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SARCOIDOSIS IN ETHIOPIA

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Summary

Six cases of sarcoidosis seen within a period of 12 months are described. They presented variously with cutaneous, lymphatic, pulmonary, hepatic, splenic, skeletal and nervous manifestations.

These 6 cases are the first to be reported from Ethiopia. A review of the archives of the Pathology Department of the Faculty of Medicine, Addis Ababa University, showed there had been 23 cases confirmed by skin or lymph node biopsy in the past 2 years. A survey of the literature concerning sarcoidosis in Africa reveals very few reported cases, but it seems likely that there are many others which are not recognised.

Résumé

L'article décrit six cas de sarcoïdose rencontrés au cours d'une année. Les malades se sont présentés avec des manifestations diverses, cutanées, lymphatiques, pulmonaires, hépatiques, spléniques, osseuses et nerveuses.

Ces 6 cas sont les premiers ê àtre rapportés en Ethiopie. Les recherches dans les archives du Services de Pathologie de la Faculté de Médecine de l'Université d'Addis Abeba, ont révélé qu'au cours des deux années passées, on a observé 23 cas confirmés par des biopsies cutanées ou des ganglions lymphatiques. Une revue de la littérature concernant la sarcoïdose en Afrique a montré que peu de cas étaient rapportés, mais il paraît probable qu'il existe de nombruex cas qui ne sont pas reconnus.

Resumen

Se describen 6 casos de sarcoidosis vistos durante un período de 12 meses, los que presentaban diversas manifestaciones cutáneas, linfáticas, pulmonares, hepáticas, esplénicas, óseas y nerviosas.

Son estos los 6 primeros casos que se informan desde Etiopía. Una revisión de los archivos del Departamento de Patología de la Facultad de Medicina de la Universidad de Addis Ababa, mostró que había 23 casos confirmados por biopsia de la piel o de los ganglios linfáticos en los últimos 2 años. Una revisión de la literatura concerniente a la sarcoidosis en Africa, revela muy pocos casos publicados, pero parece probable que haya muchos otros no reconocidos.

Introduction

Epidemiological studies in Asian and African countries suggest that sarcoidosis is relatively uncommon (Hosoda and others, 1976) although surveys have not been widely carried out in Africa. There are only a few published case reports from a limited number of countries (Ogunlesi and Rankin, 1961; Barbotin and others, 1972; Pasticier and others, 1975; Marchand, N'Diaye and Arnold, 1976) and it is generally believed that sarcoidosis is rare among black Africans. On the other hand, in North America, where sarcoidosis is relatively common, the

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American negro is known to be more susceptible to the disease than his white compatriot (Sartwell, 1976). The reason for this disparity in the prevalence of sarcoidosis among different racial groups remains unknown.

In this communication we report six cases of sarcoidosis in Ethiopians seen during 1977 in the medical teaching units of Black Lion and St Paul's Hospitals, and a review of the archives of the Department of Pathology of the Faculty of Medicine, Addis Ababa University.

Case Histories

Case 1

Z.N., a 40 year old housewife, was referred to Black Lion Hospital from Zenebework Hospital, Addis Ababa, in January 1977. She presented with pruritic skin nodules of variable size involving both arms, the chest and neck. The nodules occurred in almost every part of the body, appearing and disappearing in crops, with special affection for tattoo marks, during a period of 2 years.

Physical examination revealed small discrete, non-tender nodules over the face, neck, arms and along tattoo marks over the neck. There were small, firm, mobile lymph nodes in the neck and the tip of the spleen was readily palpable.

The erythrocyte sedimentation rate (ESR) was 40 mm in the first hour. The haemoglobin was 12.3 g/100 ml. Urinalysis and stool examination for ova and parasites were within normal limits. Liver function tests, blood urea nitrogen and serum calcium were all normal. The chest x-ray showed hilar adenopathy. The Mantoux test was negative. Biopsy of a skin nodule revealed non-caseating granuloma suggestive of sarcoid or tuberculoid leprosy; no acid fast bacilli were found. A lymph node biopsy showed granulomas suggestive of sarcoidosis, with "quite massive secondary amyloid" deposition. As the patient's symptoms were not sufficient to warrant corticosteroid therapy, she was followed in the outpatient department on no treatment.

Case 2

S.Y., a 33-year-old woman, was admitted to St Paul's Hospital in 1977 with the complaint of intermittent epigastric pain of one year's duration, and blurring of vision associated with headache and giddiness of three months duration. She also noticed small, non-pruritic swellings over the abdomen, flanks and along a tattoo mark over the bridge of her nose. She denied respiratory symptoms.

On admission, she looked well and had a blood pressure of 110/70 mm Hg, pulse rate 72 per minute and temperature 36 °C. There were several small opacities in both corneae. A small, firm, non-tender node was palpated in the right supraclavicular fossa. The respiratory and cardiovascular systems were within normal limits. The liver, palpable 5 cm below the right costal margin, was smooth and firm and the spleen was felt 8 cm below the left costal margin. There were small, indurated subcutaneous nodules over the bridge of the nose and forehead. There was a similar pea-sized nodule in the skin of the abdomen.

The ESR was 50 mm in the first hour. The haemoglobin, total white cell count, urinalysis, stool for ova and parasites were all normal. The total serum protein and albumin were 6.7 g/100 ml and 3.9 g/100 ml respectively. The serum calcium was normal. The Mantoux test, 2 units PPD, showed no induration. The chest x-ray revealed bilateral hilar lymph node enlargement. A lymph node biopsy showed non-caseating granulomas and fibrosis consistent with sarcoidosis. After 2 weeks of corticosteroid therapy the spleen regressed, the corneal opacities were clearing and the hilar lymph nodes became smaller. After 6 weeks of treatment

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the spleen was no longer palpable and the skin lesions had completely disappeared. She was discharged from hospital on a maintenance dose of prednisolone.

Case 3

F.G. was a 25-year-old housewife, admitted to St Paul's Hospital in April 1977 with a cough productive of purulent sputum of two years' duration and swellings under the jaw and axillae. She was given a trial of anti-tuberculosis therapy for 16 months and although she improved somewhat, she continued to cough and expectorate white sputum.

On admission she was emaciated, cyanotic, dyspnoeic, and coughing frequently. She had low grade fever (37.5–38.5 °C). The blood pressure was normal and the pulse rate was 92 per minute. There was bilateral cervical and right submandibular lymphadenopathy, firm, non-tender and discrete. The fingers were clubbed and cyanotic. Auscultation of the lungs revealed diffuse, bilateral, coarse crepitations. There was no evidence of cardiac failure and the abdomen was normal.

The ESR was 54 mm in the first hour and the total white cell count was normal. Sputum smear for acid-fast bacilli was negative three times. The Mantoux test, using 2 units of PPD, was negative. The chest x-ray revealed bilateral infiltrates and hilar and paratracheal lymphadenopathy.

The patient was treated with ampicillin for a presumptive diagnosis of bronchiectasis but did not improve. A lymph node biopsy at this time revealed granulomas consistent with sarcoidosis. She was started on prednisolone 60 mg daily and isoniazid 300 mg daily. She felt much better and was discharged taking prednisolone 5 mg daily.

Case 4

T.G., a 40-year-old mother of 5 children, was seen in many hospitals as an outpatient before presenting herself to the Black Lion Hospital with complaints of skin lesions involving the mucocutaneous junction of the nose, the face and fingers for 17 years and a non-productive cough for 6 years. Her skin disease began as scaly, erythematous papular lesions, starting in the right nostril, later involving the left nostril and the malar regions of the face, and was associated with recurrent nasal discharge and lacrimation of the left eye. Soon after its onset she noticed non-tender swellings of the fingers, especially the right small and middle fingers. Also, for 6 years she had had a recurrent, non-productive cough, worse at night. There was no history of haemoptysis or exposure to tuberculosis. However, at one hospital she was given anti-tuberculosis therapy for about a year without any improvement. She denied a history of syphilis or contact with lepers.

On physical examination she appeared malnourished. There were scaly, raised, excoriated, erythematous lesions in the mucocutaneous areas of both nostrils and the malar regions of the face, each of the latter being surrounded by a pale halo. Firm, non-tender lymph nodes were palpated in the neck. Some fingers were clubbed. The respiratory and cardiovascular systems were within normal limits. The liver edge was sharp, firm and about 5 cm below the right costal margin and the tip of the spleen was barely palpable. The proximal interphalangeal joints of both middle fingers and the right first finger were swollen but not painful. The rest of the physical examination was unrevealing.

Urinalysis showed an increased number of white cells but the mid-stream urine culture was negative. There were ova of ascaris species in the stool. The sputum smear for acid-fast bacilli was negative three times and the Mantoux test was negative. The serum transaminases, alkaline phosphatase, calcium and phosphorus were all within normal limits. The serum

protein electrophoresis was also normal except for a slight reduction of alpha-1 and alpha-2 globulins. X-rays of the chest revealed bilateral calcified hilar adenopathy and infiltrates involving both lower lobes, and in the hands cystic changes involving the proximal and distal phalangeal bones and the distal portion of the ulna (Fig. 1). Skin biopsies from the facial and finger lesions showed non-caseating granulomas with few giant cells. Stains for acid-fast bacilli were negative.

Because of the respiratory symptoms, disfiguring skin and finger lesions and hepatosplenomegaly, the patient was given prednisolone 60 mg daily. The skin lesions and pulmonary symptoms improved rapidly. The steroid dose was reduced to 15 mg daily within 2 weeks. Four months later she felt very well, with marks of the healed lesions on the face, nose and fingers, and impalpable liver and spleen.

Case 5

A.B., a 28-year-old driver, was first seen at Balcha Hospital two years ago because of painless mass on the right side of the neck which was surgically removed. There was no histological diagnosis. He remained well until he was admitted to another hospital in November 1976 with lymphadenopathy and splenomegaly. Again he was discharged as a suspected case of lymphoma without a histological diagnosis. About 4 months prior to his admission in December 1977, the patient had visited two other hospitals because of the sudden appearance

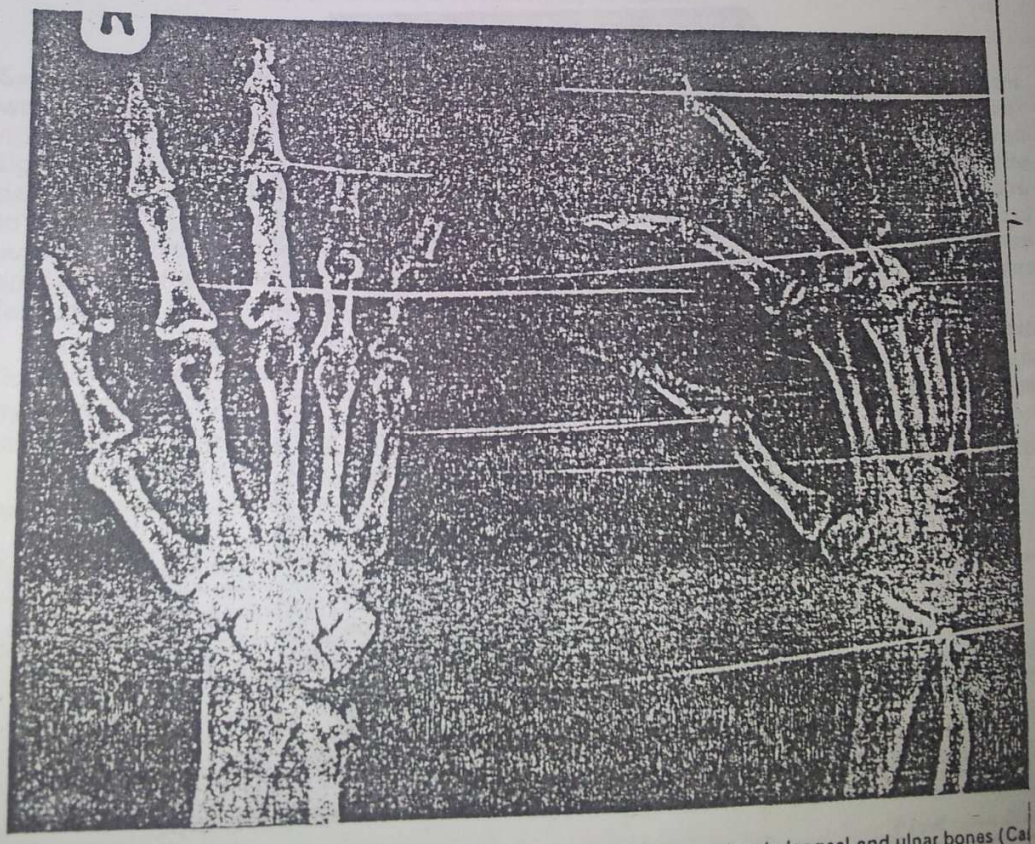


Figure 1. X-ray of the hands showing punched out lesions in the distal ends of the phalangeal and ulnar bones (Ca

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of crops of nodular skin lesions on his face. A biopsy of one of these lesions was suggestive of sarcoidosis. He denied cough or other constitutional symptoms, except vague, poorly localized abdominal pain.

On physical examination the patient appeared well and the vital signs were normal. There was no corneal opacity. There were several firm, freely mobile lymph nodes, mainly in the posterior cervical triangles. The lungs were clear. The tip of the spleen was palpated 5 cm below the left costal margin and the liver edge was just palpable on deep inspiration. There were several reddish-brown nodules over the malar regions of the face and over the nose (Fig. 2). There were similar nodules surrounded by hypopigmented areas over the extensor aspect of the forearm.

The ESR was 8 mm in the first hour. The haemoglobin was 12.5 g/100 ml and the white cell count was normal. The VDRL was non-reacting. The serum alkaline phosphatase was 15 KA units/100 ml and the serum bilirubin was 1.2 mg/100 ml. The total serum protein was 7.8 gm/100 ml. The Mantoux test with 0.5 ml. PPD was negative and the chest x-ray was clear. Both skin and lymph node biopsies were diagnostic of sarcoidosis.

After 2 weeks of treatment with prednisolone the skin lesions regressed and the hepatosplenomegaly was barely detectable.

Case 6

G.B., a 46-year-old housewife, was admitted to St Paul's Hospital because of swelling of the abdomen and lower extremities of 10 days duration. She had also noticed a painless mass



Figure 2. Case 5 showing crops of nodular lesions on the forehead, nose and malar regions of the face.

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on the right side of the neck. Except for a recurrent cough for 2 years and an episode of sudden onset of left facial weakness 7 years ago, she claimed to have been in good health previously.

On physical examination, she had a cataract in the left eye and several small, firm, mobile lymph nodes, which were not tender, in both posterior cervical triangles. There were coarse crepitations at both lung bases. The jugular venous pressure was raised and the heart was clinically enlarged. There was a pansystolic murmur which radiated to the left axilla and the second heart sound in the pulmonary area was accentuated. There were signs of fluid in the abdomen, the liver edge was 6 cm below the right costal margin and the tip of the spleen was palpable. There was bilateral leg oedema and residual signs of a left facial palsy.

The ESR was 82 mm in the first hour. The haemoglobin, haematocrit and white cell count were normal. The blood urea nitrogen was normal. The total serum protein was 6 g/100 ml, albumin 40 %. The Mantoux test with 2 units of PPD was negative. The chest x-ray revealed an enlarged heart and pulmonary congestion. The eletrocardiogram showed left ventricular hypertrophy with strain. Two lymph node biopsies were taken, one from each side of the neck, and both were reported as sarcoidosis.

After digitalization and diuretic treatment the patient lost her oedema and ascites, although the cardiac murmur persisted. However, the heart size was reduced and the electrocardiogram reverted to an almost normal pattern. The hepato-splenomegaly was significantly decreased with corticosteroid therapy. It was thought that the congestive heart failure in this patient may have been the result of cardiac involvement by sarcoidosis.

Discussion

Sarcoidosis may affect almost any part of the body and in each of our cases several organs were involved (Table I). Lymphadenopathy was observed in all 6 of our patients and splenomegaly in 5. Although the lung is most frequently affected in this disease, only 2 cases had significant pulmonary involvement as shown by the chest x-ray, while hilar nodes were detected radiologically in 4. Four of the 6 patients were concerned about recurrent skin lesions. In fact, 3 of these were sent from a leprosarium to which they had been referred because of suspected leprosy, a common condition in Ethiopia. An interesting observation was the linear appearance of nodular lesions along tattoo marks in Cases 1 and 2. Other noteworthy clinical features were cystic bony changes in the fingers of Case 4 and facial palsy in Case 6.

The tuberculin skin test was negative in all the cases. In the 4 patients with hepatomegaly the liver function tests were normal, including the serum alkaline phosphatase. There was no hypercalcaemia in any case. In every patient the diagnosis was confirmed by lymph node biopsy or skin biopsy.

All our patients except one were treated with cortico-steroids, and in every case the sarcoid lesions regressed, either partially or completely.

Table I. Clinical manifestations of 6 cases of sarcoidosis

Case no.	Parts of the body affected by sarcoidosis					
	Hilar glands	Lungs	Skin	Liver or spleen	Lymph nodes	Other parts
1	+		+	+	+	
2	+		+	+	+	Eyes
3	+		+	+	+	Bones
4	+	+	+	+	+	
5			+	+	+	Facial nerve & eyes
6						

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Country	Author	Type of study		
				1977
Africa			6	1970–77
Ethiopia	Present report	Case report	30	1960
	Present report	Pathology records	2	1961
Ghana	Ogunlesi & Rankin, 1961	Case report	1	1959–70
Nigeria	Ogunlesi & Rankin, 1961	Case report	5	1957–74
Senegal	Barbotin and others, 1972	Case report	27	1963–73
India	Hosoda and others, 1976	Survey	2679	1960–73
Japan	Hosoda and others, 1976	Survey	8	1975
Malaysia	Izumi, and others, 1975	Survey	1	1952–74
Singapore	Ong, Chew and Chiang, 1975	Case report	8	1956–75
Thailand	Bovornkitti and others, 1974	Survey	7	Each year
	Yang and Wu, 1974	Survey	35–40	
U.A.R.	Gomaa and Halim, 1965	Survey		

There is no satisfactory explanation for the small number of sarcoidosis cases seen between 1970 and 1977 in the Pathology Department of Addis Ababa University. During this period only 30 biopsy specimens were diagnosed as sarcoid, 8 from skin and 22 from lymph nodes. Twenty-three of them were seen in 1976–77. These cases came from several different parts of Ethiopia, but only a few hospitals send specimens to the Pathology Department, the number varying with the interest and enthusiasm of the physician and the availability of transport, this preventing any reliable statement on incidence.

A review of the literature found no cases of sarcoidosis reported from Eastern and Central African countries. There are only a few case reports from West, North and South Africa (Ogunlesi and Rankin, 1961; Gomaa and Halim, 1965) by individual physicians who concluded that sarcoidosis is rare among the indigenous people of Africa.

The reason for the low incidence of sarcoidosis among Africans, and in some Asiatic countries (Table II), is not well understood. Possible reasons include lack of diagnostic facilities and unawareness of its existence in a population with a high prevalence of other granulomatous disoases, especially tuberculosis and leprosy.

The finding of 6 typical cases within 12 months in two hospitals, the detection of 23 cases in a single pathology unit within less than 2 years and similar observations by others (Barbotin and others, 1972) suggest that sarcoidosis may be commoner in Ethiopia, and perhaps other parts of Africa, than has been recognised hitherto.

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ABSTRACT: *A prospective analysis of 110 hospitalized adult Cerebrospinal Meningitis (C.S.M.) cases from a military camp near Addis Ababa during 1977 was made. All were adult males admitted during the peak season (April, May and June). They presented with the classic manifestations of C.S.M. and in 55% the state of consciousness was depressed. In 40 cases where the cerebro-spinal fluid was studied most had marked pleocytosis, Gram stain showed gram negative diplococci in 31 and in 21 of these the culture was positive for Neisseria meningitidis. Serotyping done on 12 revealed group A in 10 and group C in 2; 11 of the 12 strains were resistant to sulfadiazine (MIC levels of 5 mg% or above). Case mortality was 10% and complications occurred in 9 cases. Cost benefit analysis clearly shows the advantages of vaccination. It has been recommended to use counter-current immunoelectrophoresis for rapid detection of serogroup and also conduct a mass vaccination campaign in affected areas.*

Cerebrospinal Meningitis (C.S.M.) occurs as serious outbreaks resulting in a high mortality rate in the C.S.M. zone of Africa extending from south of the Sahara to North of the Equator (1). The Central and Western parts of Ethiopia are definitely within this meningitis belt as revealed in the authors' retrospective analysis of C.S.M. in Ethiopia (2).

An adequate reporting system is necessary on the epidemiology of C.S.M., identification of the causative agent *Neisseria meningitidis* including the serotyping and also the sensitivity of the organism to antimicrobial agents for the early treatment of cases and planning control of outbreaks. Even though the cause of large outbreaks of C.S.M. in this part of Africa is *N. meningitidis* serogroup A, detection of emerging serogroups is also important.

This study includes a review of a prospective analysis of 110 cases of C.S.M. admitted in Addis Ababa hospitals in 1977 referred from a nearby military camp. The purpose of the report is to stress the early clinical and bacteriological diagnosis of C.S.M. and based on this to discuss the cost benefit of treatment as compared to chemoprophylaxis and immunization.

MATERIALS AND METHODS

A prospective study of the clinical aspect of cerebrospinal meningitis has been done in 110 patients admitted to Addis Ababa hospitals referred from a nearby military camp during a high incidence season, April to June of 1977. All these cases have been closely attended by physicians, including one of the authors, in three

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hospitals (St. Paul's, Yekatit 12, and Black Lion Hospitals). Follow-up and progress of each patient has been regularly checked by investigators. Presenting symptoms and signs, laboratory investigations, outcome of treatment and complications have been reviewed. Eighty-three patients had haemoglobin studies, 40 cerebrospinal fluid (C.S.F.) cell counts, while 31 had C.S.F. Gram stain and culture performed. Initial diagnosis of C.S.M. was made on the basis of the clinical picture, turbid cerebrospinal fluid, positive Gram stain for Gram negative diplococci and on the epidemiological situation. Complete bacteriological analysis was not done on all patients because in most patients treatment had been started prior to admission.

Bacteriological investigations included Gram stain, culture of C.S.F. on blood and chocolate agar plates followed by biochemical methods. Slide agglutination test of positive isolates was carried out using commercial antisera. Sensitivity studies on *N. meningitidis* were done by Kirby Bauer disc sensitivity test using Mueller-Hinton agar plates. Minimum inhibitory concentration (MIC) study was done separately for sulfadiazine using Mueller Hinton agar pour plates at different concentration (200, 100, 50, 20, 10, 5 and 1 microgram-ml) and each plate was inoculated with 0,5 MacFarland turbidity of an overnight broth culture of *N. meningitidis*. Control organisms with known MIC to sulfadiazine were simultaneously tested. After 24-48 hours incubation inhibition was noted when there was either no growth or fewer than ten colonies present (3). Sulfadiazine resistant organisms were recorded at 50 mg-ml or above according to other reports (4,5). All were treated with crystalline penicillin G 3 million IV every 4 hours.

The cost of treatment of C.S.M. of admitted cases has been calculated in terms of hospitalization, drugs and laboratory investigations. For this purpose, samples of 24 cases have been used from St. Paul's and Black Lion Hospitals based on average length of hospital stay, severity and complications.

RESULTS

These cases were admitted from an army camp near Addis Ababa during peak C.S.M. epidemic season in 1977 (during months of April, May and June). Thus the analysis is specific to one age group 15-50 (mean of 24 years) and male population and does not include the clinical picture and outcome of therapy of other age groups.

The duration of illness ranged from 5 to 20 days (mean of 10 days). All patients presented with the classic signs of meningitis, in 55% the state of consciousness was depressed (14 presented with coma). *Herpes labialis* was observed in 35% during the first 3-5 days of admission. There were no cases of cutaneous bleeding or seizures.

Peripheral white blood cell was elevated (greater that 10,000/cmm^3) in 73 patients (88%) and all these had neutrophilia. Anaemia was not characteristic of the disease. Erythrocyte sedimentation rate was elevated in most of the patients.

Table 1 shows the cerebrospinal fluid analysis in 40 cases. Most of the cases had marked pleocytosis greater than 5000/cmm^3 with predominant neutrophils. Those with low cell count (lowest was 120/cmm^3) had low neutrophils (48-75%). High cell count (50,000-200,000) was encountered in 4 patients. Thirty-one had positive Gram stain for Gram negative diplococci and 21 out of the 31 had positive culture for *Neisseria meningitidis*.

Serogrouping of *Neisseria meningitidis* and sensitivity tests were done in 12 cases. 10 serogroup A and 2 serogroup C were identified. All 12 strains of meningococci were sensitive to cephalothin, tetracycline,

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chloramphenicol, ampicillin, carbenicillin, gentamicin, penicillin, erythromycin and rifampicin; 10 to kanamycin, 5 to polymyxin B and 3 to streptomycin. With the exception of only one strain — meningococcus - the M.I.C. study for sulfadiazine revealed resistance by all with MIC levels of 50 mg-ml. or above.

The period of treatment ranged 1-5 days in 10, 6-10 days in 57 and eleven days or more in 39 cases (in 4 the period of therapy was not recorded). Complications occurred in 9 patients (arthritis in 4, pneumonia in 3 and facial palsy in 2). Case fatality rate was 10% and all patients who died were in deep coma on admission, they also had very high fever and high C.S.F. white cell count; two had pneumonia and one arthritis.

Cost benefit analysis was studied in selected 24 patients using costs for bed, food, drugs, laboratory and x-rays only. It was found out that to treat one patient it cost an average of 22.70 Birr daily. Had chemoprophylaxis with sulfonamide been used, the cost of protection for one person would have only been 1.00 Birr, but this is no more effective. A more effective chemoprophylaxis is rifampicin which is very expensive, costing 32.00 Birr per person. However, if vaccination is given during the early period of an outbreak a two—year protection for one person would cost only 0.70 Birr (using WHO supply).

DISCUSSION

The analysis of this prospective study of cerebrospinal meningitis cases has revealed the classic clinical picture of the disease as well as the expected outcome of therapy of an epidemic or large outbreak that is similar to others reported in Africa (5). However, the study is specific to one age group 15-50 (mean of 24 years) and male population, and does not include the clinical picture and outcome of therapy in other age groups. The early recognition of the outbreak in these cases was beneficial as it resulted in the early initiation of therapy as compared to other outbreaks in other parts of Ethiopia in 1977 where, mortality reached up to 30% (2).

Even though detailed epidemiological studies were not carried out, such as nasopharyngeal carrier rate in the camp, an immediate suspicion of an outbreak based only on rough epidemiological grounds, the finding of Gram negative diplococci in the cerebrospinal fluid, would also indicate taking serious action such as giving rifampicin chemoprophylaxis to very close contacts. Based on other reports (6, 7) that showed the advantages of rifampicin prophylaxis the investigators gave rifampicin only to very close contacts during the early period of the outbreak.

The organisms isolated in these cases were few and all but one were resistant to sulfadiazine. Similarly, resistant strains of meningococci had been found in Ethiopia (8-10). High prevalence of sulfa-resistance had been reported in other countries in the Meningitis belt of Africa, 30% from Nigeria (11) and 72% from Chad (4). Thus sulfonamide cannot be used as chemoprophylaxis unless the infective strain is known to be sensitive to sulfonamide or if the prevalance of sulfa-resistant meningococci in the region is less than 10%.

The common cause of C.S.M. in the Meningitis belt is *Neisseria meningitidis* serogroup A; however there are reports of new serogroups, namely B in the Sudan (12) and C in Nigeria (13). In our study two of the 12 strains were group C. The application of vaccination programmes and choosing vaccines require the study of emerging serogroups of meningococci as an important investigation. For this purpose the counter-current immunoelectrophoresis (C.I.E.) provides a rapid and reliable method in the detection of meningococcal polysaccharide in the cerebrospinal fluid and meningococcal antibodies in the

serum. The electrophoretic method (14) or the latex agglutination test (15) detect meningococcal polysaccharide in C.S.F. in 70-80%.

On epidemiological grounds there was no uncertainty about the clinical diagnosis of C.S.M.; thus only one drug (penicillin) was used instead of two antibiotics as reported in other "epidemics" (16).

The cost benefit analysis in this study clearly reveals the important fact that vaccination is cheaper. Group A vaccine has been shown to be effective in Egypt (17, 18) and the Sudan (19). Both groups A and C do not have serious side effects (18, 20). The trial of polysaccharide A and C vaccine during the middle part of the outbreak of C.S.M. in 1977 in the military camp near Addis Ababa showed some beneficial effect (2). It is recommended that in the future a mass vaccination campaign be conducted in the C.S.M areas of Ethiopia.

TABLE 1: W.B.C. and Bacteriological Analysis in 40 C.S.F. Specimens from C.S.M. Cases

		No.	%
White Blood Count			
<1000	/cmm³.	5/40	12.5
1000-5000	/cmm³.	7/40	17.5
5000-15,000	/cmm³.	18/40	45.0
>15,000	/cmm³.	10/40	25.0
Bacteriology*			
Positive Gram Stain		31/40	
Positive Culture		21/31	
Sero Group A		10/12	
Sero Group C		2/12	

* Serogrouping and sensitivity tests were performed only in 12 specimens.

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We would like to thank Dr. Nebiat Tafari and Dr. Ante Catipovic, who reviewed the manuscript. Our thanks are due to all the physicians in the hospitals (Black Lion, St. Paul's and Yekatit 12) for their cooperation in the study using our special protocol. The secretarial assistance of Woizerit Turunesh Damena is gratefully acknowledged.

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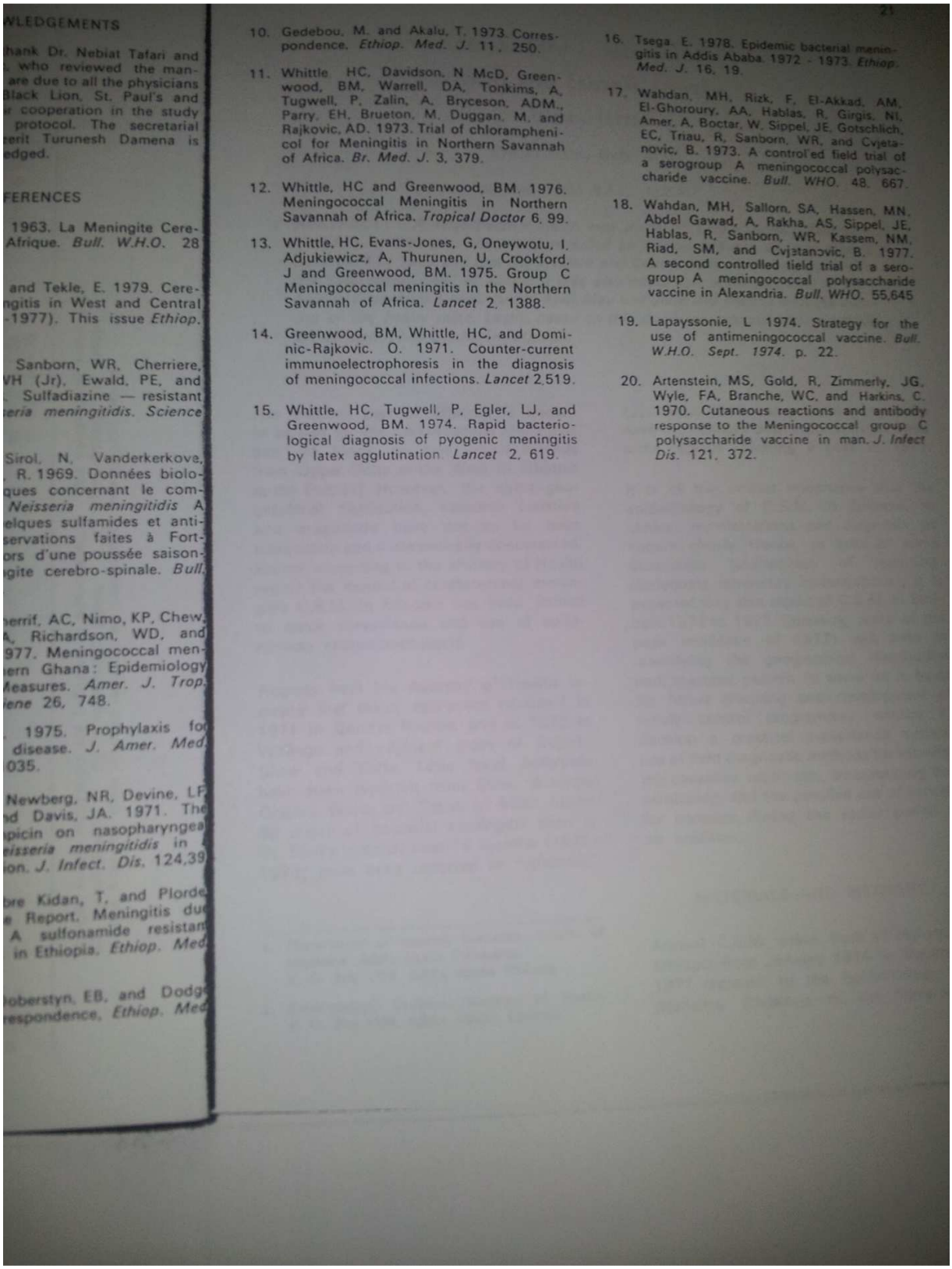
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Ranges for all parameters are indicated in parentheses. Our values show mean ± SD
a) Overall mean, b) "Professional" group, c) "Non-Professional" group
* Data from the other workers recorded as presented in their original papers.

CEREBROSPINAL MENINGITIS IN WEST AND CENTRAL ETHIOPIA

(1974 - 1977)

Eyassu Habte-Gabr M.D[1]

Estifanos Tekle B.Sc., M.P.H.[2]

ABSTRACT: *A retrospective study was made of Cerebrospinal Meningitis (C.S.M.) in Ethiopia. The study revealed an annual increase of case reports from 1974 to 1977 and that the Western and Central parts of Ethiopia fall within the "Meningitis belt" of Africa. It was also noted that epidemics start in early February reaching a peak during April, May and June and decline with the coming of the heavy rains. Lastly, based on this study, recommendations are made on the control of C.S.M. in Ethiopia.*

The western part of Ethiopia is known to be part of "the Cerebrospinal Meningitis belt" of Africa, an area which extends from Upper Volta in the West to Ethiopia in the East (1). However, the exact geographical distribution, seasonal variation and magnitude have not so far been adequately and systematically documented. Hence, according to the Ministry of Health report the control of cerebrospinal meningitis C.S.M. in Ethiopia has been limited to quick surveillance and use of sulfonamide chemoprophylaxis.

Reports from the Ministry of Health indicate that major epidemics occurred in 1971 in Gondar Region, and in 1972 in Wollega and adjacent areas of Gojjam, Shoa and Kaffa. Later focal outbreaks have been reported from Shoa, Wollega, Gojjam, Wollo and Tigrai. In Addis Ababa 38 cases of bacterial meningitis seen at St. Paul's hospital over 15 months (1972-1973) have been reported as "epidemic" (2). Since 1975, more serious outbreaks have increasingly been reported from these same regions reaching a peak in 1977.

It is of the utmost importance that the epidemiology of C.S.M. in Ethiopia, its clinical manifestations and diagnosis be known clearly. Hence, in spite of some drawbacks (inadequacy of reporting, inadequate laboratory investigations), it is expected that this report of C.S.M. in Ethiopia 1974 to 1977 (stressing more of the peak incidence of 1977) will help in identifying the geographical distribution and seasonal pattern to serve as a basis for future planning and development of timely control programmes, namely to develop a practical surveillance system, use of field diagnostic methods for identifying causative organisms, serogrouping and serotyping, and the possible use of vaccine for contacts during the earlier period of an epidemic.

MATERIALS AND METHODS

Annual C.S.M. cases from all regions of Ethiopia from January 1974 to December 1977 reported to the Epidemiology and Statistics Divisions of the Ministry of

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Health have been analysed. In addition, more information has been gathered from individual health workers who have played an active role in the control of C.S.M. in different parts of the country during these four years. Analysis of annual reports has been done by year, quarter, region and also age and sex distribution, from available records. Complete information on temperature and rainfall was only available for Shoa Region in the Central Statistics Office.

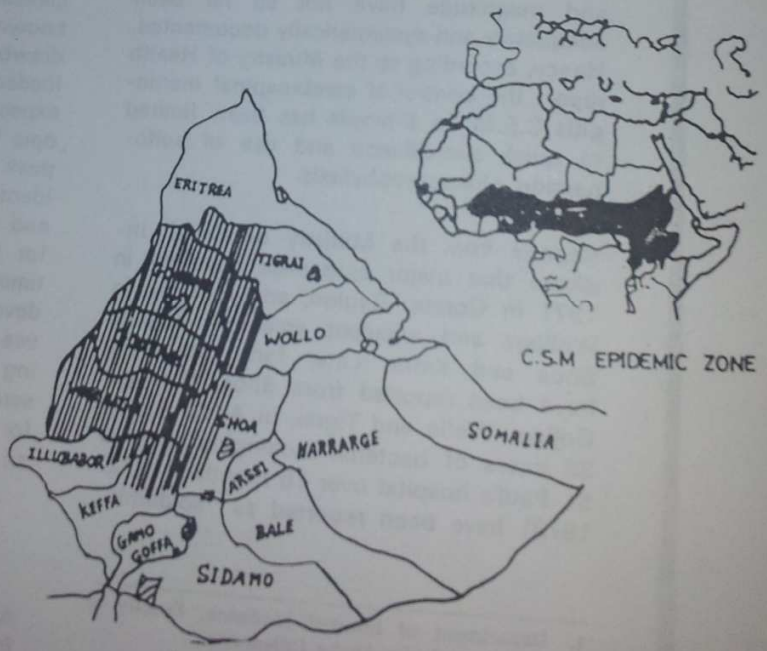
RESULTS

A) Epidemiological Situation of C.S.M. in Ethiopia

Table 1 clearly shows that there has been an increasing number of reported cases of C.S.M. in Ethiopia from 1974 to 1977. From the available data, the distribution of C.S.M. in Ethiopia (Fig. 1) has uniformly included the same regions, namely the Western and Central regions of the country or the Eastern end of the "Meningitis belt". However, from year to year there is some variation in outbreaks of C.S.M. and in 1977, in spite of all efforts to get reports on the national incidence of C.S.M., some regions affected in previous years, i.e. Gondar, Tigrai and Wollo, have not had any meningitis outbreak. Figure 2 reveals the increase in the number of cases in Addis Ababa during the hot, dry season and the rapid decrease of C.S.M. when the rains started.

Table 2 and Figure 3 reveal the peak season of C.S.M. in Ethiopia (1977) to be in the months of April, May and June. However, smaller outbreaks started in February and gradually increased in March to reach the peak incidence in the following three months,

FIG. 1



CEREBROSPINAL MENINGITIS (CSM) EPIDEMIC AREAS IN ETHIOPIA

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then dropped during the heavy rainy season, towards the end of June. Review of previous years' outbreaks also shows a similar seasonal pattern. However this pattern may not hold true for crowded areas like army barracks.

During the 1977 epidemic in Gojjam and Wollega the age group affected most was 15-44 years (60%) followed by 5-14 years (19%), 0-4 years (14.7%) and 45 years and older (8.2%). The male to female sex distribution was 1.2:1 and 1.5:1 respectively.

B. Control of Cerebrospinal Meningitis

To control the spread of C.S.M. in a large population of young adults near Addis Ababa, during the 1977 outbreak rifampicin was given to all health workers in close contact with cases and polyvalent (A and C) vaccine was given to recruits in the middle of the epidemic. All variables, i.e. crowding and climatic conditions remaining constant, there was generally a significant decrease in the number of cases. Another observation was that there was only one case in July among those who were vaccinated (92,000) and 10 cases from the unvaccinated group (7000).

However, since no systematic study was conducted and vaccination started late, we cannot with full confidence attribute this decrease to vaccination.

DISCUSSION

There are certain climatic, ecological and human habitation similarities in the Meningitis belt which favour the spread of C.S.M. Our results show that such climatic and ecological conditions for the evolution of epidemics of C.S.M. do exist in the Central and Western parts of Ethiopia. This is an agreement with other reports (1, 3, 4). In 1977, the rapid fall in the number of new cases correlates with the increase in rainfall and the low temperature.

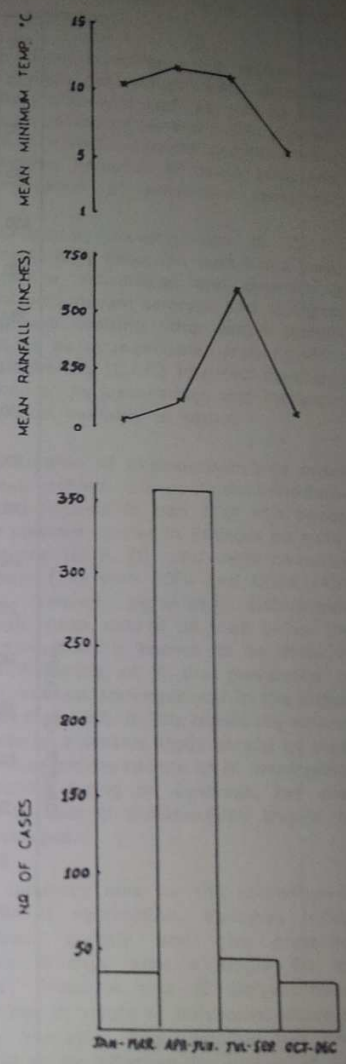


Figure 2.

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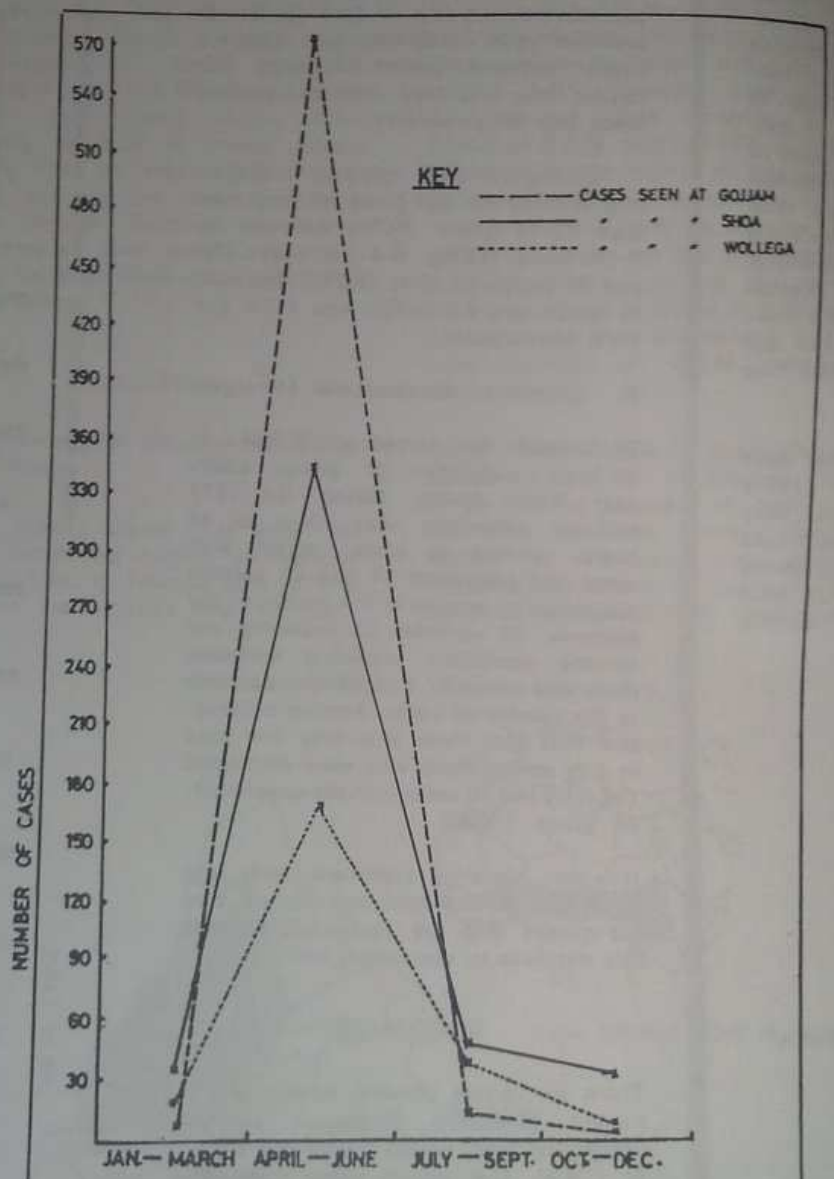


Fig. 3

CEREBROSPINAL MENINGITIS IN ETHIOPIA 1977

Outbreaks have been reported in six regions of Ethiopia yearly between 1974 and the end of 1977 but very systematic and close follow up of reports from all regions show that Wollo, Gondar and Tigrai have been free of C.S.M. This may partially be explained by the fact that as the number of carriers and cases increases the immunity of the population rises by autoregulation and another reason may be due to variation in the level of herd immunity. These reasons may be the explanation also for the years without outbreak during the interepidemic periods in the Meningitis belt.

The age distribution of C.S.M. in Africa is most frequent in the older children 5-15 years in 45-50%, followed by younger age group 0-5 years representing 25-30% (4.5). In Northern Ghana it is reported that the peak attack rate is in 10-14 age group (6). The relatively complete report of 1977 shows that in Gojjam the age distribution was 40% in age group 15-44 years, and 30% in 5-14 years; the young children may not be brought to the clinic for treatment, hence the percentage is small. As in other reports the disease is more common in males, as in Gojjam and Wollega. From this report, because of reasons mentioned we cannot comment on the age and sex distribution of C.S.M. in Ethiopia.

The high case fatality rate shown, especially in Gojjam (30%), is due to the delay in early detection and reporting, and delayed medical aid coupled with lack of facilities in the rural clinics. However, it is worth considering multiple causative organisms in some cases as with *Streptococcal pneumoniae* meningitis which is particularily lethal in 45-60%, and is also common in humid areas.

Control of C.S.M. has been successful in countries like Brazil. Based on the experiences in that country there have been recommendations (7), namely, early detection of clinical cases, reporting and surveillance:-

a) Epidemic surveillance, i.e. information on high risk groups, early detection by professional staff as well as properly motivated general public together with a well-organized communication system, detection of carrier rates and evaluation of preventive measures;

b) Laboratory investigations of C.S.F., again early detection with Gram stain, culture, sensitivities and determining of predominant serotype and emerging groups, utilizing other simple techniques as countercurrent-immuno-electrophoresis (C.I.E.) to detect meningococcal polysaccharides and meningococcal antibody in serum.

The question of chemoprophylaxis raises a major problem. Obviously the consideration of findings in part I of this paper, from previous studies in Ethiopia on sulfa-resistance (8, 9, 10) and other countries [Nigeria (11) with 30% and Chad (12) 72% resistant organism], sulfonamide though cheap, cannot be used unless the infective strain is known to be sensitive to sulfonamide or if the prevalence of sulfa-resistant meningococci in the region is less than 10%. In this regard the authors believe an extensive study should be done on the sensitivity pattern of *N. meningitidis* especially during an outbreak, but even then the use of sulfonamides should be discouraged.

The tendency now for the prevention of C.S.M. is vaccination. Vaccines induce antibody quickly and give protection about 5 days after a single 50 mg. dose; Group A and C polysaccharide vaccines in single or polyvalent doses are now available. The vaccine has been found to be effective in controlled field studies in Egypt, Sudan and Alexandria with no serious side effects (13, 14, 15, 16). However, it is expensive, not yet easily available, and because it is heat-

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labile and needs great care there is difficulty in delivering it to rural areas in the absence of a reliable cold-chain. From a review of experiences of other countries (17) mentioned above, vaccination should be started early in large outbreaks and should include all persons in the affected region except infants under 6 months of age where serological response is poor (18). In this study there was a notable difference after vaccination, when towards the middle of the epidemic season, more C.S.M. cases were reported among the non-vaccinated group. It is the authors' recommendation that in Ethiopia the efficacy of vaccine should be properly evaluated through controlled studies.

There is an indication of chemoprophylaxis for household contacts (19). Since more than 50% of new cases get the disease within less than five days after onset of the index case, immediate chemoprophylaxis with rifampicin should be given to close contacts in a household and medical personnel.

CONCLUSION

This first review of cerebrospinal meningitis in Ethiopia over four years has shown clearly that the Western and Central part of Ethiopia is within the "Meningitis belt" of Africa and that the epidemic season is between February and June with a peak in April, May and June. It gives basic information on the magnitude of this problem for the Ministry of Health and for the control of cerebrospinal meningitis, namely:-

1. **Training of manpower,** in methods of prevention and control diagnostic techniques, and in handling of vaccine, to make each region self-sufficient in combating meningococcal disease.
2. **Nationwide system of surveillance of meningococcal disease,** on clinical diagnosis, serogrouping, serotyping and sulfonamide sensitivity.
3. **Establishment of reference laboratory.**
4. **Early chemoprophylaxis** for household contacts and selected closed communities.
5. **Vaccination** in anticipation of outbreaks, and if possible routine vaccination in camps of any nature in the already identified meningitis areas.
6. **Early Warning** to health workers in these areas for careful investigation of febrile outbreaks for early detection and timely reporting especially between the months of February and June.

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TABLE 1: Cerebrospinal Meningitis in Ethiopia 1974 to 1977

Administrative Region	1974	1975	1976	1977
Gojjam	25	15	14	629
Gondar	56	77	60	—
Shoa	33	267	61	465
Tigrai	47	68	113	—
Wollega	100	115	159	202
Wollo	137	61	781	—
Total	398	603	1188	1296

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975	1976	1977
15	14	629
77	60	—
67	61	465
68	113	—
15	159	202
61	781	—
03	1188	1296

TABLE 2: Distribution of Reported C.S.M. Cases 1977 by Region and Quarter

Administrative Regions	Months Jan-Mar	Apr-June	Jul-Sept	Oct-Dec	No. Cases Total	No. of Deaths	Case Fatality
Shoa (Western part)	35	355	45	30	465	50	10.6%
Gojjam (Metekel + Agewmidir Awrajas)	6	583	35	5	629	187	29.7%
Wollega (Horogudru and Nekempt Awrajas)	18	173	9	2	202	31	15.3%
Total	59	1111	89	37	1296	268	21%

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VALUE OF MANTOUX TEST IN LYMPHADENOPATHY

Bayu Teklu, MD[1] and Berhanu Getahun, MD[2]

ABSTRACT: *The results of Mantoux test in 71 consecutive Ethiopian patients with peripheral lymphadenopathy and a definite histologic diagnosis have been documented. All the 37 patients with tuberculous lymphadenitis had positive Mantoux test. In the lymphomas and metastatic malignancies the Mantoux test was positive in about 50 percent. The Mantoux test was not positive in any of the patients with sarcoidosis or chronic non-specific lymphadenitis. Therefore, even though therapeutic trial is a common clinical practice in developing countries with limited facilities, antituberculosis therapy has no place in patients with peripheral lymphadenopathy and negative Mantoux test.*

INTRODUCTION

Generalized or localized lymphadenopathy is a common clinical finding in diseases such as bacterial infections, Hodgkin's disease and lymphomas, leukemias, sarcoidosis and metastatic carcinomas. It is well known that the Mantoux test is usually positive in tuberculous lymphadenitis and negative in malignancies (1-3). The purpose of this study was to evaluate Mantoux reactions in Ethiopian patients with lymphadenopathies not due to obvious causes like localized soft tissue infections or lymphangitis.

MATERIALS AND METHODS

The study consisted of a retrospective chart review of patients with either localized or generalized lymphadenopathy admitted to the teaching medical wards at St. Paul's and Black Lion Hospitals from December 1973 until January 1977. All patients who had lymphadenopathy (not due to localized skin or soft tissue infection), Mantoux test (2u or stabilized PPD-RT23) and a definitive diagnosis confirmed by histology were included. There were 71 patients that fulfilled all these criteria.

RESULTS

Table 1 gives a summary of the findings in the 71 patients with lymphadenopathy. There were 37 patients with tuberculous lymphadenitis; 7 tuberculous peritonitis; 3 tuberculous pleurisy; 4 chronic non-specific lymphadenitis; 4 lymphomas; 10 secondary carcinomas and 6 sarcoidosis. In the tuberculous lymphadenitis patients there were 20 males and 17 females.

The Mantoux test was positive in all cases of tuberculous lymphadenitis and in fifty percent of the lymphomas and secondary carcinomas in lymph nodes. None of the six sarcoidosis patients nor the patients with chronic non-specific lymphadenitis had positive Mantoux, even though three of the latter had reactions in the doubtful range (5-9 mm. induration). Of the 31 tuberculous lymphadenitis patients with haemoglobin results, only 5 had levels of 14 gm. percent and above and there were 9 with less than 10 gm. percent. Four patients had white blood counts of less than 3,000 and six had over 10,000 per cu-mm. The Mantoux test was 20 mm. induration or greater in more than fifty percent of tuberculous lymphadenitis patients. Of the 20 patients with weight records, 7 weighed 50 kg. and above and 6 weighed less than 35 kg., the lowest weight being 24 kg. with a Mantoux reaction of 26 mm. induration.

DISCUSSION

Simple excision biopsy gives the definitive diagnosis in most patients with peripheral lymphadenopathy if there is a pathology

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service. However, in developing countries where facilities and financial resources are limited, one has to resort to inexpensive and simple tests to reach a reasonable diagnosis. One such simple test is the Mantoux test.

High positivity of Mantoux test in tuberculous lymphadenitis has been reported before (2) where none of the patients had cutaneous anergy, while in other forms of tuberculosis, anergy has been reported in 2-17 percent of the cases (2,4,5). This study suggests that the Mantoux test is not affected adversely by anaemia, or the poor nutritional status of patients with tuberculous lymphadenitis, even though debility in tuberculosis is one of the factors giving false negative reactions to PPD (5). The fact that Hodgkin's disease, lymphomas and various malignancies depress cellular immunity has been well documented (2,3,6) and is again well demonstrated in our patients. It is also of interest to note that none of the six patients with sarcoidosis had any skin reaction to PPD. Cellular immunity is depressed more in those with widespread than those with localized malignancy (2,6) and cellular immunity reverts to normal in some cases of localized malignancy after successful curative surgery (7).

The present study demonstrates that one hundred percent of patients with tuberculous lymphadenopathy had positive skin test to intermediate strength PPD, and that in all other non-tuberculous conditions encountered the positivity was zero to fifty percent. Therefore, in patients with peripheral lymphadenopathy and negative Mantoux test, there is no clinical justification for therapeutic trials with antituberculous drugs as the diagnosis of tuberculosis is extremely remote.

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TABLE 1: Sex and age distribution, type of disease and Mantoux reaction in 71 Ethiopian patients with lymphadenopathy

Diagnosis	No. of Patients	Sex		Age In Years						Age Range	Mean Age	Positive Mantoux %
		M	F	14-20	21-30	31-40	41-50	51-61	61 & above			
1. Tuberculous lymphadenopathy	37	20	17	11	11	8	5	2	—	14-60	30	100
2. Tuberculous peritonitis	7	4	3	1	5	1	—	—	—	19-32	26	86
3. Chronic non-specific lymphadenitis	4	2	2	2	2	—	—	—	—	15-25	21	0
4. Tuberculous pleurisy	3	3	—	1	—	1	1	—	—	14-42	31	100
5. Lymphomas	4	3	1	2	—	—	1	—	1	14-74	39	50
6. Metastatic carcinomatous lymphadenopathy	10	6	4	2	—	2	3	1	2	14-62	43	46
7. Sarcoidosis	6	2	4	—	2	3	—	1	—	25-55	38	0

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Zawde, D, Workneh, F, Habte-Gabre, E. 1978. *Ethiop. med. J.* 16.

CASE REPORT

MUNCHAUSEN'S SYNDROME

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ABSTRACT: A 24 year old female patient who fits the classical descriptions of Munchausen's syndrome and who had recently come under our care for flank pain, haematuria, fever, leg oedema and other symptoms, with a background of prolonged repeated hospital admissions, is presented. A documentation of her previous admissions together with the variety of symptoms she had presented with is made and commented upon. The present presumed causes of the syndrome are also discussed.

In 1951, Asher (1) who described the characteristic features of this syndrome named it after the fabled German Baron Munchausen who died in 1797 leaving behind exaggerated tall stories of his daring exploits and adventures (2). Since Baron Munchausen was not known to have been concerned with illness, other names that have been proposed, but used less often than Munchausen's syndrome, include Hospital Hoboes (3) Hospital Addiction (4) and Chronic Factitious Illness (5).

Ireland *et al.* (6) in their review of all the reported cases of Munchausen's syndrome point out that Munchausen's syndrome as a diagnostic entity applies to persons who, in the absence of appropriate medical or surgical need, have made hospitalization a primary way of life. The characteristic features of the syndrome being: 1) feigned severe illness of a dramatic and emergency nature, the symptoms of which may or may not be borne out by physical examination, 2) factitious evidence of disease, surreptitiously produced by interference with diagnostic procedures or by self mutilation, 3) evidence of many previous hospital procedures particularly laparotomy scars and cranial burr holes, 4) pathological lying, 5) aggressive unruly behaviour and "a mixture of truculence and evasiveness in manner", 6) departure from the hospital against medical advice, 7) a background of many hospital admissions and extensive travel, 8) the absence of any discernible ulterior motive.

In this report, we describe a case of Munchausen's syndrome, in order to create an awareness of those patients who may unnecessarily be overburdening the already meagre health resources, and to facilitate their early recognition in other hospitals here.

CASE REPORT

M.A. a 24 year old girl who gave her occupation as a baby sitter was admitted to the surgical wards of Black Lion Hospital, Addis Ababa in March 1977. This was her tenth hospital admission. She reportedly fell from a double deck bed two months before admission and had made several out-patient visits with complaints of flank pain and haematuria. She was transferred to medicine three months later after various investigations, which included cystoscopy, intravenous and retrograde pyelography, urine studies including cultures, had all yielded negative results, despite frank haematuria, fever and leg oedema being demonstrated by the patient intermittently.

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Upon transfer to medicine, she gave a detailed account of prolonged, repeated hospital admissions which started in the town of Nazreth in 1968, and frequent out-patient visits during a period of nine years, 1968-1977, seeking medical care with various problems (Table 1).

She had during her previous admissions been subjected to a number of investigative procedures, which included x-ray studies of the G. I. on six occasions, intravenous pyelography, on three occasions, retrograde pyelography twice and oesophago-gastro-duodenoscopy and cystoscopy once each. Several laboratory studies, haematological and biochemical, had been made, all of which were within normal range. She had undergone six laparotomies (Table 2) at three different centres.

She evaded questions about social and family histories and was noted to be aggressive when her narratives relating to past complaints of abdominal distension, crampy pain, vomiting, constipation, inability to pass urine for several days, etc., were not promptly heeded to.

Physical examination revealed no abnormalities except for a distended abdomen with several post operative scars and trace pre-tibial oedema.

While further investigations were being contemplated, a suspicious nursing staff had made the following observations:

1) The patient was applying tourniquets on her legs prior to morning rounds to demonstrate oedema.

TABLE 1. Summary of M.A'S hospital admissions

Month and year of admission	Hospital stay in days	Presenting symptoms	Procedures - diagnosis
1. July 1968	13	Abdominal pain epigastric burning pain	Symptomatic Medical treatment offered
2. August 1968	64	Abdominal pain epigastric burning pain, abdominal distention and vomiting.	Ulcer disease suspected Negative Upper G.I. series. Medical treatment given.
3. August 1970	27	Same symptoms.	Normal Barium studies.
4. Sept. 1970	186	Same symptoms.	Discharged with diagnosis of hysteria.
5. May 1971	252	Epigastric burning pain and vomiting, haematemesis.	Negative Upper G.I. series. Laparotomy performed for suspected ulcer.
6. June 1972	14 14	Abdominal distention, haematemesis and bloody diarrhoea.	Prepared for laparotomy, discharged against medical advice.
7. July 1973	246	Abdominal distention with crampy pain and haematemesis.	Upper G.I. series and i.v.p. were normal. Intestinal obstruction suspected and four abdominal surgeries done.*
8. June 1974	91	Same complaints.	Negative G.I. x-ray studies. Exploratory laparotomy.
9. May 1975	29	Persistent vomiting with occasional haematemesis abdominal distention.	Normal oesophago-gastro-duodenoscopy. Psychiatric consult made. Discharged as psychoneurotic.
10. March 1977 (present)	178	Abdominal distention, flank pain, fever, haematuria and leg oedema.	i.v.p. retrograde pyelography & cystoscopy normal. Symptoms were proved

TABLE 2. Abdominal surgeries performed on M. A.

Month and year of surgery	Type	Comments
June 1971	Exploratory laparotomy	No ulcer found at laparotomy.
July 1973	Subtotal gastrectomy	Negative diagnosis.
August 1973	Resection of sigmoid	? Volvulous.
October 1973	Closure of colostomy	Post-operative draining fistula persisted.
November 1973	Exploratory laparotomy	? Intestinal obstruction.
February 1974	Laparotomy	Adhesiolysis. Partial intestinal obstruction due to bands.

2) Catheter urine specimens obtained by the nursing staff were clear as opposed to the frank haematuria she was producing for demonstrations on occasions.

3) She was manipulating thermometers in her mouth resulting in 'false' high readings whereas temperatures taken with a staff member standing by were normal.

CAUSES

These patients consiously simulate illness but their symptomology is more complex than simple malingering. Hysterical mechanisms are said to be partially responsible in the pathogenesis of their illness. Hysterical symptoms, however, are not consciously produced. Though these patients act consciously to produce symptoms, these individuals may be no more in control of their actions than their hysterical counterparts (6) and must involve considerable masochistic needs (7). Some of these patients in fact manifest symptoms of hysteria while others may be schizophrenic or sociopathic (6,7). Childhood deprivations and relationships with aloof and sadistic parents may predispose these individuals to a persistent unsatisfied need to get attention through illness and repeated hospitalizations often involving traumatic procedures

COMMENT

Our patient fulfils all features of this hospital addiction syndrome. She has spent well over a thousand days in hospitals in nine years, 1968-1977, and perhaps more for which documents were not available to us. In the same review by Ireland *et al* (6), 61 percent had undergone laparotomy, our patient had undergone six laparotomies on record performed between 1971 - 1974. Fifteen percent had haemoptysis, a presenting symptom presumably fictitious on earlier admissions of our patient, 14 percent had pyrexia proved fictitious as it was in our case, in 7 percent haematuria was a presenting symptom and several more have been reported since (8,9,10). This was her main problem during this last admission, again not borne out by investigations. She had left one hospital against advice, probably because she was required to pay for this admission.

She had been noted to be evasive and at times even aggressive and in keeping with what has been described of the syndrome At no time during her hospitalization was it possible to obtain a reliable family and social history.

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ABSTRACT. In order to find a safe and palatable mixture of *Kosso* and oats, exploratory feeding, using different concentrations of crude female *Kosso* flowers prepared in pellet forms, was carried out in 7 groups of mice for about 2 weeks. *Kosso* was found toxic to mice in high concentrations, toxicity being manifested by paralysis of extremities followed by sudden death. After this, a second experiment was designed using 9 groups of mice and employing provocative factors, paracetamol and starvation, that might render the liver susceptible to the effect of *Kosso*. Thus, after 6 months of feeding *Kosso* of different concentrations to the different groups of mice, it was found that *Kosso* was not hepatotoxic in normal, starved and paracetamol-fed mice. On the other hand, *Kosso* was fatal to mice, fatality being maximum during periods of starvation. It is suggested that the effects of *Kosso* on the nervous and muscular systems of mice and other animals should be studied in detail.

INTRODUCTION

Hagenia abyssinica (Bruce) Gmel., also commonly known as *Kosso*, is a dioecious tree which grows on the highlands of Ethiopia and other parts of East Africa. Although *Kosso* had been used as a taenicide by Ethiopians for many centuries, its taenicidal value was first reported to the rest of the world in the eighteenth century by the Portugese Jesuit Almeida and by the Scottish traveller James Bruce [1]. Though there has been for several years considerable interest in the elucidation of the chemical constituents of *Kosso*, it was only recently that the structures of four phloroglucinol derivatives derived from *Kosso* have been reported [2,3]. The female flowers are popularly used to treat tapeworm, a very common infestation among Ethiopians due to the age-long practice of eating raw beef by a large sector of the population. A variable amount of the dry flower suspended in water is taken, either to treat tapeworm infestation or to relieve nonspecific abdominal complaints. It is not uncommon for many Ethiopians to take *Kosso* as often as once every two months for several years.

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† Presented at the 14th Annual Ethiopian Medical Association Conference on May 26, 1978

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Hepatitis-like illnesses after ingestion of *Kosso* have been observed by some clinicians [4]. However, *Kosso* may have been taken coincidentally during the prodromal phase of hepatitis to relieve symptoms. Because of such observation, and particularly because of the high prevalence of liver diseases in Ethiopia, this study was conducted to find out if *Kosso* is hepatotoxic in mice.

MATERIALS AND METHODS

A. *Exploratory feeding:*

In order to find a palatable mixture of *Kosso* and oats *(Semolina)*, four groups of 5 mice each were fed samples with a concentration of 1:1, 1:2, 1:3, and 1:4, respectively. A fifth and sixth group, three mice in each were fed *Kosso*-oat mixture in a ratio of 1:10 and 1:20, respectively. A seventh group of 3 mice was fed only oats to serve as control.

B. *Experimental feeding and design:*

Sun dried and ground up flowers of female *Kosso* collected in January 1977 from the Addis Ababa region and oat flour were mixed in a ratio of 1 part *Kosso* to 5 parts oats and 1 part *Kosso* to 10 parts oats. The mixture was made into pellets by wetting it with water and then allowed to dry. For the groups of mice requiring paracetamol 350mg per kg body weight of Panadol Elixir (Winthrop Products Inc., New York, N.Y., USA) was added to the feeds in such a way that the total amount of paracetamol was absorbed and retained by the pellets. Thus the single total calculated dose of paracetamol was fed to the appropriate mice within a period of 6 to 12 hours. Since paracetamol had to be administered only once, subsequent feeding of *Kosso* and oats was resumed after the mice had completely consumed the paracetamol containing mixture.

Forty *albino* mice, each about 2 to 3 weeks old and with an average body weight of 23.6g (range: 20-28.5g) were divided into 9 groups according to Table 1.

All the mice were kept in the same room at atmospheric temperature; starving mice were kept in isolation to prevent cannibalization. Water was provided *ad libitum* to all groups, including the starving mice. Starvation in groups 7 to 9 was achieved by restricting the amount of feed to one third of that given to the rest of the mice, *i.e.*, groups 1 to 6, per day. Paracetamol was administered on the same day to group 9 after one month of starvation; following this, starvation feeding was continued until the mice died or till the end of

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TABLE 1

Experimental design showing type of feeds and number of mice in each group

Group	Type of feed	Number of mice	Number of cages
1	*Kosso* 1:5	5	1
2	*Kosso* 1:10	5	1
3	Normal feed (N.F.) only	5	1
4	Paracetamol	5	1
5	Paracetamol + *Kosso* 1:5	5	1
6	Paracetamol + *Kosso* 1:10	5	1
7	Starvation only	4	4
8	Starvation + *Kosso* 1:5	3	3
9	Starvation + *Kosso* 1:5 + Paracetamol	3	3

the experiment. A mouse was removed and weighed as soon as it was found dead and submitted for autopsy and histological study of the liver. The total study or observation period was 6 months (August 7, 1977 until February 8, 1978).

RESULTS

A. *Exploratory feeding:*

Kosso is found to be neurotoxic to mice. The degree of toxicity depends on the concentration of *Kosso* consumed by the mice. Thus, no mouse survived for more than 6 days in group 1-4 (Table 2). The clinical presentation was paralysis of all 4 extremities followed by sudden death. In group 5, all 3 mice were found dead overnight without preceding neurological signs. The 3 mice in group 6 and the 5 control mice in group 7 were alive and well after an observation period of 17 weeks.

B. *Experimental feeding results:*

As shown in Table 3, mice in the control group and those fed paracetamol alone in group 4 lived longer than those mice in the other groups. However, the survival period, like in groups 1,2 and 5,6 as well as groups 8 and 9, is comparable. Therefore, the addition of paracetamol did not alter the response of the mice to *Kosso*.

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TABLE 2

Results of exploratory feeding of *Kosso* (Different concentrations) to mice

Group	No. of mice	Feed mixture ratio (*Kosso*:oats)	Day 3 alive normal	Day 3 alive paralyzed	Day 3 dead	Day 4 alive normal	Day 4 alive paralyzed	Day 4 dead
1	5	1:1	-	3	2	-	-	5
2	5	1:2	2	3	-	-	-	5
3	5	1:3	3	2	-	-	-	5
4	5	1:4	2	2	1	-	-	-
5	3	1:10	-	-	3	-	-	-
6	3	1:20	3	-	-	3	-	-
7	5	only oats	5	-	-	5	-	-

TABLE 3

Effect of *Kosso* on different groups of mice

Group	No. of mice	Type of feed	Survival period* (days)
1	5	*Kosso*/oat 1:5	14, 51, 51, 120, 130
2	5	*Kosso*/oat 1:10	40, 109, 118, 122, 151
3	5	Control (normal Feed = N.F.)	
4	5	N.F. + Paracetamol	141, 144, 151, 155*, 155*
5	5	N.F. + Paracetamol + *Kosso*/oat 1:5	76, 78, 82, 86, 122
6	5	N.F. + Paracetamol + *Kosso*/oat 1:10	123, 132, 139, 141, 147
7	4	Starvation only	139, 139, 144, 152
8	3	Starvation + *Kosso*/oat 1:5	14, 21, 29
9	3	Starvation + *Kosso*/oat 1:5 + Paracetamol	14, 27, 30

* The total feeding or observation period of 155 days was survived by all the mice in group 3 and by 2 mice in group 4. These 7 mice were sacrificed at the end of the experiment.

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Mice fed *Kosso* while on starvation diet, *i.e.*, groups 8 and 9, died much earlier than those in other groups. Starvation alone did shorten the survival period appreciably when compared to the control group or those fed paracetamol. Therefore, *Kosso* toxicity seems to be maximum during periods of starvation. No mouse revealed paralysis of extremities prior to death.

Fig. 1 shows that all mice fed on *Kosso*-oat were far below normal weight at the time of death.

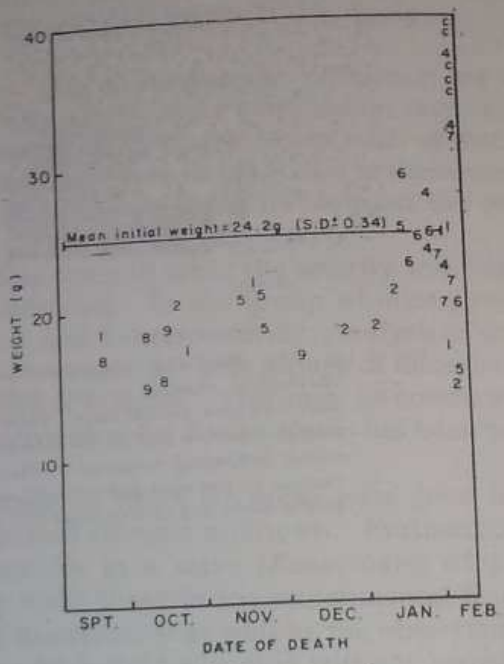


Fig. 1.

Again, the addition of paracetamol did not bring any change either to the control or the *Kosso*-oat fed groups. The mice in the restricted diet group 7, but without *Kosso*, did not gain weight like the control group, suggesting that starvation was achieved.

Histologically, no mouse developed hepatic necrosis, cirrhosis or hepatic carcinoma (Fig. 2 (a) - (d)).

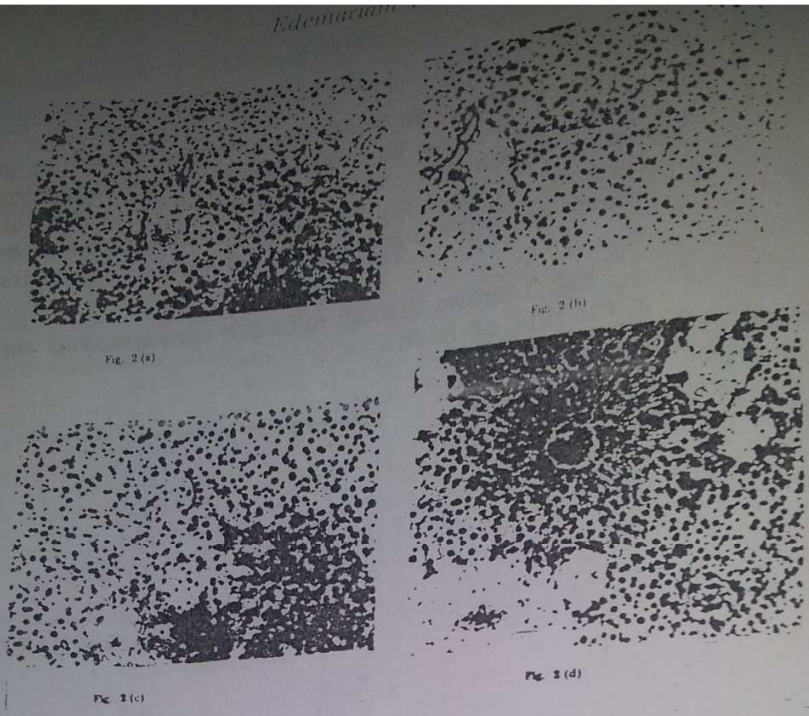


Fig. 2(a)

Fig. 2(b)

Fig. 2(c)

Fig. 2(d)

Fig. 2 (a) - (d). With the exception of one mouse in group 9, Fig. 2(d), the hepatic histological changes are very slight. Each figure contains at least one portal tract and one central vein. There is a variable degree of atrophy of cells not referable to any part of the lobule. The centrilobular necrosis seen in only one mouse belonging to group 9, Fig. 2(d), with no intermediate stage of partial damage to the cells and without any response by inflammatory cells is unusual. This is likely due to a peculiar post mortem autolysis.

DISCUSSION

Schoental and Coady [5] have shown that, of 40 different Ethiopian plant materials, 10 species of plants of the genera *Senecio*, *Crotalaria*, *Heliotropium* and *Cynoglossum* are hepatotoxic in rats. Anthelmintics, including *Kosso*, did not cause hepatic damage after feeding the plant material to rats for a period of one month or less. In this experiment, the same negative finding was observed in mice fed *Kosso* 1:5 and 1:10 for a period of 6 months.

It has been suggested that known hepatotoxic substances given to animals previously rendered cirrhotic by another known and predictably hepatotoxic agent may result in more pronounced liver damage [6]. Thus, paracetamol,

known to cause predictable and reversible histological changes in the liver when given in a dose of 350mg per kg body weight, was administered to 3 groups of mice who were later fed *Kosso* at a concentration of 1:5 and 1:10. There was no difference between the hepatic histology of these groups and that of the control group. Therefore, whether *Kosso* is given to mice with normal livers or to mice with livers previously injured by a known agent, it is not hepatotoxic. It is possible, however, that paracetamol did not cuase any hepatic damage or, if there was any injury at all, complete recovery had taken place. However, since no hepatic damage was noted in group 9 mice that were fed paracetamol which died within 4 weeks, the former is very likely.

Hepatic changes due to nutritional deficiency are well established fact [7,8]. The additional ingestion of hepatotoxin may aggravate or worsen the nutritional liver disease. Accordingly, *Kosso*, with or without paracetamol, was fed to starving mice. The effect of the *Kosso* in these mice, *i.e.*, group 8 and 9, was disastrous, resulting in early death but without any evidence of liver injury.

Kosso is definitely toxic to mice; the severity and fatality depending on the concentration administered. In the group of mice given *Kosso* in concentrations of 1:1, 1:2, 1:3, and 1:4,respectively, paralysis of extremities followed by sudden death were observed. In these groups of mice neurological involvement of respiratory muscles is possible. This may be correlated with an earlier finding in which optic nerve atrophy due to *Kosso* has been noted [9].

However, the cause of death of those mice given lower concentration of *Kosso* over a long period remains unknown. Furthermore, it is not clear why mice given feed mixture in a ratio (*Kosso*:oats) of 1:10 died early in the exploratory feeding while those in the experimental feeding survived for more than 50 days. This discrepancy as well as the observation of the 3 mice in the exploratory feeding which suddenly died without preceding neurological signs may be because of variation in the amount of *Kosso*-feed mixture eaten by the mice, since the exact amount of mixture consumed by each mouse was not monitored.

Although extrapolation of data from mice to man requires extreme caution, more detailed physiological and biochemical studies with emphasis on the nervous and muscular systems are necessary in order to understand the suspected toxicity of *Kosso* in man.

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A recent report on type and sensitivity pattern of tubercle bacilli from Addis Ababa by S.R. Pattyn *et al.* (1) is of great interest to those practising medicine in Ethiopia, and especially to those dealing with tuberculosis.

The study consisted of identification and sensitivity studies on 184 consecutive isolates of mycobacteria cultures at the Central Laboratory and Research Institute in Addis Ababa. These tubercle bacilli were grown from the sputa of patients seen at the Tuberculosis Demonstration and Training Centre in Addis Ababa. Sputa were cultured from (a) tuberculosis suspects with 3 negative acid-fast bacilli (AFB) smears, (b) treatment failures, and (c) relapse cases.

Identification and sensitivity testing on these isolates were carried out at the Prince Leopold Institute of Tropical Medicine in Antwerp, Belgium, as proper facilities for these tests were non-existent in Ethiopia. Even though one of the purposes of the study was to look for *Mycobacterium africanum*, identified in other parts of Africa (2), all the 184 strains proved to be *M. tuberculosis* with some biochemical peculiarities. No *M. bovis* was identified. The results of the sensitivity tests, as taken from the report, are shown in Tables 1 and 2.

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TABLE 1. Double and triple resistance among Ethiopian strains of *M. tuberculosis*

Double resistance		%	Triple resistance		%
INH + PAS	27/109	25	INH + PAS + TSC	16/109	14
			INH + PAS + KAN	5/66	7
INH + TSC	28/112	20	INH + TSC + SM	18/112	16
			INH + TSC + KAN	6/66	9
INH + SM	32/112	28	INH + SM + PAS	17/109	15

TABLE 2. Drug sensitivity of Ethiopian *M. tuberculosis*

	INH	SM	PAS	TSC	KAN	RMP
Number resistant/ number examined	52/112	52/112	52/109	33/113	21/66	0/66
% resistance	46	46	47	29	31	0
Relapses	17/42	17/42	20/40	13/42	12/28	0/28
% relapses	40	40	50	31	42	0
Treatment failures	12/32	8/21	8/21	5/23	1/6	0/6
% failure	52	35	38	21	17	0

INH : isoniazid
PAS : para-aminosalicylic acid
TSC : thiosemicarbazone (thiocetazone)
SM : streptomycin
KAN : kanamycin
RMP : rifampicin

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As can be concluded from the study, INH resistance is very high (40% to 52%). Indeed, even multiple drug resistance is unacceptably high: INH and PAS, 25%; INH and TSC, 20%; INH and SM, 28% and INH, TSC and SM, 16%. There were no strains that were resistant to rifampicin, demonstrating that this drug has not been used extensively in Ethiopia.

The fact that relapse and treatment failures showed a high degree of resistance was no surprise. Even in one of the most developed countries, USA, a recent report revealed that resistance in previously treated cases was as high as 68% (3). As the resistance in both relapse and treatment failure cases was similar, Pattyn *et al.* concluded that most probably the resistance was primary. Of course this does not follow the strict definition of *primary drug resistance*, that is, resistant organisms isolated from a patient who has *never* previously had antituberculosis chemotherapy (4). In fact, since patients may not always be truthful, it is impossible to determine primary drug resistance accurately. Therefore, *initial resistance*, which is defined as resistance in patients who *deny* previous antituberculosis therapy, is a preferred term (4), even though several studies use the phrases *primary drug resistance* and *initial drug resistance* interchangeably (1,3,5).

Initial drug resistance (primary drug resistance) varies with each country: 3.8% in Australia (6); 4% in Great Britain and USA (5,7); 10% in France (8); 22% in India (9); and 30% in Hong Kong (10). Even in Hong Kong, with such a high prevalence of primary drug resistance, routine tests for sensitivity would prevent only 5% of failures (4). Similarly in Great Britain, with 4% resistance, it was extrapolated that only 0.7% of failures would be prevented if sensitivity tests were carried out routinely.

Therefore, in Great Britain, an editorial (4) concluded that routine sensitivity tests on previously untreated patients could be stopped for reasons of economy, without appreciably compromising patient treatment. It presupposes, however, that these tuberculosis patients are closely monitored by sputum examinations for response to therapy.

It must be borne in mind that continued surveillance for primary drug resistance in any community is essential. The Centre for Disease Control, in co-operation with 17 public health laboratories throughout the United States, reported the results of a survey for primary drug resistance that had been conducted since March 1975 (11). Resistance to isoniazid was 4.3%, very similar to the results in a report of more than a decade earlier (7). The study (11) found resistance to streptomycin 4.3%; rifampicin (0.2%) and ethambutol (0.5%) had the lowest rates of resistance. It was also noted that resistance was 14% and 18% among Hispanics and Asians respectively. Resistance was higher in the young than in the elderly.

The study by Pattyn *et al.* (1) has a number of flaws: (a) the methodology of sensitivity testing has not been given in detail, nor does the article quote published methods; (b) it does not define relapses, treatment failures or drug resistance; and (c) no details are given about the patients. If, for example, as it appeared, all patients were ambulatory, it would be impossible to ascertain their drug intake, and it would therefore be difficult to distinguish relapses from treatment failures.

What Ethiopia needs today is an accurate account of the prevalence of primary drug-resistant tubercle bacilli, for a rational approach to the control of tuberculosis. The fact that we have only INH, TSC and SM available for the majority of patients (95% or more) makes the determination of primary drug resistance mandatory.

If primary drug resistance is very high in Ethiopia, then we cannot afford to dish out INH left and right, as is at present being done. We must undertake routine sensitivity tests on all tuberculosis patients, and, for the resistant cases.

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other antituberculosis drugs should be available. If, with luck, primary drug resistance is low, we may be able to afford to plod along as we are doing — but not for too long!

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TETANUS IN GONDAR PUBLIC HEALTH COLLEGE HOSPITAL, ETHIOPIA: A REVIEW OF 72 CASES

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ABSTRACT: Records of 72 tetanus cases admitted during a two year period to the Gondar Public Health College Hospital have been analyzed. The males were predominant. There were 8 neonates, 22 between 29 days and 9 years, 33 between 10 and 39 years, and 9 above 40 years. The mortality rate and form of tetanus was the same in non-neonatal cases of both sexes. There was no difference in the various combination of relaxants in so far as the outcome is concerned. The disease was more common during the dry season. All patients were prone to one type of trauma or another because of the nature of their activity, and as a result of ignorance, poverty, and social and cultural practices. The site of injury was known in 59 cases (82%), the commonest being the foot. All neonatals with severe form of tetanus died. Sixty-seven percent of severe and 25 percent of moderate form of non-neonatal tetanus cases died. The overall mortality was 61 percent. The various complications and the causes of death are discussed. The study strongly justifies the need for a special unit for better and continuous care using trained health assistants without additional cost. The cost benefit analysis clearly demonstrates the vital importance of active immunization programmes and appropriate health education.

Tetanus is an acute intoxication of the nervous system with manifestations of neuromuscular dysfunction resulting from fixation in the central nervous system of a soluble exotoxin (Tetanospasmin) elaborated by a spore-forming gram-positive anaerobic bacillus, *Clostridium tetani*. Although tetanus is a world-wide disease, it is more prevalent in those areas where the climate is warm and damp, and where the soil is rich in organic matter. Two major problems of tetanus (1) are the lack of naturally acquired immunity and the difficulty of implementation of immunization programmes, especially in the tetanus-prone communities of the developing countries. Because of these, the incidence of tetanus still remains high. In developed countries, like USA and Britain, where immunization has become routine, there has been a tremendous reduction in the incidence of the disease (2, 3, 4). Other factors like socioeconomic changes also play a role in the epidemiology of the disease (5). In Ethiopia there is no nation-wide study on the incidence and mortality rates of tetanus; the only available data being a review of 79 cases admitted to three hospitals in Addis Ababa with an overall mortality of 32 percent (6). Analysis of 1971-72 admissions to Gondar Public Health College Hospital (7) indicated that tetanus was a common cause of mortality with the highest case specific death; it stood third in the proportional mortality rate after malnutrition and cirrhosis of the liver.

Tetanus is a lethal but preventable disease. The mortality rate in various continents of the world is different. However, all in all 423,000 people in the world die from tetanus each year (8). The case fatality rate, even in developed countries where the management facilities are much better, is still high (9). This clearly indicates the need for and importance of preventive

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measures. Yet the emphasis put on prevention, which is quite cheap and effective (10,11), is very poor in developing countries. In Ethiopia, immunization programmes for tetanus are practically non-existent except in some MCH centres in the capital city and some provincial towns.

In this paper 72 tetanus cases with poor socioeconomic backgrounds, admitted to the Gondar Public Health College teaching hospital over a two year period, are reviewed with the following objectives:

1) to study the problem of tetanus in terms of a) frequency of admission, b) geographical distribution, c) seasonal variation, d) occupation, e) clinical picture, f) care and outcome, g) cost of care,

2) based on the above findings, to recommend ways of reducing the mortality rate without incurring additional costs.

MATERIALS AND METHODS

The records of 72 tetanus cases admitted over two years (January 1975 to December 1976) to the Gondar Public Health College Hospital were analyzed according to age, sex, occupation, seasonal variation, geographical distribution, how the infection was acquired, incubation, frequency of admission to hospital, presenting symptoms, severity of tetanus and physical findings. The progress and outcome of these cases were studied. The neonatal and non-neonatal tetanus cases have been studied separately. Moreover, an attempt was made to relate the continuity of care to the outcome. The cost of each case was calculated in terms of drugs, hospitalization and laboratory charges only. The factors which have led to a high case fatality rate have been studied so that feasible recommendations to increase the survival rate could be made.

RESULTS AND ANALYSIS

Frequency of tetanus hospitalizations: The total hospital admission in this study period was nearly 7,000 with a male: female ratio of 1: 1.2. The frequency of tetanus admissions was 1.07 percent. There were eight neonatal and 64 non-neonatal tetanus cases. The incidence of tetanus in Ethiopia cannot be properly assessed because of poor reporting systems. Furthermore, the authors believe the traditional beliefs and practices, combined with communication problems in the region, have resulted in a lower figure.

Age and sex distribution: Table 1 showsthe age and sex distribution, the youngest six days old and the oldest 66 years. There were 44 males and 28 females. (M:F - 1.6:1) and males predominated in all age groups. Higher incidences in males have been observed by several workers (12, 13) in all ages. There was no difference between the two sexes in so far as the severity and mortality are concerned. The mortality in the under 10 year age group was 62 percent in contrast to 68 percent in Massawe's report (4) from Mulago Hospital in Uganda.

Geographical distribution and occupation: Twenty-seven (37.5%) were from Gondar town, 13 from Gondar vicinity, and the rest from places over 30 kms away. All cases were from places below 2300 meters above sea level, 47 of the cases (65.3%) were from rural areas, and 25 (34.7%) from urban. A higher proportion of cases from urban areas died and this may be explained by the fact that more children came from urban communities where the fatality rate was 77 percent.

All cases were prone to one type of trauma because of the nature of their activity and as a result of ignorance and poverty (nearly all of them wore no shoes). Children staying at home, farmers, housewives and pupils constituted a high proportion of the cases (Table 2).

Seasonal variation: Forty-nine cases (68%) were admitted during the dry season, and the rest (32%) during the wet season.

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The cost of maintaining this patient during all these years of free hospital medical care (by one calculation, the cost of intravenous fluid alone exceeds 2000 Eth. Birr), time consuming and expensive investigations and surgical interventions is prohibitive.

Observations by the ward nursing staff were crucial in reaching the diagnosis.

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TABLE 1: Tetanus in Gondar Public Health Hospital: Age, sex distribution and case fatality

AGE	Male			Female			Total	
	Total Case	% of total	% of case fatality	Total case	% of total	% of case fatality	No.	Case fatality
Neonatals (< 29 days)	7	87.50	85.71	1	12.50	100.00	8	87.50
29 days- 9 yrs	13	20.31	61.54	9	14.06	55.56	22	63.64
10 yrs-19 yrs	8	12.50	37.50	7	10.93	85.71	15	60.00
20 yrs-39 yrs	11	17.19	54.44	7	10.93	28.57	18	44.44
40 yrs +	5	7.81	80.00	4	6.25	50.00	9	66.67
Total (Non-neonatal)	37	57.81	59.46	27	42.19	55.50	64	57.81

TABLE 2: Occupation of 72 tetanus cases

Occupation	Number	% Total
Stay at home (children)	27	37.50
Farmer	15	20.83
House wife	12	16.67
Student	8	11.10
Daily labourer	2	2.78
Tella seller	2	2.78
Weaver	1	1.39
Servant	1	1.39
Merchant	1	1.39
Unknown	3	4.17
Total	72	100.00

This seasonal variation is statistically significant ($0.005 < P < 0.001$). There has been controversy about the seasonal variation in the incidence of tetanus in Africa. Tompkins (15), Baker (16), Adeuja (17) and Sènècal (18) reported that tetanus is common during the dry season. On the other hand Massawe (14) found no significant monthly variation. There is a communication problem in this administrative region which is reflected in lower patient attendance in the hospital during the wet season. However, of the 40 cases from Gondar town and its vicinity, where transport facility is available all the year, 30 were admitted during the

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dry season. This may support the argument that tetanus is commoner during the warm and dry season. Detailed studies (19) from various countries have shown that, in areas with cool and temperate climates, cases of tetanus occur during the warm season but in tropical areas the seasonal variation of the incidence is less pronounced.

Portals of entry of infections: Table 3 shows the incidence of various modes of infection and their relative mortality. The commonest portal of entry was trauma in 45.8 percent, thorn-prick to foot and other foot injuries being the commonest. Other causes of trauma were car accident, bullet injury with retention of foreign material in the dry tissues, burn and dog bite. Ten cases had tetanus related to home delivery, five of puerperal sepsis and five neonatal following umbilical sepsis. In 10 cases, mode of infection was other crude, traditional surgical practices, namely excision of uvula (in four, three were neonates), extraction of deciduous teeth and incision of gums in two, and in four others following jigger extraction, thorn removal and incision. Four were associated with otorrhea (one with foreign body in the ear), three cases with skin infection and one with a cold abscess. In 11 cases (15.3%) there was no information on the portal of entry.

Table 4 shows the suspected sites of injury. In 59 cases the site was known, the commonest site being lower limbs. Foot as site of injury accounted for 35.6 percent of the known sites and 29.2 percent of the total. Similar observations have been noted by Ayim (20) and Adeuja (17) and Vakil *et al* (21). Portal of entry was unknown in 11 cases (15.3%) and this is similar to a report with larger series (22), in contrast to observations by Braganza (23) and Cox (4) who reported over 50 percent.

Clinical picture: (Table 5). In this study the cases were classified as severe, moderate and mild, using criteria by Dastur *et al* (24). There were 56 (77.8%) severe (five were neonatals), 15 (21%) moderate (three were neonatals), and only one case of mild form of tetanus. All five severe and two out of three moderate neonatal tetanus cases died. Mortality is high in this series and also in other reports, ranging from 80 to 95 percent (22,25). Lower mortality however has been reported in rural Haiti, 47 percent (26), and India, 56.8 percent (27). In nonneonatal tetanus there were 51 cases of severe, 12 cases of moderate and mortality was 66.7 percent and 25 percent respectively; there was only one case of the mild form and this survived. There was no difference in severity or mortality in both sexes.

The incubation period could be determined in number of days (1-37) in 55 cases.

TABLE 3.

Mode of Infection	Number Admitted	% Total Admission	No. Died	Dead
A Trauma	33	45.83	17	51.52
B Umbilical and uterine sepsis (home delivery)	10	13.89	7	70.00
C Traditional practices (other than cutting umbilical cord)*	10	13.89	9	90.00
D Miscellaneous	8	11.11	4	50.00
E Unknown	11	15.28	7	63.64
Total	72	100.00	44	61.11

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TABLE 4. Site of injury and case fatality of tetanus

Site of Injury	Neonatal			Non-Neonatal		
	Total cases	%of total	% Case fatality	Total cases	% of total	% case fatality
Head	3	37.50	10.00	8	12.50	62.50
Upper limb	—	—	—	6	9.38	66.67
Chest	—	—	—	5	7.81	80.00
Umbilicus	5	62.50	80.00	—	—	—
Birth canal	—	—	—	6	9.38	66.67
Lower limb	—	—	—	26	40.62	46.15
Unknown	—	—	—	13	20.31	61.54
Total	8	100.00	87.50	64	100.00	57.81

TABLE 5: Tetanus — Classification according to severity* and case fatality

	Total No.	Severe			Moderate			Mild		
		No.	Death	%Death	No.	Death	%Death	No.	Death	%Death
Neonatal	8	5	5	100.00	3	2	66.67	—	—	—
Non-neonatal	64	51	34	66.67	12	3	25.00	1	—	—
Total	72	56	39	69.64	15	5	33.33	1	—	—

*Scoring criteria (21) was used considering a) frequency of spasms, b) temperature above 38°C c) tachycardia ,d) rigidity (trismus, opistothonus, abdominal and limb rigidity).

There were 22 cases with incubation period less than seven days, 27 cases 7-15 days, and six cases above 15 days. The further the site of entry from the head, the longer the incubation period. The case fatality was lower in those with the longer incubation period, 33.5 percent with incubation period greater than 15 days, 50 percent 7-15 days, and greater than 80 percent in less than seven days in non-neonatals. All neonatal cases that died had an incubation period of less than seven days.

The onset was documented in 39 cases and it ranged between 24 hours to nine days. In 23 of these cases the onset was less than 24 hours. Eighty-seven percent of these cases died. Forty-four percent of those with onset greater than 24 hours died. None of the patients had received tetanus antitoxin or toxoid before admission.

Almost all patients had trismus and spasm, 71.7 percent of the cases had rigidity. Eighty-three percent of the cases were

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*Scoring criteria (21) was used considering a) frequency of spasms, b) temperature above 38°C c) tachycardia ,d) rigidity (trismus, opistothonus, abdominal and limb rigidity).

There were 22 cases with incubation period less than seven days, 27 cases 7-15 days, and six cases above 15 days. The further the site of entry from the head, the longer the incubation period. The case fatality was lower in those with the longer incubation period, 33.5 percent with incubation period greater than 15 days, 50 percent 7-15 days, and greater than 80 percent in less than seven days in non-neonatals. All neonatal cases that died had an incubation period of less than seven days.

The onset was documented in 39 cases and it ranged between 24 hours to nine days. In 23 of these cases the onset was less than 24 hours. Eighty-seven percent of these cases died. Forty-four percent of those with onset greater than 24 hours died. None of the patients had received tetanus antitoxin or toxoid before admission.

Almost all patients had trismus and spasm, 71.7 percent of the cases had rigidity. Eighty-three percent of the cases were

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conscious. Over 80 percent of the patients had tachycardia, fever and opisthotonus. Dysphagia, neck-stiffness, and pain occurred in over 50 percent of cases. Less common presenting clinical pictures were refusal to feed, hypotension, convulsions, sweating, irritability, constipation, and difficulty in urination.

MANAGEMENT OF PATIENTS IN THE HOSPITAL

There is no special unit for tetanus patients in the hospital, though there is a 22 bed ward where there are three rooms for patients with tuberculosis and one room with three beds for cases of meningitis, hepatitis, tetanus, etc. There is a physician responsible for the patients and close supervision of assistants. However, the whole unit is run by one advanced health assistant and two practical health assistants during working hours and only one practical health assistant during off hours (evenings, nights and holidays). Over the study period, 49 non-neonatal tetanus cases were admitted to this unit and 15 non-neonatal tetanus to the other wards. Eight neonatal cases were admitted to the paediatrics ward. Case fatality in the non-neonatals admitted to this unit was 24/49 (49%), while 20/23 (86.9%) in other wards.

All adult patients were given crystalline penicillin 8 to 12 million units I.V. per 24 hours in divided doses for 10 days. In the absence of crystalline penicillin, procaine penicillin 800,000 I.U. I.M. b.i.d. was given for the same length of time. Neonatals and children were also given crystalline penicillin 1.2 to 4 million units I. V. per 24 hours in divided doses. When crystalline penicillin was not available, procaine penicillin 400,000 to 800,000 units I.M. twice per day was used. Twenty-five patients were given chloramphenicol in addition to penicillin for complications. All except two patients received tetanus antitoxin treatment. The reason why the two patients who were admitted during off hours did not receive the tetanus antitoxin was not clear. Adults were given 50,000 units of tetanus antitoxin (TAT) stat, and a second dose of 50,000 units after six hours. Then, depending on the severity of the case, a daily dose of 10,000 units for five days was given. On the other hand, neonatals and children were given tetanus antitoxin, 5,000 - 500,000 units over one to five days. There were two adult and one child tetanus cases who were sensitive to tetanus antitoxin and all were successfully desensitized. The cases were few to compare the different doses of TAT. Optimum dose of TAT or TIG (tetanus immune globulin), both equally effective, has not been made but the fact that serological therapy in tetanus is effective has been supported by various studies in humans (28) as well as in animals (29,30).

Various combinations of relaxants were used in this study. Neonatals and children were given phenobarbitone 2-3 mg/kg IM/24 hours, and chlorpromazine hydrochloride (largactil) 2 mg-kg IM/24 hours in divided doses alternating four to six hours. Diazepam (valium or stezolid) 1-2 mg/kg IV per dose was also used whenever there was severe spasm. Adults were also treated with chlorpromazine hydrochloride 50 mg IM alternating with diazepam 10 mg IV every four to six hours. Diazepam was often used on P.R.N. basis for severe spasms. There was no significant difference in the outcome using different combinations of relaxants. However, our general observation was that in many non-neonatal tetanus cases relaxants were used more on P.R.N. basis and this was more effective for severe and frequent spasms and this method has been supported in another report (31).

Other important methods for the management of tetanus included giving oxygen, surgical toilet of wounds and oropharyngeal suctioning, plus nursing care. Various problems have been encountered, namely lack of oxygen supply, suction machine not available in time and lack of continuous nursing care during off-hours. 45

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Outcome of tetanus management: Twenty-eight patients (39%) survived and the average period of hospitalization of the survivors was 26 days (range of 9-59 days), while 44 died (61%), ie 87.5 percent neontal death and 57.8 percent non-neonatal death and the average period of hospital stay was 5.4 days (range 1-23 days). Fifty percent of deaths occurred within four days of admission (all neonatal and 17 non-neonatal deaths), 39 percent between 5-10 days and 11 percent after 10 days of admission. In the under 9 year age group only two cases survived out of 28. The case fatality rate decreased in those patients above 10 years of age. Moreover, this study has revealed that the traditional medical practices and home delivery as modes of infection (Table 3) have resulted in higher mortality than trauma. The total estimated cost of care of 72 tetanus patients was 11,514.34 Birr (US $ 5,757.17). On the other hand the cost of tetanus toxoid would have been 138 Birr (US $ 69) only, if immunization had been done on these patients.

Cause of death in tetanus patients: Table 6 indicates the causes of death. The most frequent causes of death, accounting for 40 percent and 30 percent, were respiratory spasm and respiratory failure (secondary to aspiration and pneumonia) respectively. In three neonates cause of death was unknown. Causes of death unrelated to tetanus were sepsis in two patients and one due to hypertensive encephalopathy in a 66 year old man. Such high causes of mortality of respiratory origin have been reported in large series (21). These could have been avoided if proper and continuous nursing care, especially during off-hours, had been given, together with continuous supply of oxygen and suction machine.

Complications during the course of management occurred, urinary retention in 17, diarrhoea in seven, pneumonia in nine, nervous system complications (depression, cranial nerve palsy and foot drop) in three and serum sickness in one. These complications occurred in the first 10 days in those who died.

DISCUSSION

It is the investigators' belief that social and cultural factors, lack of an active immunization programme, along with very limited MCH activities and many home deliveries by untrained local midwives, must contribute significantly to the incidence of tetanus. Vaccination and frequent

TABLE 6: Causes of death in tetanus patients (both neonatal and non-neonatal)

Cause	Number	% Total death
1. Respiratory spasm	18	40.91
2. Respiratory failure (aspiration, pneumonia and lung abscess)	13	29.55
3. Circulatory failure	5	11.36
4. Hyperpyrexia	2	4.56
5. Unknown (neonatal)	3	6.81
6. Unrelated (sepsis, hypertensive encephalopathy)	3	6.81
Total	44	100.00

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intramuscular injections by untrained personnel have not been observed in our study to be the cause of injury resulting in tetanus. It is interesting also to note that there were no tetanus cases in this study from amongst carpenters, mechanics and bricklayers, even though they are subject to frequent trauma. It is expected that incidence of neonatal tetanus is higher because of customs of cutting the cord with various unsterilized instruments, such as knife, blade, etc. and the practice of putting on the umbilical stump various dressings.

The cause of death by and large was associated with conditions that could have been prevented, ie adequate basic supplies and, what is more, by continuous nursing care especially during the critical period, namely the day of admission and subsequent four days. A special effort has been made to teach health assistants in the special ward where 49 non-neonatals were admitted the management of tetanus patients. Out of 25 admitted during regular hours when continuous nursing care was given, only six died (24%) while mortality was high in those admitted during off hours, 18 out of 24 (75%), and there is a strong statistional difference ($p \leq 001$). Such high mortality during off-hours had been due to lack of staff (only one practical health assistant on duty, not only for tetanus patients but for 20 other patients), and delay in early management. Modern methods of tetanus treatment as set out by Cole and Youngman (32) and Robles (10) including high level trained staff, use of currarization, tracheostomy, artifical respiration and hyperbaric oxygen, are impossible and far fetched to envisage in our setting for economic reasons and because of the lack of available experts. On the other hand, a modified intensive care unit has been recommended by Ayim (20) for use in developing countries. The writers strongly emphasise the need for a special unit which could be even more economical if trained health assistants were used to give the continuous nursing care. We also recommend intensive teaching of relatives taking care of patients. Simpler and cheaper would be to use nasogastric tube for giving relaxant as well as for feeding. This has shown good results (33).

The cost of treatment of one tetanus patient in this study was, on the average, 159.92 Birr (US $ 79.96). This did not take into account financial value on human life or work lost through the disease or cost of personnel. On the other hand, it would have cost only 139.8 Birr (US $ 69.9) or 1.2 Birr ($ 0.60) to 3 Birr (1.50) for each person to prevent tetanus in all 72 patients. Reports gathered by Cvjetancvic *et al* (34) from different parts of the world show that the cost of immunization ranges from $ 0.1 to $ 3.3, while that of treatment ranges from $ 50 to $ 900. This finding is in agreement with ours.

The clear message from this analysis is that prevention of tetanus by active immunization is very considerably cheaper than the management of clinical cases. The vital importance of routine immunization programmes to high risk groups of patients as in Maternal and Child Health Clinics and casualties needs to be emphasised in the strongest terms. Furthermore, the cultural and social factors related to tetanus must be considered not only in terms of active and widespread immunization programmes but also as a basic important part of all health education.

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CASE REPORT

PSYCHOSIS DUE TO ISONIAZID

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ABSTRACT: Two malnourished tuberculous patients with no previous history of mental disorder developed psychotic behaviour while taking isoniazid in a dosage of 6 to 8 mg per kgm body weight daily. The clinical manifestations of these patients were resentment, confusion, hallucination, disorientation, refusal to take medications, argumentativeness, complaining of trivialities and a tendency to run away from the hospital. The two cases responded well to pyridoxine while they were still on isoniazid. The role of isoniazid in the induction of psychosis is discussed and the literature is reviewed. It is recommended that such highly predisposed patients should be given supplementary pyridoxine containing Vitamin B complex to prevent the multiple side effects of isoniazid.

It is now over two decades since isoniazid, the cheapest and probably the most effective drug, became available for the treatment of tuberculosis (1). It is commonly used in countries like Ethiopia where tuberculosis is very prevalent.

The use of isoniazid as an antituberculous drug is not always without side effects even though they are infrequently encountered. Its neurotoxic effects are well documented; the commonest being peripheral neuropathy (2). Psychosis is another well known neurological disturbance produced by isoniazid (2-8). The psychosis is an effect of a metabolic defect induced by the drug, even when used in the standard dose (2,3). The increased incidence of psychosis in patients with existing malnutrition has been commented upon by Haynes (5). Isoniazid complications are seen more frequently among slow than among rapid inactivators of isoniazid (2,7,9,10).

In late 1976, the first author became aware of a tuberculous patient who developed psychosis while he was on Tb450 (isoniazid 300mg plus thiacetazone 150mg). He received chloropromazine to begin with but did not improve. The possibility of isoniazid induced psychosis was then thought of and pyridoxine was given. He showed a remarkable improvement. It was after this patient that we had two other cases.

As far as we know, psychosis due to isoniazid has never been previously reported in Ethiopia. Therefore, the purpose of this paper is to record two cases who developed psychosis while getting isoniazid in a dosage of 6 to 8mg per kgm daily in the Public Health College Hospital, Gondar.

CASE REPORT

Case 1. A.M. (Hosp. No. 41243), a 20 year old male daily labourer from Gondar town was readmitted to the medical ward on 26-2-77 because of malnutrition and suspected sarcoidosis. However a repeat lymphnode biopsy showed tuberculous lymphadenitis. Streptomyin, lgm im daily, and Tb450, 1 tablet per day, were started on 15-4-77. His general condition improved. Nevertheless, on 9-5-77 he refused to take his medication. He became resentful and argumentative, and had a tendency to run away. Later he developed confusion, disorientation to time and visual hallucination. He had no history of mental instability in the past. He used to drink the local beer occasionally

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but had abandoned drinking for over one year because of gastritis. Neurological examination disclosed no abnormality. He was given oral pyridoxine, 50mg twice a day, while Tb450 was still continued. His mental changes improved after three days and he started behaving cooperatively as before. After ten days, pyridoxine was discontinued. Two weeks later, he began behaving abnormally as before and took his own discharge from the hospital shortly afterwards. He was seen after three months in good mental condition. He had then stopped taking Tb450.

Case 2. A.B. (Hosp. No. 44858), a 55 year old emaciated male merchant from Gondar town, was admitted to the isolation unit on 13-1-77 because of open pulmonary tuberculosis. Antituberculous treatment with Tb-450, 1 tablet per day, and streptomycin, lgm im daily, was started on the day of admission. A month after admission, pyridoxine containing multivitamin and ferrous sulphate, each in a dose of 1 tablet thrice daily were begun. The multivitamin was discontinued on 10-3-77. Ten days after this he started complaining of trivialities, refused to take his medication and wanted to run away. Later he became confused and disoriented to time and place. He had no past history of such mental changes but used to drink the local beer regularly. Neurological examination revealed no abnormality. Pyridoxine, 100mg im, daily, was given together with the antituberculous treatment. He responded well and started behaving normally. Pyridoxine was then discontinued and four days later he began behaving abnormally as before. He improved remarkably when he was put back on pyridoxine again.

DISCUSSION

The mental changes seen in these two cases are all compatible with toxic psychosis, which is most probably dependent on their poor nutritional status. There is no direct evidence to implicate isoniazid as the aetiologic agent of the psychosis in these cases. On the other hand, it was not possible to determine urinary excretion of pyridoxine or xanthurenic acid in our cases since there was no facility. However, since there was no past history of mental instability and since their behavioural changes were similar to other reported cases, together with the good clinical response to pyridoxine, it can be concluded that the psychosis was due to isoniazid.

Obviously, our cases did not receive pure isoniazid as in other reported cases. Instead, they received Tb450 which contained both isoniazid and thiacetazone What role thiacetazone played in the psychosis is unknown and we were not able to find in the literature repored cases of psychosis due to thiacetazone.

The mechanism involved in psychosis due to isoniazid is in general believed to be related to deficiency of vitamin B (3). Zabad (6) reported one case of isoniazid induced psychosis which responded to nicotinic acid. Aspinall (7) reported a case with peripheral neuropathy, pellagra-like lesions and a toxic psychosis while receiving isoniazid. This case responded to nicotinic acid and vitamin B complex One of the five cases in Jackson's series (3) responded to nicotinamide. There are other similar reported cases of psychosis due to isoniazid who responded to nicotinic acid. Therefore, it is unlikely that isoniazid toxicity can be attributed to a single member of the vitamin B complex although thiamine itself plays no role. (3)

According to Adams (2) the effect of isoniazid on the peripheral nerves is different from its effect on the central nervous system. The neuropathy is believed to be due to a deficiency of pyridoxine. Hence, he thinks that fhe adminisfration of pyridoxine, which has a protective action against the development of peripheral neuropathy, is ineffective in the prevention of psychosis, fits and ataxia. In contrast, our cases responded well to pyridoxine while isoniazid therapy was still continued. They developed psychosis again upon discontinuing the pyridoxine. Case 2 showed improvement when pyridoxine was restarted. This observation of the preventive and curative role of pyridoxine supports other authors' views and findings (4,9,10,11,12, 13).

The role of pyridoxine in the metabolism of the brain has been demonstrated (11) The decarboxylation of glutamic acid to gammaaminobutyric acid is a pyridoxal dependent reaction which is specific to the central nervous system. The gamma-

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aminobutyric acid plays a role as a regulator of neuronal activity centrally. Hence, the central nervous system changes which result from isoniazid or from pyridoxine deficiency or from the administration of pyridoxine antimetabolite like deoxypyridoxine may be ascribed to a reduction in the activity of the glutamic acid decarboxylase with subsequent decrease in the quantity of gamma-aminobutyric acid, which is believed to be essential for the regulation of neuronal activity. The administration of pyridoxine or gamma-aminobutyric acid improved the central changes.

There are various opinions about how the deficiency of pyridoxine in isoniazid treatment occurs. Instead of the competitive blocking of pyridoxine by the isoniazid molecule, Biehl and Vilter (10) considered that isoniazid interacted with pyridoxine in the tissues to form a pyridoxal isoniazid complex which they found was excreted in the urine in large amounts. This finding was supported by other authors also. On the other hand, it has been shown in *E. coli* that isoniazid exerts a competitive antagonism the pyridoxine-catalysed reaction (12).

In closing, the complications of isoniazid are multiple (3,7,13) and are associated with the deficiency of various members of the vitamin - B complex. Our cases were all malnourished and this probably predisposed them to psychotic reaction which was well controlled with pyridoxine Therefore, in such predisposed groups it is worthwhile giving pyridoxine containing vitamin - B complex to prevent the multiple side effects of isoniazid.

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above sea level, and location in the north-western part of Gondar administrative region. Except for one patient who had stayed in Setit-Humera for 9 days only, the rest had been in the area for over 9 months. The prisoner was from Gondar town itself.

The 12 patients from Setit-Humera had a diet which included porridge prepared from boiled sorghum flour and mixed with a sauce made from lentil and red pepper. Vegetable oil was used for cooking purposes. The porridge was taken twice a day and was followed, each time, by two cups of tea with sugar. Eleven patients had meat twice a month, and only 2 patients had cabbage occasionally. Three patients used to drink the local beer. The diet of the prisoner consisted of "Injera" (bread) made from sorghum, plus sauce prepared from beans and red pepper, with vegetable oil added for cooking.

The symptoms of the disease are given in Table 1. The duration of illness ranged between 2 and 20 weeks.

TABLE 1. Symptoms in 13 dry beriberi cases

FEATURE	YES	NO
Heaviness of legs	12	1
Numbness of legs	12	1
Swelling of legs	12	1
Burning pain in the legs	10	3
Inability to walk	13	—
Inability to rise from a squatting position	13	—

TABLE 2. Clinical signs in 13 dry beriberi cases

FEATURE	YES	NO
Inability to rise from a squatting position	13	—
Tenderness in the legs	13	—
Swelling of leg	12	1
Vibration sense impaired	13	—
Position sense impaired	13	—
Brisk knee jerk	12	1
Brisk ankle jerk	12	1
Reduced heat, pain, touch sensations	9	4

Table 2 shows the clinical signs of the disease. Twelve of the 13 patients had a hard swelling on one or both calf muscles. Eight patients had the swelling on the right calf muscle alone. There was one patient with wasting of both leg muscles. There was no evidence of cellulitis, thrombophlebitis or peripheral nerve paralysis in any of the patients. There were 2 patients with fever; the fever in both subsided without treatment within 24 hours of admission.

Eleven patients had anaemia with a haematocrit ranging between 13% and 31% (mean 22.6%). The peripheral red blood cell morphology in all the anaemic patients showed microcytic, hypochromic, polychromatophilic and poikilocytic red blood cells. The erythrocyte sedimentation rate was taken in 10 patients, in all of whom it was significantly elevated ranging between 60 and 146mm. (mean 106.5mm.) in the first hour. The stool examination showed hookworm ova in 4 patients. The white blood-cell count was within the normal range except in 3 patients, where it was 3100 per cu.mm., 2910 per cu.mm. and 3450 per cu.mm. respectively. There were 2 patients with eosinophilia of 12% and 37% respectively, and both had hookworm infestation. A chest X-ray which was taken of 3 patients was normal.

In addition to the well-balanced diet that was given in the hospital, all patients received oral thiamine, 100 mg. daily. The patients with anaemia were also given oral iron, 300 mg. thrice daily; and they showed improvement. Following thiamine therapy, it took between 3 and 13 days, or 6 days on the average, for the patients to be able to walk. The ability to rise from a squatting position, after thiamine therapy, took a relatively longer

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time, which ranged between 5 and 17 days, or 10 days on the average. Swelling of the calf muscle resolved after 10 to 30 days, or on the average 21 days. The 9 patients who had a reduced sensation for heat, pain and touch took 35 to 58 days, or 43 days on the average, to recover their normal sensation. Thus, it took 6 weeks on the average for these 9 patients to recover completely from the disease with thiamine therapy.

DISCUSSION

It is now over 60 years since the aetiology of beriberi was fully established and methods of preventing it have been known. It is a disease that can be eradicated, provided measures of prevention and changing of the national diet are taken (6).

Beriberi is a variable disease with regard to its course, duration and outcome (1). In some patients it may present with a generalized neuritis and meningeal signs, together with the other clinical findings described in these patients (Mulugetta Mengistu and Mallede Maru, "A case of dry beriberi", unpublished data). Infantile beriberi may present with a pseudomeningeal form in which the clinical picture resembles tuberculous meningitis or an encephalitis (7).

All the patients in our series were young males. However, the data are too few and biased to draw any conclusion from.

Twelve patients had swelling of the legs. Eight of these had swelling of the right leg alone. The authors could not explain the reason why this preponderance occurred. One of the most useful diagnostic signs in the early stages of the disease is the alteration of the knee and ankle jerks. The patellar reflexes may be exaggerated during the first week of the disease, but thereafter they are absent (1). The deep tendon reflexes (Table 2) in 12 of the patients, with a duration of illness of more than 2 weeks, were exaggerated. This was an unusual finding, which the authors again could not explain. The deep tendon reflexes in the series described by Belcher *et al.* (5) are intact, whereas in other reports (2, 8) they are either diminished or absent. Tenderness on squeezing the calves and difficulty in rising from a squatting position, which are both useful diagnostic signs of beriberi (1), were elicited in all patients (Table 2).

The daily requirement of thiamine in adults is 0.4 mg. per 1000 calories. However, the need for thiamine increases wth conditions such as fever, physical exertion and high environmental temperatures (8, 9, 10). The staple diet in our patients was sorghum, which when uncooked contains an adequate amount of thiamine (4). However, since thiamine is heat-labile and water-soluble (9, 11), boiling of sorghum for a longer period of time, as in the preparation of porridge, may be associated with thiamine losses. Therefore, in 12 of the patients, the high environmental temperature of Setit-Humera, the excessive physical exertion and the fever due to malaria (10 patients) may have led to an increased demand for the vitamin, and this demand was apparently not satisfied by the diet which these patients had.

None of the patients died, and the response to oral thiamine therapy was dramatic. All the patients started to walk within a week following thiamine treatment. On the other hand, the 9 patients who had reduced sensation required a 6-week course of thiamine therapy to recover their normal sensation. This duration of time for recovery is in agreement with the findings of Bressa (10).

Obviously, biochemical tests confirm the diagnosis of beriberi. The estimation of the transketolase activity of the red blood-cell haemolysates is a simple, specific and sensitive test (3, 11) for this purpose. Unfortunately this test could not be performed. Therefore, in the absence of supportive laboratory data, the diagnosis of beriberi was made on the basis of environmental and dietary histories, the clinical picture and the response to speci-

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fic therapy with thiamine. Finally, it is suggested that beriberi should be considered as a differential diagnosis in those cases with a similar clinical picture.

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...PARUM INFECTION:
A REPORT OF TWO CASES WITH A REVIEW
OF THE ENGLISH LITERATURE

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SUMMARY

Two cases with acute plasmodium falciparum infection who developed acute urticaria are presented and discussed. The English literature is reviewed. The importance of malaria in the differential diagnosis of acute urticaria in areas where malaria is endemic is emphasized.

INTRODUCTION

Urticaria is a distinctive reaction of the skin, which is a localized oedema. The lesions develop suddenly, the colour varies from normal to pink or white and the configuration may assume bizarre, linear, or round patterns. Even though it is a very common skin disease, the incidence and aetiologic factors in the general population are still undetermined. In the United States probably more than 20% of persons experience at least one episode of urticaria and/or angioneurotic oedema during their lifetime (1). In Sweden in a survey of 36,347 persons 0.11% of the males and 0.14% of the females had objective signs of urticaria (2).

The commonest aetiologic factors that have been implicated in the causatio n of urticaria are drugs (e.g. penicillin, aspirin), psychic factors, inhalant allergens, physical agents, intestinal parasites, and infections such as filariasis, schistosomiasis, and malaria.

In a review of the English medical literature, we were unable to find any report of urticaria due to malaria infection, except in two old textbooks of dermatology and malariology by Ormsby and Montgomery (3) and Russel, West and Manwell (4) respectively where there was a passing mention. The following is a report of two cases of acute urticaria due to plasmodium falciparum infection which were seen at the Public Health College Hospital in Ethiopia.

MATERIALS AND METHODS

Case reports.

Case 1, K. K. M. (No. 45048), was a 30-year-old male Ethiopian from the Gondar area who was admitted to the medical service of the Public Health College Hospital (PHCH) on 4th July 1977 with a sudden onset of abdominal cramps, frequent bloody diarrhoea, vomiting, chills, and fever of 18 hours duration. Patient had been to a malaria

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area one month prior to admission. On examination he looked acutely sick, with an axillary temperature of 38.6°C, and a generalized urticaria, of different shapes and sizes ranging from 1–10mm in diameter, involving the extremities and the abdomen. He had slight epigastric tenderness. The rest of the examination was normal. The laboratory showed normal white blood cell count, haematocrit, and urinalysis. The stool and blood film for haemoparasites were negative. Patient was treated with intravenous fluid and Allercur (clemizole hydrochloride) 10mg IM for the allergic reaction. On 5th July 1977 the diarrhoea, fever, vomiting, and urticaria subsided. During the night of 6th July 1977 patient started to have headache, vomiting, frequent watery diarrhoea, fever, and generalized urticaria. In the morning, he started to have chills with a drop of his BP from 100/80mm Hg to 80/40mm Hg and a tachycardia of 116 per minute. He was found to be slightly dehydrated and was started on intravenous fluid. Stool and blood cultures and repeat films were sent. The patient was given epinephrine subcutaneously and prednisone 25mg intravenously. The blood film revealed plasmodium falciparum ring forms and the stool was positive for strongyloides larvae. He was immediately started on intravenous injection of chloroquine 250mg. This was repeated every 6 hours until patient was able to take orally. His condition improved gradually with a return of his vital signs to normal within four hours. The urticaria subsided and the diarrhoea improved with only intravenous fluids. Patient was kept in the hospital for 15 days without treating his strongyloides. He was followed for three months without any recurrence of his symptoms.

Case 2. H. D. (No. 49933), a 33-year-old Ethiopian was seen in the outpatient department of the PHCH, on 5th October 1977 complaining of headache, chills, and fever of sudden onset. He had been to a malaria area about three weeks prior to the onset of his present illness. Examination at that time revealed that he was acutely ill looking with axillary temperature of 38°C. The rest of the examination was negative. He was then admitted to the medical unit on 6th October 1977 for further examination and management. On admission, he complained of burning sensation all over and itchiness, headache, chills, and fever. The only physical findings on admission were a low grade fever (37.5°C), rose-red, circular to oval shaped, firm wheals with a diameter of 1–20mm, numerous in number and located on the left posterior and lateral chest. The stool examination was negative for ova and parasites. Full blood count and urinalysis were normal. The Widal test showed a titre "O" (E_O = 1/160). A repeat peripheral blood smear was positive for plasmodium falciparum malaria. He received a full course of chloroquine. The itching and burning sensation as well as the lesions on the chest and the fever disappeared soon after being treated for malaria and he was sent home in good condition. Although he did not look clinically a typhoid case, he was given chloramphenicol for 14 days, upon discharge, on the basis of the high titre.

DISCUSSION

Urticaria is a common disease of unknown incidence in the general population. The aetiologic causes of urticaria are many and varied. The study of Habte-Gabr, Tiruneh and Hailu (5) of the Gondar prison-mates showed a high incidence of urticaria due to intestinal parasites. Malaria as a causative agent of urticaria has been mentioned by Ormsby and Montgomery (3), and Russel *et al* (4). In our hospital malaria cases are seen frequently all the year round with a peak incidence from May to November. Low grade fever and urticaria may be the only presenting symptoms when the patient is seen in the outpatient department.

The first case had two episodes of urticaria associated with chills and fever. The urticaria disappeared with the treatment of the malaria. Strongyloides infestation has been reported to cause urticaria (6). In this patient the strongyloides infection was not treated for two weeks to see if the urticaria is due to the strongyloides.

The second case was also admitted with headache, fever, chills, and an itchy urticaria which again subsided only with the treatment of malaria. This patient had elevated E_O titre 1/160. However, the patient had no other symptoms or signs of acute typhoid fever.

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These two patients demonstrate that malaria may present with low grade fever, chills, and itchy generalized urticaria. Patients who present with the above signs and symptoms in a malaria area should have a blood smear for malaria parasites before embarking on more expensive and time-consuming studies.

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BOOK REVIEWS

Endometrial Cancer. Brush, King and Taylor. Bailliere Tindall.

This is the Proceedings of the Second International Symposium on Cancer of the Endometrium held in London in 1977. It consists of papers presented by 120 clinicians and scientists from Europe and North America giving an authoritative and up-to-date review of the current knowledge of endometrial cancer.

The book opens with a few articles on the epidemiology of the disease. Then follows a detailed discussion on the thorny subject of relationship between long-term oestrogen replacement therapy in menopausal women and risk of subsequent development of cancer. The authors leave very little doubt that all such women require regular endometrial biopsies irrespective of whether they have symptoms or not. Adenomatous hyperplasia is to be viewed as pre-cancerous and should be managed accordingly. An innovative aspect of the symposium is the contribution of a lay person, Wendy Cooper, who is a journalist interested in medicine. She reviews the subject of hormone replacement therapy from the patients' point of view which many doctors tend to ignore.

The book also goes on to cover various aspects of diagnosis and treatment of endometrial cancer, such as methods of outpatient diagnostic endometrial biopsy, the value of surgery, radiotherapy, and the recently introduced progesterone therapy. The last section of the book is devoted to cell biology and how presence or absence of oetrogen and progesterone receptors in the cells influence the response to hormone therapy.

The book will appeal to those interested in epidemiology and pathology of endometrial cancer, as well as the clinician faced with the difficult question as to whether to prescribe replacement hormone therapy to menopausal women. To the research scientist the book will form a good source of bibliography.

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MALARIA IN GONDAR, ETHIOPIA, 1975-1978: A REVIEW OF 435 CASES WITH SPECIAL EMPHASIS ON CEREBRAL MALARIA

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ABSTRACT. *A total of 435 cases of malaria, admitted consecutively over a four-year period (January, 1975 to December, 1978) were studied. The overall incidence of malaria was 5.2%. There were 52 cases of cerebral malaria of which 14 (26.9%) died. Only 7.7% of these cases had a classical malaria picture, while 25% had no fever at the time when the malaria parasite was demonstrated in the peripheral blood film. As a result of the varied clinical presentations of the disease, 44.2% of the cerebral malaria cases were misdiagnosed on admission. The treatment of cerebral malaria requires meticulous care. In this series intramuscular chloroquine was used in over 80% of the cases initially, followed by oral chloroquine. The preferred route for initial administration of this drug, however, is the intravenous route. Hydrocortisone was used in only four cases. But dexamethasone is the steroid of choice and should be administered routinely in the treatment of cerebral malaria. The administration of fluid and electrolyte should be individualized and must be rigidly controlled. Finally, since the presentation of malaria is at times misleading, as was seen in this study and in other reports, we suggest that a blood film for malaria must be a routine procedure, particularly in those patients who have come from a malarial area.*

Malaria is a major cause, world-wide, of morbidity and mortality in all age groups (1,2,3). Chang (4) ranked it among the 12 most frequent communicable diseases in Ethiopia, and Wang (5) reported it the ninth cause of admission among 20 common diseases there. Analysis of medical admissions to Gondar Public Health College Hospital by Molineaux *et al.* (6) showed that malaria plus splenomegaly (probably due to the disease) accounted for 3.6% of total admissions; Habte Gabr *et al.* (7) reported that malaria was the thirteenth most frequent cause of admission; in 1978 Zein (8) ranked malaria and other febrile diseases of lesser frequency seventh in the most frequent diseases seen in the out-patient department.

During the 1958-1959 malaria epidemic in Ethiopia, 3 million people suffered from the disease; 150,000 (5%) died, and many others subsequently fell victim to starvation and economic disaster (9). In the epidemic of 1964 in Begemidir and Semien province (now Gondar Administrative Region), 100,000 people developed malaria, of whom between 5,000 and 7,000 (5% to 7%) died (10).

This paper reports on malaria admission to the Public Health College Teaching Hospital, Gondar, in general, and on cerebral malaria in particular.

MATERIALS AND METHODS

The records of all cases admitted for malaria from January 1975 to December 1978 were examined. Out of a total of 518 cases, 435 with positive blood films were analyzed in detail. There were 52 cases with cerebral malaria; these were analyzed according to age, sex, clinical picture, treatment and outcome. The criteria for cerebral malaria, besides a positive blood smear, were impaired consciousness

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convulsion or coma. There was only one algid malaria case. There was no record of the parasite density count.

During the period studied, there were two health officers and a general practitioner (M.D.) working in the out-patient department. A paediatrician, an internist and a general practitioner cared for paediatric and medical in-patients. There was no change in the clinical laboratory staff.

RESULTS AND ANALYSIS

Incidence. Table 1 shows the annual admission of cerebral and non-cerebral malaria cases. About 2,651 paediatric and 5,643 medical patients were admitted during the four-year period, a total of 8,294. The overall incidence of malaria was 5.2%, and among those cases the incidence of cerebral malaria was 12.0%. The incidence of cerebral malaria in males and females was 8.0% and 25.8% respectively. The incidence in age groups 0 to 14 years and 45 or above was 23.2% and 36.4% respectively. Thus, in this study, cerebral malaria was more commonly seen in the extremes of age and among the female population, even though 44.2% of cases were in the age group 15 to 29 years. The reason for this preponderance is not clear.

Only *Plasmodium falciparum* and *P. vivax* were found, in the ratio of 4.6 : 1.0. It has been observed in Ethiopia that *P. falciparum*, *P. vivax* and *P. malariae* are seen in that order of frequency, while *P. ovale* is rarely reported (4).

TABLE 1. Yearly malaria admissions to Gondar Public Health College Hospital

YEAR	NON-CEREBRAL MALARIA		CEREBRAL MALARIA		TOTAL
	FALCIPARUM	VIVAX	FALCIPARUM	VIVAX	
1975	3	6	0	0	9
1976	46	7	17	1	71
1977	65	6	6	0	77
1978	194	56	27	1	278
TOTAL	308	75	50	2	435

Age and Sex. Age and sex are given in Table 2. Ages ranged between 5 months and 62 years (mean age 17.2 years). The male to female ratio was 3.5 :1

TABLE 2. Age and sex distribution of 435 malaria cases.

AGE (YEARS)	NON-CEREBRA MALARIAL		CEREBRAL MALARIA		TOTAL	% CEREBRA MALARIA
	MALE	FEMALE	MALE	FEMALE		
0 - 14	25	18	3	10	56	23.2
15 - 29	217	38	13	10	278	8.3
30 - 44	55	16	4	4	79	10.1
45 +	14	0	7	1	22	36.4
TOTAL	311	72	27	25	435	12.0

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Address. The locality from which patients came is shown in Table 3. About 93% of the total cases came from Chilga, Gondar and Wogera *Awrajas*. About 60% of the cases came from Metema (Chilga *Awraja*) and Setit-Humera (Wogera *Awraja*), which are well-known malarial areas.

TABLE 3. Address of 435 malaria cases

PLACE	ALTITUDE (METRES)	NON-CEREBRAL MALARIA	CEREBRAL MALARIA	TOTAL	% TOTAL
CHILGA *AWRAJA*					
METEMA	600	101	7	108	24.8
SERABA	2320	6	1	7	1.6
GONDAR *AWRAJA*					
GONDAR TOWN	2100	45	7	52	12.0
GONDAR *ZURIA*	> 2000	45	21	66	15.2
DEMBIA	1720	12	6	18	4.1
WOGERA *AWRAJA*					
SETIT HUMERA	650	143	8	151	34.7
DABAT	2500	2	0	2	0.5
SEMIEN *AWRAJA*					
ADI ARKAI	1460	21	1	22	5.1
DEBARK	2620	7	1	8	1.8
GAINT *AWRAJA*	2500	1	0	1	0.2
TOTAL		383	52	435	100.0

TABLE 4. Presenting symptoms and signs in 52 cases of cerebral malaria.

FEATURE	NUMBER	% TOTAL
*SYMPTOMS		
HEADACHE	20	43.5
CHILLS	15	32.6
VOMITING	14	30.4
ANOREXIA	14	30.4
ABDOMINAL PAIN	10	21.7
NO FEVER	8	17.4
COUGH	6	13.0
SWEATING	5	10.8
DIARRHOEA	4	8.7
BACKACHE	3	6.5
CONSTIPATION	2	4.3
URINARY INCONTINENCE	1	2.2
SIGNS		
FEVER	39	75.0
IMPAIRED CONSCIOUSNESS	36	69.2
**HYPOTENSION	25	59.5
SPLENOMEGALY	17	32.7
COMA	14	27.0
JAUNDICE	13	25.0
MENINGISMUS	7	13.5
ABDOMINAL TENDERNESS	7	13.5
HEPATOMEGALY	6	11.5
CONVULSION	6	11.5
RESPIRATORY DISTRESS	3	5.8

*AVAILABLE ONLY IN 46 CASES.
**BLOOD PRESSURE WAS RECORDED IN 42 CASES.

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Signs and Symptoms. Table 4 shows the signs and symptoms in 52 cases of cerebral malaria. Only 7.7% presented the classical picture as defined by O'holohan (11). There were 9 cases (17.3%) with fever and chills, and 4 cases (7.7%) with sweating and/or rigor and fever. It is noteworthy that the diagnosis of malaria was clinically suspected only in 55.8% of cerebral malaria cases on admission. The rest (44.2%) were suspected of having hepatitis, 7; pneumonia, 4; typhus, 3; acute gastritis, 2; meningitis, 2; peptic ulcer crisis, 1; epilepsy, 1; relapsing fever, 1; pyelonephritis, 1; and anaemia, 1. There was a child with cerebral malaria clinically indistinguishable from tetanus. The haematocrit was recorded in 46 cases; it ranged between 10% and 53% (mean 24.1%). The peripheral blood film was positive for *Plasmodium falciparum* in 50 cerebral malaria cases (96.2%). Two cases were due to *P. vivax*; both were in a state of coma.

Treatment and Outcome. Over 80% of the cerebral malaria cases were initially given chloroquine, 5 to 10 mg per kgm per dose, intramuscular (IM), and later nearly all took the drug orally to complete the course. A 3-day course of hydrocortisone, in a dosage of 100 mg, intravenous (IV), 6-hourly, was given to 4 patients with cerebral malaria. Phenobarbital, 2 to 3 mg per kgm per day, was used for 5 children who had convulsions, while the only adult case who presented as epilepsy received phenobarbital, 100 mg IM every 8 hours, and valium, 10 mg IV, as need arose. There were 3 cases with hypostatic pneumonia, and one case of urinary tract infection; these received respectively procaine penicillin, 800,000 International Units IM every 12 hours, and chloramphenicol, 500 mg orally every 6 hours. All patients with anaemia were given oral iron. Intravenous fluid — dextrose in water or saline 1000 ml to 2500 ml — was given daily.

The non-cerebral malaria patients were treated with oral chloroquine. In addition, cases with either the simple or cerebral forms of malaria with the gametocyte of *P. falciparum* or *P. vivax* infection received a full course of primaquine.

There was no death from the uncomplicated type of malaria. The only patient with algid malaria died, in spite of conventional treatment. Out of 52 cerebral malaria patients, 14 died, giving a mortality rate of 26.9%; of these, 9 (17.3%) were females, and 5 (9.6%) were males. Over 85% of the deaths occurred in the age group below 29 years, but there was none above the age of 45 years. In the 0 to 14 age group, there were 5 deaths out of 13 cases. There were 7 cases below the age of 5 years, of whom 3 died. Of the total deaths, 50% occurred in the age group 15 to 29 years. Over 78% of deaths occurred within the first 24 hours of admission. The illness of 7 who died was misdiagnosed at the time of admission.

DISCUSSION

The yearly malaria admission in Gondar Public Health Teaching Hospital has progressively increased (Table 1). Even though this does not reflect the true incidence of malaria in the community, it nevertheless gives an idea of the seriousness of the problem. One reason for the increas in the number of malaria cases is the interruption of the control programme in the region in the last three years (personal communication, Regional Office for Malaria Control).

About 12% of the total malaria cases, including infants and children, came from Gondar town itself, which has an altitude of about 2100 metres; most of these cases had never been out of the town. There were also cases from other areas where the altitude is over 2000 metres (Table 3), but for whom a history of travel to a malarial area was not documented. Malaria transmission above 2000 metres was also reported by Kebere Demissie (unpublished data).

The clinical picture of malaria nowadays is rather misleading. In O'holohan's series

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(11), only 16% had a classical presentation; 49% of cases in the series had no fever. Ramachandran and Peresa (12) also commented that the clinical presentation did not conform to the classical malaria syndrome. In this report, only 7.7% of cerebral malaria cases presented with classical malaria (11), while 25% had no fever at the time when the malaria parasite was demonstrated in the blood film. The two cerebral malaria cases in Illangasekera and De Sylva's report (13) had no fever on admission.

As a result of the varied clinical presentation, cases with malaria are being misdiagnosed. In an autopsy study, the cause of about 57% of deaths in children in Nigeria was misdiagnosed in life (14). About 44% (23 cases) of our cerebral malaria cases were misdiagnosed at the time of admission because of the atypical clinical picture (Table 4). The diagnosis of malaria in these cases was established from 4 to 35 hours (average 8 hours) after admission. It is evident that a prerequisite of the early diagnosis of malaria is an awareness of its possible existence, and a peripheral smear must be taken immediately; the importance of early diagnosis has been stressed by other authors (15, 16, 17).

The treatment of cerebral malaria requires meticulous care. In our series, chloroquine, intramuscular, was used initially, and oral chloroquine was given once the disease had been brought under control. Diop Mar *et al.* (18) used intravenous quinine or chloroquine in combination with sulphadoxine and pyrimethamine. The intravenous route is preferred to the oral or intramuscular route because of poor absorption from the small bowel and slow absorption from the muscles, due to peripheral vascular collapse (19). The use of dexamethasone in the prevention or treatment of malaria complications has been emphasised by several authors (13, 20—24). Four of our cerebral malaria cases were given hydrocortisone, and they were cured. The administration of fluid and electrolyte should be rigidly maintained, even although oedema can develop independently of fluid or electrolyte imbalance or both (23). Sitprija (25) suggests that 3000 ml of fluid daily can be given safely with a small dose of frusemide administered intravenously at intervals. In this series, 1000 ml to 2500 ml of intravenous fluid was used over 24 hours, and no frusemide was administered.

Of the cerebral malaria cases, 14 (26.9%) died. A similar result was reported by Diop Mar *et al.* (18) and Lafaix *et al.* (26). In the age group 0 to 14 years, 38.6% of our cases died, as compared to 21.6% in Rothe's report (27).

The degree of parasitaemia in the prognosis of the disease is well documented (28). However, there was no record of parasite density count in our series. The two cerebral malaria cases due to *P. vivax* were cured. There have been reports of cerebral malaria due to *vivax* by other authors also (29—32).

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CHRONIC RENAL FAILURE IN ETHIOPIANS

Berhanu Habte, *MD and Bayu Teklu, **MD

ABSTRACT. *The clinical picture of chronic renal failure in 45 Ethiopians (33 males and 12 females, with an average age of 42.2 years) admitted to Black Lion Hospital, Addis Ababa, is described. Chronic glomerulonephritis was the commonest cause (53%), followed by diabetic nephropathy (11%) and chronic pyelonephritis (7%). Uraemic pericarditis, uraemic coma, and hiccough each independently carried a poor prognosis, none of them was related to the level of blood urea nitrogen. We were impressed by the finding of two secondary amyloid kidneys, proven at autopsy, as further causes of chronic renal failure. The hospital mortality was 67%.*

Future prospective studies, using kidney biopsies, can more clearly elucidate the aetiology of chronic renal failure in Ethiopians, and add further details to the clinical picture.

INTRODUCTION

Analysis of hospital admissions from various parts of Ethiopia show that chronic renal diseases comprise from 1.2% to 2.8% of all medical admissions (1,2,3). In other parts of Africa - Nairobi, Coast Province in Kenya, Ibadan and Kampala - the figure is 0.8% to 4.1% (4-7). However, from 7% to 8% of all medical deaths in hospitals are due to chronic renal disease (3,4,6), thus shown to be an important cause of morbidity and mortality, even in Africa, where infectious diseases predominate.

Renal dialysis and transplants have improved the prognosis (8, 9). But in developing countries like Ethiopia, these facilities are lacking, even blood chemistry tests are not performed in the majority of hospitals, and the disease therefore progresses relentlessly. Since there is a lack of documentation of chronic renal failure in Ethiopians, we set out to describe the clinical picture.

MATERIALS AND METHODS

All patients with chronic renal failure admitted to the medical wards of Black Lion Hospital, Addis Ababa, from December 1975 to July 1979 were studied. Much of the study was a retrospective review of clinical charts, but patients admitted from the latter part of 1978 to July 1979 were observed prospectively.

The criteria for inclusion in the study were elevated blood urea nitrogen (BUN) (> 20 mg%) and/or creati-

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nine (> 1.5 mg%) not secondary to acute renal or extrarenal diseases, and some of the clinical symptoms and signs (Tables 1 and 2). There were 55 clinical charts with the final diagnosis of chronic renal failure or chronic renal disease, but 10 were not analysable, because of either very incomplete work-up or untenable diagnosis. All available information with regard to history, physical examination and laboratory data was carefully extracted, and only signs and symptoms expressed either negatively or positively were included in the study.

TABLE 1. Symptoms of chronic renal failure on admission

Symptom	No. of patients questioned	No. positive (percentage in parentheses)
Loss of appetite	35	34 (97)
Weakness	39	37 (95)
Nausea	44	31 (70)
Vomiting	42	28 (67)
Decreased urine output	29	19 (66)
Dizziness	37	24 (65)
Dyspnoea	41	22 (54)
Leg oedema	42	20 (48)
Facial swelling	38	17 (45)
Flank pain	36	15 (42)
Abdominal swelling	42	13 (31)
Dysuria	26	7 (27)
Epistaxis	40	5 (13)
Haematuria	40	3 (8)
Gum bleeding	41	2 (5)

TABLE 2. Physical findings on admission

Physical finding	No. checked	No. positive (percentage in parentheses)
Ophthalmoscopic changes	11	10 (91)
Pallor	45	40 (89)
Chronically ill	40	29 (73)
Hypertension	45	28 (62)
Leg oedema	43	20 (47)
Ascites	42	14 (33)
Acute distress	39	11 (28)
Pericardial friction rub	44	6 (14)
Elevated JVP	42	5 (12)

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RESULTS

From 3,530 patients admitted, 45 (1.3%) - 33 males and 12 females - had well-documented chronic renal failure; there was only one foreigner during the study period. The Ethiopians were from 19 to 79 years of age, with a mean of 42.2 (median age of 40). The average age of the males was 44.2 (median age 47), and of the females 36.8 years (median age 40).

Renal disease had been diagnosed in 25 of the 45 patients from 8 months to 25 years prior to their last hospitalizations (on average, 5.4 years). Hypertension had been present in 14 patients for from 5 months to 8 years (average 3.2 years). Five patients had had diabetes mellitus for from 8 to 15 years (average 11.5 years). Of 11 patients with ophthalmoscopic records, 10 had arterial narrowing, exudates and haemorrages; 2 of these 10 had diabetes mellitus. (Symptoms and signs on admission are shown in Tables 1 and 2 respectively.)

The admission laboratory results are shown in Table 3. Urine cultures grew *Escherichia coli* in 2 patients, *Klebsiella* and *E. coli* in a third patient on 2 different occasions, and *Klebsiella* alone in a fourth patient on 3 different occasions. Colony counts were 10^5 or greater per cubic millilitre in all cases.

Ninety-six per cent had a haemoglobin of less than 12 gm%. The lowest haemoglobin was 2.8 gm%, and the highest 16.1 gm%; both of these cases had chronic glomerulonephritis. The patient with 2.8 gm% gave no evidence of bleeding or jaundice.

Thirty-one patients had serum creatine of from 2.5 mg% to 23 mg%. Serum sodium and potassium were determined in 23 patients. One had a serum sodium of 118 meq/L, 2 had serum potassium of 2.7 meq/L and 3.2 meq/L respectively, and 4 had serum potassium above 5 meq/L. Serum calcium was determined in 13 patients, with values ranging between 4.6 mg% and 10.1 mg% (average 7.2 mg%); in 11 of these 13, the serum calcium was less than 9 mg%. Most of the electrolytes were determined only once during hospitalization.

TABLE 3. Laboratory findings on admission

Laboratory test	No. tested	No. positive (percentage in parentheses)
Urine		
SG≥1010	16	5 (31)
Proteinuria	45	40 (89)
RBC (>5/HPF)	36	22 (61)
WBC (>10/HPF)	35	23 (66)
Granular cast	36	20 (56)
Hyaline cast	36	3 (8)
RBC cast	36	2 (6)
Blood and ESR		
Haemoglobin (<12 gm%)	45	43 (96)
ESR mm/hr.		
0-20	38	4 (11)
21-75	38	14 (37)
76-100	38	8 (21)
101 and above	38	12 (32)
Blood chemistry		
BUN, mg%		
20-50	45	4 (9)
51-100	45	18 (40)
101 and above	45	23 (51)
Creatinine, mg%		
2-5	31	12 (39)
6 and above	31	19 (61)
Uric acid, mg%		
>7	8	7 (88)
Serum Na (≤125 meq/L)	23	1 (4)
Serum K (<3.5 meq/L)	23	2 (9)
Serum K (>6 meq/L)	23	4 (17)
Serum Ca (<9 mg%)	13	11 (85)

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Chest X-ray was normal in 12 patients, 5 had cardiomegaly, and 10 had either pulmonary congestion or effusion. Three patients had hilar adenopathy. The intravenous pyelogram (IVP) was normal in 1, non-functional in 6, and 2 had bilaterally contracted kidneys. No bone changes were described in any of the X-rays.

Table 4 shows the salient symptoms and signs that developed during hospitalization. The hospital stay before discharge or death varied from 3 to 60 days, with an average of 22 days. Eleven patients stayed 10 or fewer days; all of these died.

TABLE 4. Important signs and symptoms developed during hospitalization

Symptoms and signs	No. checked	No. positive (percentage in parentheses)
Mental changes	38	27 (71)
Kussmaul breathing	40	27 (68)
Haematemesis	39	9 (23)
Uraemic frost	41	9 (22)
Twitching/seizures	34	6 (18)
Pericarditis	43	8 (19)
Oropharyngeal bleeding	39	7 (18)
Hiccough	37	6 (16)
Asterixis	38	5 (13)

Pericarditis, detected by pericardial friction rub, developed in 8 patients after hospitalization; thus there was a total of 14 with uraemic pericarditis, of whom only 3 were females. Nine had chronic glomurelonephritis; 2 amyloid kidneys (autopsy-proven); 1 chronic pyelonephritis; 1 diabetes mellitus; and 1 systemic lupus erythematosus. Although the average age of these patients was 36 years, 9 were 35 years old or younger. Of these 14, 5 had dyspnoea and chest pain, and 2 others developed hypotension. None had cardiac tamponade. Only 1 of the 14 had electrocardiographic (ECG) changes consistent with pericarditis.

The 8 that developed pericarditis after admission died from 1 to 25 days after clinical detection of pericarditis; the average survival was 10 days. The 6 who had pericardial friction rub on admission died within from 3 to 24 days, with an average of 9 days.

Of the 45 chronic renal failure patients, 30 died in hospital, of whom 23 were males. Ten were relatively stable at time of discharge; 5 (3 males and 2 females) were discharged against medical advice in critical condition.

All but 2 of the 30 patients who died developed mental changes that progressed to deep coma before death. In 19 of these 28 patients, records

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were available on the duration of coma: between 3 hours and 17 days, with an average of 3.3 days before death.

Three patients were tested for BUN on the day of death, with values of 56, 132 and 208 mg%; the day before death, 3 had values of 68, 90 and 119 mg%; 2 days before death, BUN was determined in 4, with values of 42, 93, 109 and 170 mg%; in 2 patients, 3 days before death, BUN was 160 and 185 mg%. The mean BUN measured 0-3 days before death in these 12 patients was 120 mg%.

Six patients developed hiccough terminally; they had BUN of 68 to 118 mg%.

The final diagnoses obtained from discharge summaries are shown in Table 5. There were 2 patients with systemic lupus erythematosus, clinically diagnosed from positive lupus erythematosus cells. The periarteritis nodosa patient was a 32-year-old man, who had proteinuria for 5 years with a persistent eosinophilia (14% - 25%), without evidence of allergy or intestinal parasites.

Only 1 successful needle biopsy was made *post mortem*, revealing membranous glomerulonephritis. Two autopsies were performed; both patients had extensive renal amyloidosis. The first was a 32-year-old man with tuberculosis of the thoracic vertebrae and draining sinuses in the thigh, and the second was a 19-year-old man who had Hodgkin's lymphoma with lung involvement. These 2 patients had between 2+ to 3+ proteinuria and pyuria; the ESR was 115 and 155 mm/hr, and the BUN was 60 and 65 mg%, respectively. Both developed pericarditis terminally.

TABLE 5. Final clinical diagnosis in 45 patients with chronic renal failure

Final diagnosis	Number of patients (percentage in parentheses)
1. Chronic glomerulonyphritis	24 (53.3. . .)
2. Diabetic kidney disease	5 (11.1. . .)
3. Chronic pyelonephritis	3 (6.6. . .)
4. Systemic lupus nephritis	2 (4.4. . .)
5. Secondary kidney amyloid	2 (4.4. . .)
6. Periarteritis nodosa	1 (2.2. . .)
7. Renal tuberculosis	1 (2.2. . .)
8. No diagnosis	2 (4.4. . .)
9. Miscellaneous (benign prostatic hypertrophy, renal stones, etc.)	5 (11.1. . .)
Total	45 (100)

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DISCUSSION

The clinical picture of chronic renal failure in our study was similar to others described previously (8,9,10). However, though reported in almost 100% of cases by others, hypertension was present in only 69% of our patients, and was mild to moderate, with diastolic pressure of 140 mmHg in only 2 patients on a few occasions.

Our patients with uraemic pericarditis presented a clinical picture almost identical with those reported by Wackner and Merrill (11). In contrast to our experience, others reported cardiac tamponade, and advised that the electrocardiogram was very helpful in diagnosing pericarditis (12,13,14).

The commonest cause of chronic renal failure in our series, as well as in others, was chronic glomerulonephritis (8,9,10, 15). Of interest was that the 3 commonest causes in Nigerian patients (15) were identical with ours.

Although large series on diabetes in Ethiopians (16,17) have reported that it was about twice as common in males as in females, only 1 of our 5 patients with diabetic kidney failure was a female. Two per cent of 94 diabetic patients reported from Gondar had chronic renal diseases, but none of the 9 deaths in that series was from chronic renal failure (17). In contrast, 10 of 404 patients (2.4%) from Addis Ababa died of chronic renal failure, and nephropathy was reported in 17% of 358 patients (16). Our diabetics developed chronic renal failure, and died after an average of 11.5 years. On the other hand, reports from USA indicated that diabetes was present in adults 15.9±1 years before diabetic nephropathy required dialysis (18), suggesting more severe diabetes or less well controlled diabetes in Ethiopians.

The male-to-female ratio of 3:1 in our patients was also difficult to explain, for the medical beds were almost equally divided between the sexes. Several of our patients presented with features of chronic renal failure for the first time, and had a rapidly fatal course: 11 died within 10 days of admission. This might be the result of our patients' lack of awareness of the early non-specific symptoms of renal failure.

All 14 patients who developed pericarditis and all 6 who had hiccough died, and this had no correlation with the degree of uraemia, anaemia or electrolyte imbalance. Thus, pericarditis, hiccough and coma each independently carried a very poor prognosis in our patients.

This paper has attempted to present some of the clinical features of chronic renal failure in 45 Ethiopians. There are still pertinent questions left unanswered, however, because of the inherent defect of all such retrospective studies. Future prospective studies of chronic renal failure with accurate recording of the clinical picture, laboratory studies and needle renal biopsies are therefore desirable.

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CASE REPORT

RHINOCEREBRAL MUCORMYCOSIS IN ASSOCIATION WITH DIABETES MELLITUS

Mallede Maru,* MD, Mulugetta Mengistu,** MD and Bitew Bayuh*

ABSTRACT. *A patient with rhinocerebral mucormycosis associated with poorly controlled diabetes mellitus is reported. The high invasiveness of the saprophytic phycomycetes in patients with diabetes, ketoacidosis and other diseases that compromise the host resistance is discussed. Our patient died soon after the diagnosis was established, without receiving any antifungal drug. The drug of choice for mucormycosis is amphotericin B. The prognosis of patients with mucormycosis is dependent on the early identification of the fungus, with prompt and appropriate therapy to the organ involved.*

Mucormycosis (phycomycosis) is a disease caused by saprophytic fungi in a compromised host. It is the most rapidly progressive, fulminant fungal disease known (1). The fungi of the genera *Mucor, Rhizopus* and *Absidia* belong to the class phycomycetes, and are characterized in tissue sections by broad, aseptate, branching hyphae, 6 to 50 microns in width (2). They are usually found in decaying vegetation, fruits high in sugar content, soil and manure, and are frequently contaminants in cultures of human body orifices. The fungi may become invasive in patients with certain underlying diseases. Diabetes mellitus with ketoacidosis is the most frequent of such underlying conditions, and is most often associated with the rhinocerebral form (3,4). Other predisposing factors include uraemia, diarrhoea with acidosis, leukaemia, malnutrition, antimetabolites, antibiotic therapy, steroids, severe burns and other conditions well-known to impair the body's defences (5). The following is a report of a case of rhinocerebral mucormycosis in an alcoholic diabetes mellitus patient who was admitted to the Gondar Public Health College Hospital.

CASE REPORT

T.G.M. (Hospital No. 32131), a 43-year-old male Ethiopian, was a known alcoholic and diabetic patient for several years. He was readmitted to the hospital on 2 June 1978 for the third time, with severe rheumatic pain and stiffness of both legs, swelling of the right side of the face, headache, and fever of 5 days' duration. His diabetes had been controlled for about 4 years on protamine zinc insulin, 40 units daily. However, prior to this admission the patient had been on glibenclamide (Daonil), 5mg by mouth daily, and apparently his dia-

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betes was then , poorly controlled. On examination, he was emaciated and had a non-pitting swelling of the right side of the face, including the orbit. His blood pressure was 130-70 mmHg, pulse 120-min., regular, respiration 24-min. and temperature 37.5° (axillary). The pupils were equal and reactive to light. The ears, nose and oral cavity were normal. The neck was supple. There were crepitations in both lung bases. The rest of the examination was unremarkable.

The abnormal laboratory findings were urine sugar 4+, acetone trace, and a sputum examination showing gram positive diplococci and streptococci. The spot blood sugar on admission was 500mg%. The patient was then given insulin on sliding scale, and antibiotic.

On 7 June 1978 the swelling of the right side of the face and of the right orbit markedly increased, with ptosis and swelling of the conjunctiva, which had a dark brownish discharge. The possibility of rhinocerebral phycomycosis was considered, but microscopic study of the conjunctival scraping for fungus was negative. On 9 June the patient also developed severe headache, with weakness of the right side of the face, and right ophthalmoplegia. Soon afterwards he lapsed into coma, possibily because of the spread of fungal infection into the cavernous sinuses and the brain, for a repeat conjunctival scraping in potassium hydroxide solution revealed a large number of fungi with the characteristic broad, branching, aseptate hyphae which are typical of phycomycetes. The patient died during the night of that same day, without getting any specific antifungal drug. The fungal culture that grew after the death of the patient was also typical of phycomycetes.

This is the first reported case of phycomycosis from Ethiopia. Our patient illustrates that uncontrolled diabetes mellitus is closely linked with invasiveness of phycomycetes, especially of the rhinocerebral form. For an early diagnosis of the disease, a high degree of suspicion and a prompt search for the causative agent from appropriate scrapings and biopsies are essential. Patients who present with dull, steady, localized facial or orbital pain, lid drop, localized anaesthesia about the eye, dark bloody nasal discharge of brief duration on the side of the pain, ptosis of the eyes with limitation of motion, loss of vision, grey-black appearance of nasal turbinates, septum or roof of mouth, and lethargy progressing to coma should be highly suspected for rhinocerebral phycomycosis, and appropriate investigations should be made.

In our case the diagnosis was suspected on the patient's fifth hospital day, from the signs and symptoms that progressively appeared while he was in hospital. However, a definitiv diagnosis was only arrived at after the seventh hospital day, from a second conjunctival scraping in potassium hydroxide solution examined with the light microscope. The culture on Sabouraud medium which became available after the patient's death also confirmed the diagnosis. The characteristic broad, branching, aseptate hyphae that were isolated by culture are shown in Figures 1 and 2.

The prognosis of the patient is determined by the severity of the associated disease and the pattern of organ development. In the rhino-

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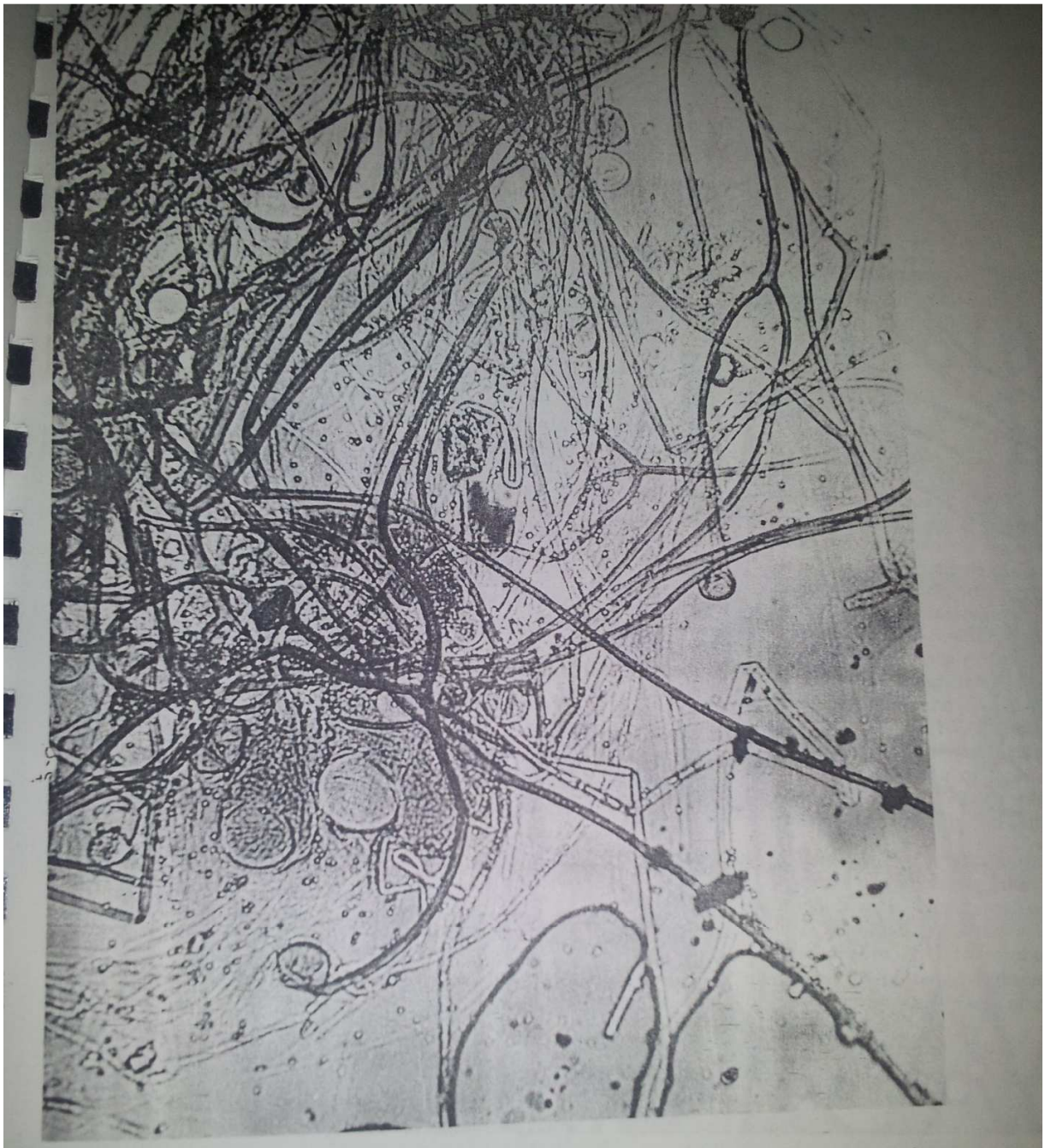


FIGURE 1. *Mucor* sp. (magnification x 250) shows aseptate hyphae forming single or branched sporangiophores arising from hyphae. No rhizoids are present. Sporangia are spherical and have a columella.

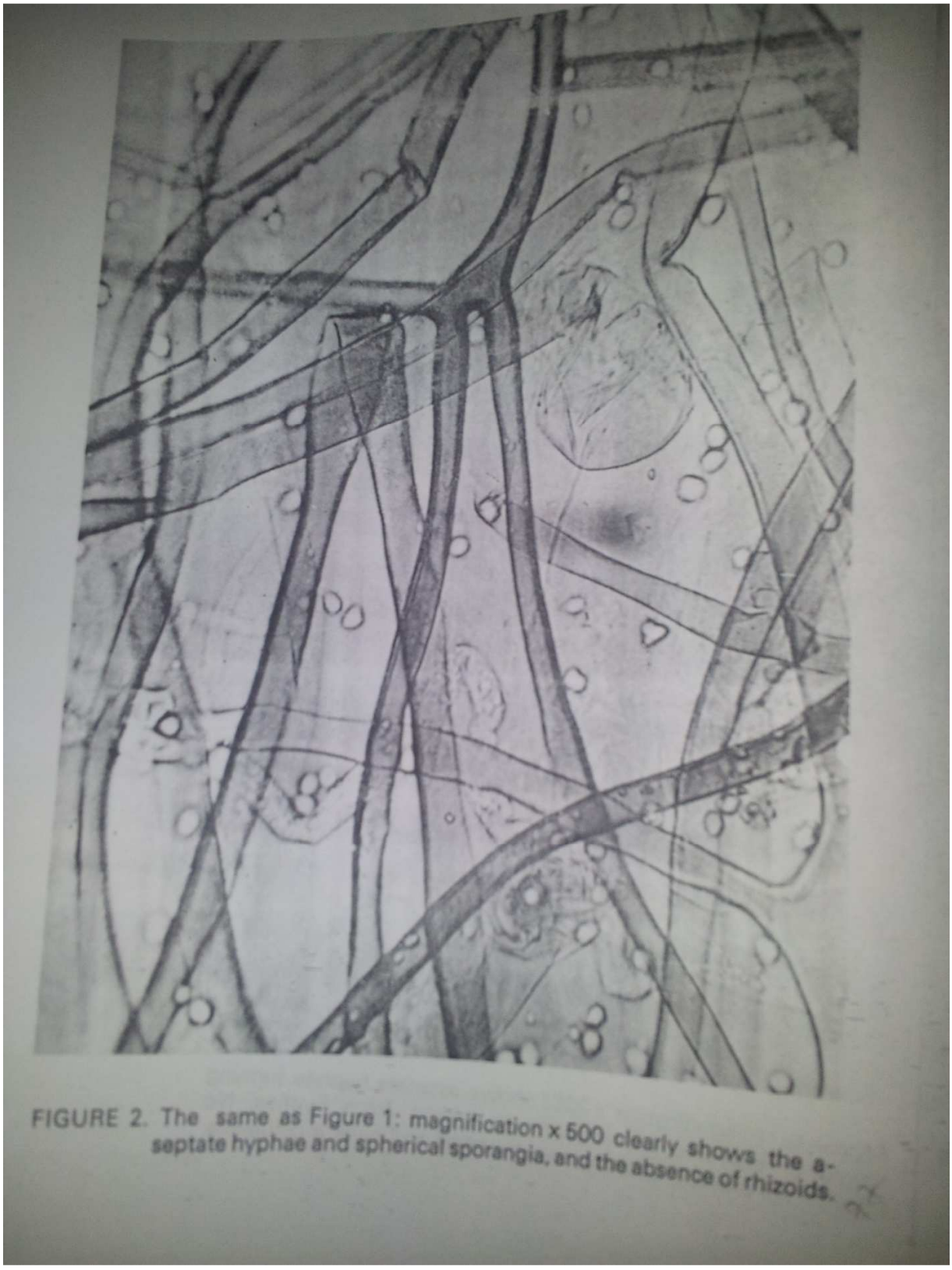


FIGURE 2. The same as Figure 1: magnification x 500 clearly shows the a-septate hyphae and spherical sporangia, and the absence of rhizoids.

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INVESTIGATIONS INTO THE CONTROL OF SCHISTOSOMIASIS AT THE HVA WONJI-SHOA SUGAR ESTATES IN ETHIOPIA

2. Interim evaluation of the project

Redda Teklehaimanot, MD[1] and Peter H Goll, MSc.[2]

ABSTRACT: *An account is given of the attempt to control transmission of* Schistosoma mansoni *by the use of molluscicides on a sugar estate in Ethiopia. Annual fluctuations of populations of snails* (Biomphalaria pfeifferi) *and their distribution in various habitat types are discussed in relation to application of the molluscicides, N-tritylmorpholine and niclosamide. The use of these products in their respective situations was successful in controlling snail populations, but results of a 10 percent random stool survey of 14 plantation villages indicated that a low level of transmission persists. The most likely modes of transmission are considered and improvements in the application of the control methods are suggested. Clinical aspects of the infection are discussed briefly but there is little evidence of severe symptoms in this locality.*

The background to the project has been described by Duncan and Lemma (1). This paper constitutes an interim evaluation of the control measures adopted during the period until June, 1973, when the HVA Medical Services Department maintained continuous monthly snail surveys on the basis of which molluscicide applications were made covering the entire estate. Routine examination of *Biomphalaria pfeifferi* for infection with *Schistosoma mansoni* was introduced in order to locate possible transmission sites and to discover any seasonal fluctuations of infected snails.

Results of stool surveys will be presented together with some observations of the water contact behaviour of estate residents. Comments will be made on the extent of disability in clinical and social terms caused by the disease.

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MATERIALS AND METHODS

Intermediate snail host surveys: Representative examples of the types of water body to be found on the estates, in main and secondary supply canals, tertiary or field drains, main drains and wadooks (night storage reservoirs) were surveyed monthly and all molluscs recorded according to the methods of Duncan and Lemma (1). Rainfall and temperature data were provided by the Agricultural Services Department of HVA Wonji/Shoa. Water temperature was not recorded until 1973 but for discussion of the influence of this factor before 1973 air temperature was taken as a suitable indication.

Molluscicide applications: During the period under review the timing of the molluscicide treatments was determined by increased abundance of *B. pfeifferi* populations. N-tritylmorpholine (Frescon) as a 16.5 percent weight/volume emulsion concentrate was used at a concentration

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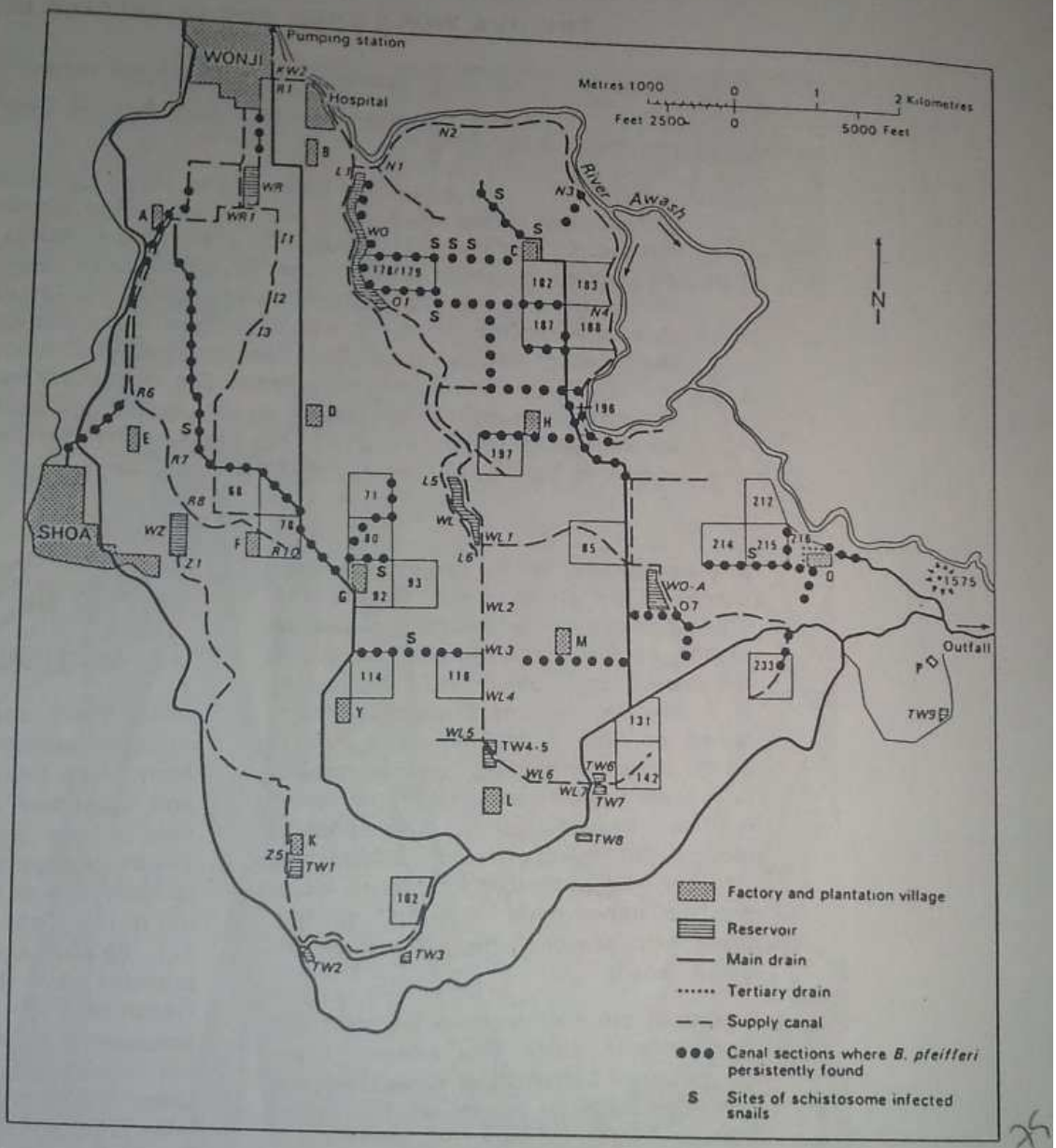


Figure 1. Sketchmap of Wonji-Shoa Sugar Estates indicating water distribution and drainage network; factory and plantation villages; and distribution of *B. pfeifferi* populations.

of 0.025 ppm for 72 hours on two occasions, 20 days apart, while niclosamide (Bayluscide) as a 70 percent wettable powder was used at 0.25 ppm for eight hours.

The use of these molluscicides was initially integrated, the former being used in the main supply and the latter in smaller secondary supplies and the tertiary drainage system. Applications of N-tritylmorpholine were protracted and cumbersome, and often rendered impracticable by irrigation practice, so that by 1972 it was partially replaced by niclosamide applications.

One branch continued to be treated with N-tritylmorpholine from KW2 (figure 1) with a booster dispenser at WR, but on the other branch niclosamide was dispensed from L1 and N1 to avoid dissipation of chemical into wadook WO. Discharges from wadooks, WO, WL, WZ and WR (figure 1) continued to be treated with niclosamide.

Distribution of the chemicals was monitored by analysis of water samples according to the methods of Beynon and Thomas (2) and Strufe (3) for N-tritylmorpholine and niclosamide respectively. Bioassay, using previously collected *B. pfeifferi*, was also carried out.

Cercarial examination: The infection rate of *B. pfeifferi* with *S. mansoni* was assessed from samples collected mostly from field drains at 100 m intervals using a drag scoop. From each drain 200 - 300 specimens were collected. The method of shedding was essentially that of Webbe (4). If schistosome-type cercariae were shed, then snails from the positive samples were exposed individually on the following day in order to determine percent infection rate. This routine was considered to be less time-consuming and less subject to error than the crushing method, although only patent infections were detected.

Population under survey: There are about 3000 permanent and 2000 seasonal labourers who together with dependents comprise a population of about 20,000. They are housed in two large factory villages, one attached to each of the two mills, and 14 smaller plantation villages distributed throughout the estate, designated alphabetically in figure 1.

Stool examination: Until 1970, all stool samples at Wonji Hospital were examined by the direct (unpreserved) film method, where two faecal smears were made on the same slide. One smear was stained with D'Antoni's iodine solution and the other with 2 percent Eosin and both were read by the same technician. The routine diagnostic procedure adopted in 1970 for all stool examinations was Ritchie's formol ether concentration method which had been recommended as the method of choice by Duncan *et al.* (5) and which is more efficient in detecting light infections (6).

The direct smear method was repeated in 1973 in order to allow some comparison with pre-1970 data but the definitive prevalence was the estimate obtained by the concentration method. This 10 percent random survey for *S. mansoni* infection among the plantation villages was considered suitable as an interim evaluation of the efficacy of the first three years of control measures.

RESULTS

Snail populations: The main and secondary supply canals and field drains, which were surveyed regularly are indicated in figure 1. The density fluctuations of *B. pfeifferi* are shown in figure 2, where the monthly data for the supply canals and for the drains have been aggregated in each case and a mean number of snails per sample plotted. Throughout the three years of this report the pattern for field drains was roughly parallel to that for the affluent system. Wadooks and the proximal sectors of their discharge systems were surveyed initially on a regular basis

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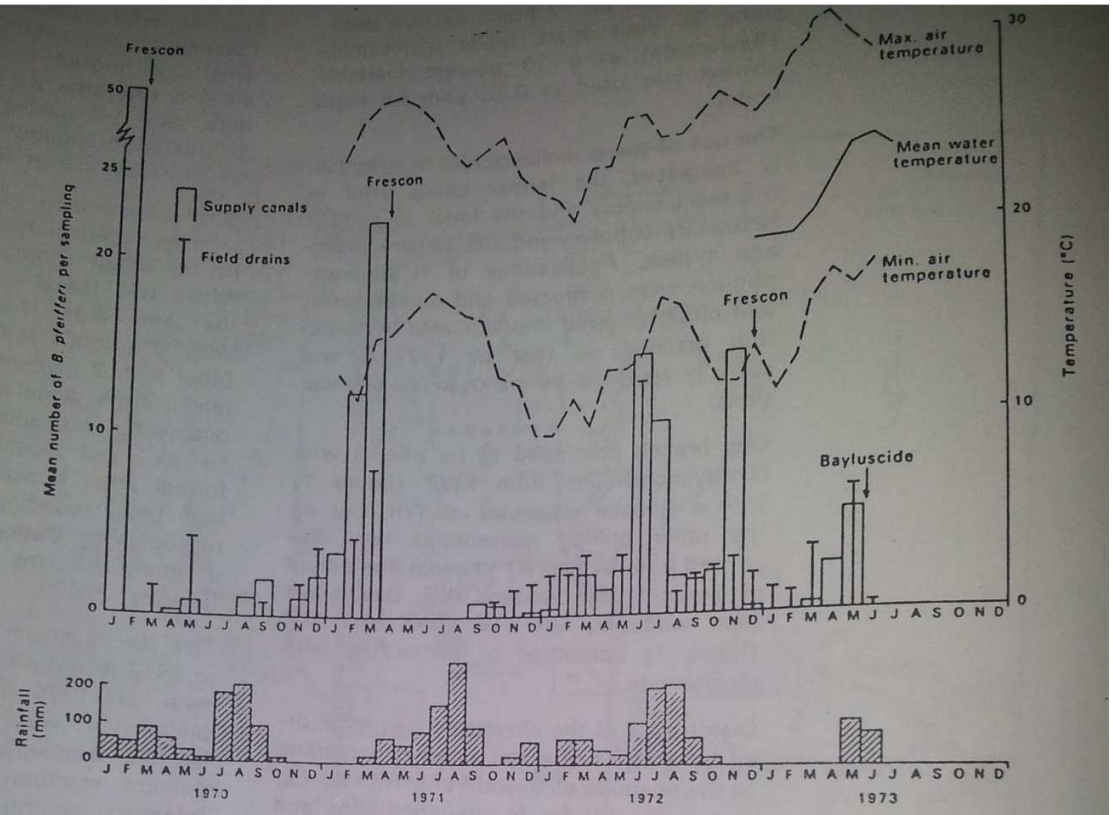


Figure 2. Density fluctuations of *B. pfeifferi* in supply canals and field drains in relation to rainfall and temperature. Molluscicide applications to the supply system are indicated.

but only isolated specimens were found occasionally so sampling was abandoned.

Molluscicide applications: Figure 2 shows that, apart from the increase observed in January 1971 when molluscicide application was unavoidably delayed until March, there was a marked reduction in density of *B. pfeifferi* after each chemical treatment. In general field drains remained free of snails for many months after treatment.

Infection of B. pfeifferi with S. mansoni: Table 1 shows a distinct seasonal fluctuation in the recovery of infected snails. In 1972 no infected snails were found until June, after which time the occurrence and percentage infected increased from 0.5 percent to a peak of about 2 percent for individual drains in mid-September. In 1973, although one isolated infected population was found in January (but none of four mice which were exposed to cercariae derived from it became infected), no infections were found until May, increasing to a peak in November after the period under review. The infection rate per sample varied between 0 - 3 percent and 0.5 - 2 percent for individual drains sampled, these being measures of the intensity and distribution of infection in the irrigation system respectively. All these data were from field drains but infected *B. pfeifferi* were occasionally found in the secondary supply system, R6 — R8, and in the main drain near Camp C, adjacent to field 176.

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TABLE 1: Examination of *B. pfeifferi* for infection with *S. mansoni* in field drains, where the total number of snails is the pooled collection from a variable number of drains sampled over the course of one month.

Date	Total number of snails examined	Number infected	Percentage infection rates for individual drains
1972			
January	Not recorded	0	
February	"	0	0
March	"	0	0
April	1342	0	0
May	2732	0	0
June	3072	1	0.5
July	2740	13	0.5-1.9
August	—	—	—
September	1704	5	0.5-1.1
October	3030	15	0.4-1.0
November	2154	0	0
December	1575	0	0
1973			
January	703	3	0.4
February	429	0	0
March	552	0	0
April	1988	0	0
May	2740	2	0.4
June	772	2	0.5
July	891	0	0
August	1710	12	0.4-1.9
September	1908	3	0.5-1.0

Sampling of field drains was erratic so that no drain could be sampled continuously or for the same months each year, but the combined results from all the drains indicate widespread, intermittent occurrence of infected snails throughout the estates, although they are probably absent at the southern end.

Stool survey of plantation villages:

Sample structure: In order to ensure that the 10 percent random sample of the plantation village survey was representative of the population, and in the absence of a complete official census, a subsidiary survey of three villages was carried out. The age structure of the combined data for males and females is compared with that of the sample in figure 3. It can be seen that, with the exception

TABLE 2: Prevalence of *S. mansoni* infection in a 10 percent random survey of plantation villages in 1973

Plantation village	Total number examined	Percentage positive: Direct smear	Percentage positive: Concentration
A	66	13.6	19.7
B	67	0	6.0
C	79	7.6	12.7
D	76	2.6	13.2
E	105	6.7	17.1
F	93	6.5	32.3
G	77	5.2	16.9
H	70	2.9	15.7
K	85	2.4	10.6
L	112	0.9	7.1
M	127	3.1	15.7
O	69	2.9	5.8
P	18	0	16.7
Y	147	2.0	10.9
MEAN PREVALENCE	—	3.9	14.3

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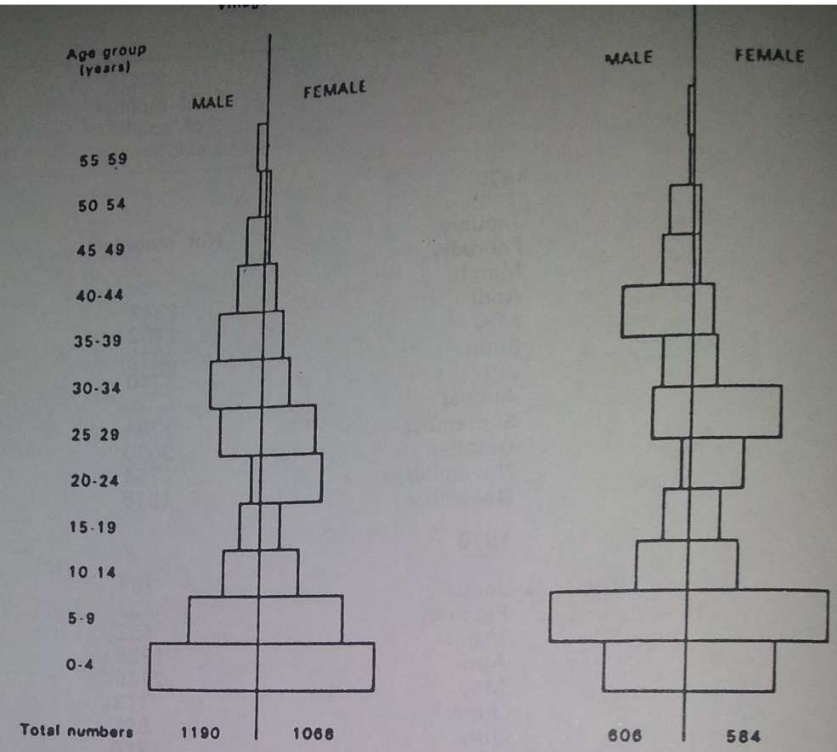


Figure 3. Age frequency pyramids for plantation population and stool survey sample.

of children aged less than four years, there is a very close correspondence between the two.

Stool survey: As shown in Table 2, in 1973 the concentration method gave an overall estimate of prevalence three times that obtained by the direct smear. However, there is no clear indication that the value of 14.3 percent represents a significant increase during those five years.

Table 3 also shows the variation in prevalence between villages, from 5.8 percent in village 0 to 32.3 percent in village F.

The distribution of *S. mansoni* infection in relation to sex was examined. The mean infection rate was 24.5 percent for males and 5.1 percent for females. When viewed according to age (figure 4) there is an apparent bimodal distribution for infected males about the ages of 12 and 29 years, while females show a much smaller single peak at age 12 years.

TABLE 3: Prevalence of *S. mansoni* amongst schoolchildren from both plantation and factory villages

Year	Number examined	Number positive	Percentage prevalence
1971	238	22	9.24
1973	238	31	13.00

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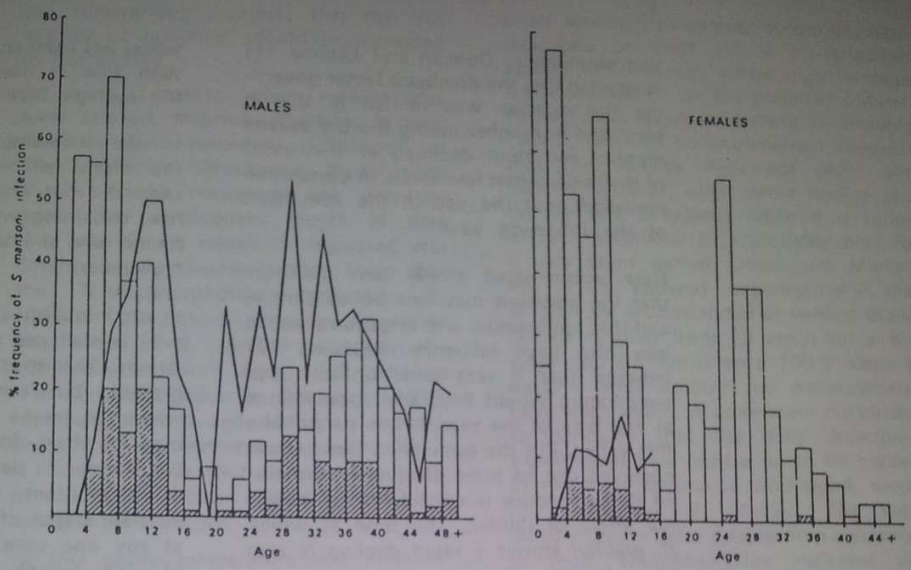


Figure 4. Age distribution and percentage frequency of *S. mansoni* infection in males and females at Wonji-Shoa Sugar Estates in 1973. Open histogram is total number in age group examined; hatched histogram is number positive; solid line is percent infected.

Survey of schoolchildren: In 1971, 238 children (13 - 15 years old) born on the estates and drawn from factory and plantation villages were examined for *S. mansoni* infection. Another group of 238 was examined in 1973 in the same age group, and from Table 3 it can be seen that there was an increase in prevalence of 3.5 percent, although the difference is not statistically significant. In addition, 189 of the 238 examined in 1971 were re-examined in 1973 and it can be seen from Table 4 that there was an increase of infection rate of 6.0 percent.

DISCUSSION

The programme of snail control initiated by Duncan and Lemma (1), and its continuation reviewed here, is essentially a demonstration of the integrated use of well-tested molluscicides in a novel irrigation system in Ethiopia, the results of which, it is hoped, will be of use in future irrigation schemes in the Awash River basin and elsewhere in the country. That population of *B. pfeifferi* in the various ecosystems found on these estates can be controlled by molluscicides is without doubt but the evidence of continued transmission of the infection as shown by the survey of 1973 suggests that a reappraisal of the measures is required.

Snail populations and control by molluscicides: Populations of *B. pfeifferi* vary in abundance with respect to time and habitat type. In Wonji Shoa, temporal fluctuations are the product of both climatic factors and water management practice, while the nature of the irrigation system itself, by provision of a variety of habitats, influences spatial distribution

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and abundance. Duncan and Lemma (1) suggested that the dominant factor governing this species was rainfall in that it increased in number during the dry season months and then declined at the onset of the rains, when low levels of population prevailed until the rise in the early part of the following year.

Data accumulated since then indicates that the situation may not be as simple, and that temperature and irrigation practice may also have influence. Bruijning (7) believed that it was most unlikely that temperature would limit snail populations at any time of the year in this part of the Rift Valley. But the population fluctuations observed can be more adequately explained if temperature is considered to modify the effect of rainfall. The time at which *B. pfeifferi* shows a rapid decline is also when irrigation is stopped and the character of habitats is liable to change.

Thus, in the dry season of October, 1970, to February, 1971, there was a steady rise in populations of *B. pfeifferi* in the supply system which accorded with expectation. Unseasonal rain fell in November and December, 1971, and levels remained very low until an abrupt rise in June, 1972, just at the onset of the rains. They declined in July and by August were down to pre-rain levels. During the following season there was a dramatic rise within one month of the end of the rains, which had not been seen before.

Onset of the rains is usually accompanied by a fall in mean temperature followed by a steady rise through the dry season, December to May, and this was the case in 1970 - 1971 when *B. pfeifferi* populations followed the expected pattern. In 1971 - 1972, a continuous fall in temperatures accompanied the unseasonal rain and they remained low until February and *B. pfeifferi* was apparently suppressed until May. Measurements of daily water temperatures from November to April suggest that they were less than optimal for breeding of this species, which elsewhere has been [illegible] with little or none at 18°C, which was the average here.

In the following season, 1972 - 1973, the slight fall in temperature after the rains did not occur and it continued to rise, remaining well above the optimum; hence the dramatic expansion seen in November.

In an irrigation system, it is not obvious why rainfall *per se* should control populations. The stress of water flow is ever present, but minimal during the rains when the intake is closed. The converse may be true for the drainage system. Field drains in particular represent a series of intermittent habitats which are at different stages of an ecological succession at any one time according to the stage of cane growth of adjacent blocks. The average density of *B. pfeifferi* in seven such drains which were known always to contain the species unless treated revealed a similar pattern to that of the affluent system. Peaks were seen in March, 1971, June, 1972, and May, 1973, corresponding with major peaks in the supply canals. This similarity contrasts with the situation described by Dazo *et al.* (8) in an irrigation system in Egypt, where there was a distinct seasonal difference in the pattern of density fluctuations of *B. truncatus* living in supply canals and those living in drains. The former showed a peak in June and the latter in December. The synchrony seen at Wonji-Shoa emphasises the dominant effect of climatic factors which may be modified by water management practice.

The parallel fluctuations of populations in different parts of the system also suggests that the sampling programme was reasonably efficient. However, since the object was to detect the point at which populations were entering a phase of rapid expansion and so to apply molluscicides, the fact that such sudden increases took place in June and November, 1972, with-

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out forewarning suggests that the frequency of sampling should be increased to fortnightly.

On each occasion when molluscicides were applied, massive reductions in snail numbers were recorded. Distribution of the chemicals throughout those parts of the system concerned was generally good. The subsequent length of time that populations remained depressed was determined by climatic factors. Thus, after the N-tritylmorpholine application in March, 1971, there was no significant population of *B. pfeifferi* present in the supply system until June, 1972, whereas after the application in December, 1972, repopulation occurred within six months, prompting a treatment in June, 1973. It would appear that one treatment per annum of the affluent system is insufficient to maintain control.

In this study temperature and irrigation practice have been observed to cause fluctuations in the populations of snails. Could these fluctuations observed during three years be due to natural variations in response to these factors alone or has the use of chemical induced or contributed to the changes? In 1971 there was no peak observed at the end of the dry season following the use of N-tritylmorpholine in March. In 1972, there was a massive increase in November soon after the resumption of irrigation.

What is the situation in the main drains and wadooks? The former do support *B. pfeifferi*, especially in the upper reaches, but except for the one close to Camp C (figure 1) they do not present an obvious hazard owing to their inaccessibility. Water volume and velocity increase down the course of the drain and daily fluctuations of level discourage colonisation by snails, unless the drain is overgrown. Treatment of these would be problematic but it should probably be restricted to focal application in places where habitual water contact is known to occur.

Wadooks support only very sparse populations of *B. pfeifferi* or, more often, none at all, which is in contrast to the situation described by Shiff (9) in an irrigation system in Rhodesia, where night storage dams seemed to be the preferred habitat. Nevertheless, work elsewhere in Ethiopia (Aram; personal communication) suggests that this species does not settle and flourish in large, open water bodies and on the rare occasions when it is found in such situations it is probably only for a very short period. Jobin and Michelson (10) showed experimentally that *B. glabrata* was stranded at vertical drawdowns ranging from 23 cm/h on a 5:1 slope and 0.1 cm/h on a 100:1 slope in daytime and, although no measurements have been made, it does seem reasonable to conclude that the daily drawdown experienced here, where up to 50 percent of the total volume is discharged, would not encourage *B. pfeifferi*. The steep sided margins deter people from swimming in most wadooks. This indicates that such wadooks are not important as transmission sites.

S. mansoni infections in B. pfeifferi: Until 1971, the need for the application of molluscicide had been determined on the basis of snail density, but now that there is evidence from the human infection survey that measures applied so far have not been entirely successful in interrupting transmission it seems reappraisal is necessary. One important parameter not utilized previously was the rate of *S. mansoni* infections in *B. pfeifferi*. Data accumulated to date suggest that infected snails are only found towards the end of the dry season and until a month or so after the rains. The reason for seasonal cercarial production is not obvious. The length of the prepatent period for *S. mansoni* in *B. pfeifferi* was shown by Foster (11) to vary with temperature and perhaps with the relatively low water temperatures, frequently below 18°C. Low temperatures are recorded between November and February and they cause delays in the maturation of infections acquired just before and during this period, giving rise to a bunching of

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cercarial emergence in May/June. The peak infection rate seen towards the end of the rains would reflect the extent of infection in the early rains which apparently increased after irrigation ceased and when flow rates were minimal.

The time of peak infection rate is analogous to that found at Adwa, Tigrai Administrative region (Lemma; unpublished data), 1000 km north of Wonji-Shoa. Not only was cercarial production maximal in September) October, but it also occurred at a time when snail densities were low. This could be explained by the greater chance of stools containing viable eggs being washed from the rocky watercourses into proximity with snails by the next rainstorm, whereas in the dry part of the year dessication would be more likely. Similarly, at Wonji-Shoa ova from stools deposited on the closely vegetated banks of canals or drains will have a greater chance of hatching and the resulting miracidia locating and infecting through the agency of surface rainwater (or flood conditions) than would occur otherwise. There is also the possibility that empty drains and canals which provide cover for defeacation will be flushed through from time to time by storm-water with the same results as suggested above.

Cercarial examination of samples of *B. pfeifferi* which was introduced in 1971 in order to define possible transmission sites has revealed that infected snails are widespread. Paradoxically, plantation camps, such as A and F, where high infection rates were found among workers and their families were in areas where snail densities are low and also where molluscicide applications had repeatedly been made, which suggests that transmission was occurring in water bodies not previously considered hazardous.

S. mansoni infection in the estate population: The overall prevalence rate for plantation villages of 14.3 per cent would seem to be low. Data from the direct smear examinations in 1968 and 1973 do not indicate an unequivocal increase during those five years, but there is reason to believe that there has been a marginal one. The data available for shorter periods are conflicting; examination of 238 schoolchildren in 1971 and 1973 showed no significant increase of prevalence (Table 4) but the rate of 13 percent is at variance with the rate of 50 percent for boys between 10 - 14 years in the plantation survey of 1973, which should give cause for concern. Bruijning (7) quoted a 31.25 percent prevalence in Camp F, a result based on simple smear preparations, yet in 1973 the estimate was still only 32.3 percent by the concentration method. It does seem fairly certain however that there has been a change in the distribution pattern of infection in the population, since in 1968 there was no evidence of substantial transmission in children.

TABLE 4: Incidence of *S. mansoni* amongst the same group of schoolchildren between 1971 and 1973.

1971/1973	Positive	Negative	Percentage prevalence
Positive	18	11	15.3
Negative	1	159	—
% prevalence	10.0	—	189

Incidence = 1 — 0.84 (12/30) = 7.0%

The relatively low overall prevalence rate obscuring the high rates found in boys 10 - 14 years and men 24 - 30 years was a consequence of the very low rates in females, in whom incidence is confined to 10 - 14 year olds. In all age groups there is a significant difference (p 0.01) in the infection rate in males and females. The significance of the apparently bimodal distribution in males rather depends on how the age data is grouped. If the sample is divided into three groups, 5 - 14, 15 - 24, and 25 - 40 years, then the chi-square analysis shows there was no difference, but if the narrower bands are chosen, 10 - 14, 16 - 20, and 28 - 34 years, there was a difference at the 5 per-

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cent level. Lack of firm statistical support for this distribution may be due to the small sample number in the age group, 16 - 20 years. Nevertheless, in biological terms it could still be a fading reflection of the way in which schistosomiasis transmission was established at Wonji-Shoa; introduction by immigrant labour (the disease was not previously known in the area of the estates); continued occupational transmission (or simply past infections) within the same age groups producing the older peak; acquisition of infection by children, particularly boys, at the ages when swimming and playing in infested water is indulged as a daily routine, producing the younger peak. If detectable transmission continues then the two peaks will coalesce, but if control is successful then both peaks would shift simultaneously to older age groups. Enhancement of the peak in 25 - 35 year old men no longer occurs since the rigid screening of new labour for *S. mansoni* infection was introduced.

Application of the 'Sign' test to the data from the sample of 189 children examined in 1971 and 1973 indicated that the increase of 11 cases was significant. An estimate of the incidence according to the formula:

$$\text{Incidence} = 1 - x^{(12/y)}$$

where x is the proportion remaining negative for y months, gave a value of 7 percent over a 30 month period. There is no doubt that transmission is occurring amongst children, but the true extent needs elucidation.

Analysis of the variation of prevalence rates of the plantation camps indicated that, with the exception of Camp F, the situation was a homogenous one. This suggests that the factors governing transmission are similar throughout the estates and that village location is not important. However, the prevalence of 32 percent in camp F is outside the range expected (chi-square increased from 16.81 to 42.76 when n—l = 12 and 13 respectively) and the difference is highly significant. As yet no special features in the vicinity of the village have been identified to account for it. It should be noted that villages G and Y, housing principally cane cutters, showed no differences from other villages, so that there is no special association between that occupation (including the extra mobility of these workers) and excessive transmission.

The only causative variable that correlates with individual village prevalence rates is the number and proximity of water contact points. Villages A and F have the highest prevalence and numbers of such sites on adjacent canals used for laundering, bathing and swimming, although the absence of infection in adult females suggests that laundering as an activity, and the secondary supply canals themselves are not involved in transmission. In the spite of the provision of piped artesian well water to all villages, it is claimed that it is unsuitable for washing clothes and Awash River water is preferred; the concrete constructions found on secondary supply canals are also convenient for this activity. However, water flow rates generally exceed 35 cm/sec in daytime and, combined with rising and falling levels, discourage *B. pfeifferi*. During the period of no irrigation, from July to September, when there is a risk of infected snail populations these canals are either empty or the water level too low for laundering.

Clinical features and chemotherapy: Presence of *S. mansoni* eggs in the stool does not always signify the presence of symptoms (12, 13) and at Wonji-Shoa in 30 percent of the infected cases there were no obvious symptoms. Otherwise abdominal pain with an upset bowel habit, and/or blood and mucus in the faeces were common but the presence of concomitant parasites makes differential diagnosis difficult. In a small percentage of patients there was pyrexia, malaise or general febrile reaction and eosinophilia was common.

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the need for long term availability of irrigation water at a time when plantation requirements tend to be erratic whereas it would be necessary if N-tritylmorpholine was used. This procedure should be carried out annually without reference to snail densities and combined with at least one interim treatment, so raising the annual number of treatments to a minimum of three.

4. Attempts should also be made to define those sites responsible for the elevated transmission amongst males, particularly in the period August - November when infection in snails is thought to be high, but also at a time when irrigation is restarted causing changes in distribution and character of water bodies. Careful observation of sites favoured by children for swimming and further water contact studies in the villages with high prevalence rates, such as A and F, might be profitable as outlined by Farooq (17). A survey of the two factory villages is also essential; the pattern of infection in populations of these two villages could provide further information on the location of transmission sites so far overlooked.

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TETANUS IN GONDAR PUBLIC HEALTH COLLEGE HOSPITAL, ETHIOPIA: A REVIEW OF 72 CASES

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ABSTRACT: Records of 72 tetanus cases admitted during a two year period to the Gondar Public Health College Hospital have been analyzed. The males were predominant. There were 8 neonates, 22 between 29 days and 9 years, 33 between 10 and 39 years, and 9 above 40 years. The mortality rate and form of tetanus was the same in non-neonatal cases of both sexes. There was no difference in the various combination of relaxants in so far as the outcome is concerned. The disease was more common during the dry season. All patients were prone to one type of trauma or another because of the nature of their activity, and as a result of ignorance, poverty, and social and cultural practices. The site of injury was known in 59 cases (82%), the commonest being the foot. All neonatals with severe form of tetanus died. Sixty-seven percent of severe and 25 percent of moderate form of non-neonatal tetanus cases died. The overall mortality was 61 percent. The various complications and the causes of death are discussed. The study strongly justifies the need for a special unit for better and continuous care using trained health assistants without additional cost. The cost benefit analysis clearly demonstrates the vital importance of active immunization programmes and appropriate health education.

Tetanus is an acute intoxication of the nervous system with manifestations of neuromuscular dysfunction resulting from fixation in the central nervous system of a soluble exotoxin (Tetanospasmin) elaborated by a spore-forming gram-positive anaerobic bacillus, *Clostridium tetani*. Although tetanus is a world-wide disease, it is more prevalent in those areas where the climate is warm and damp, and where the soil is rich in organic matter. Two major problems of tetanus (1) are the lack of naturally acquired immunity and the difficulty of implementation of immunization programmes, especially in the tetanus-prone communities of the developing countries. Because of these, the incidence of tetanus still remains high. In developed countries, like USA and Britain, where immunization has become routine, there has been a tremendous reduction in the incidence of the disease (2, 3, 4). Other factors like socioeconomic changes also play a role in the epidemiology of the disease (5). In Ethiopia there is no nation-wide study on the incidence and mortality rates of tetanus; the only available data being a review of 79 cases admitted to three hospitals in Addis Ababa with an overall mortality of 32 percent (6). Analysis of 1971-72 admissions to Gondar Public Health College Hospital (7) indicated that tetanus was a common cause of mortality with the highest case specific death; it stood third in the proportional mortality rate after malnutrition and cirrhosis of the liver.

Tetanus is a lethal but preventable disease. The mortality rate in various continents of the world is different. However, all in all 423,000 people in the world die from tetanus each year (8). The case fatality rate, even in developed countries where the management facilities are much better, is still high (9). This clearly indicates the need for and importance of preventive

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measures. Yet the emphasis put on prevention, which is quite cheap and effective (10,11), is very poor in developing countries. In Ethiopia, immunization programmes for tetanus are practically non-existent except in some MCH centres in the capital city and some provincial towns.

In this paper 72 tetanus cases with poor socioeconomic backgrounds, admitted to the Gondar Public Health College teaching hospital over a two year period, are reviewed with the following objectives:

1) to study the problem of tetanus in terms of a) frequency of admission, b) geographical distribution, c) seasonal variation, d) occupation, e) clinical picture, f) care and outcome, g) cost of care,

2) based on the above findings, to recommend ways of reducing the mortality rate without incurring additional costs.

MATERIALS AND METHODS

The records of 72 tetanus cases admitted over two years (January 1975 to December 1976) to the Gondar Public Health College Hospital were analyzed according to age, sex, occupation, seasonal variation, geographical distribution, how the infection was acquired, incubation, frequency of admission to hospital, presenting symptoms, severity of tetanus and physical findings. The progress and outcome of these cases were studied. The neonatal and non-neonatal tetanus cases have been studied separately. Moreover, an attempt was made to relate the continuity of care to the outcome. The cost of each case was calculated in terms of drugs, hospitalization and laboratory charges only. The factors which have led to a high case fatality rate have been studied so that feasible recommendations to increase the survival rate could be made.

RESULTS AND ANALYSIS

Frequency of tetanus hospitalizations: The total hospital admission in this study period was nearly 7,000 with a male: female ratio of 1: 1.2. The frequency of tetanus admissions was 1.07 percent. There were eight neonatal and 64 non-neonatal tetanus cases. The incidence of tetanus in Ethiopia cannot be properly assessed because of poor reporting systems. Furthermore, the authors believe the traditional beliefs and practices, combined with communication problems in the region, have resulted in a lower figure.

Age and sex distribution: Table 1 showsthe age and sex distribution, the youngest six days old and the oldest 66 years. There were 44 males and 28 females. (M:F - 1.6:1) and males predominated in all age groups. Higher incidences in males have been observed by several workers (12, 13) in all ages. There was no difference between the two sexes in so far as the severity and mortality are concerned. The mortality in the under 10 year age group was 62 percent in contrast to 68 percent in Massawe's report (4) from Mulago Hospital in Uganda.

Geographical distribution and occupation: Twenty-seven (37.5%) were from Gondar town, 13 from Gondar vicinity, and the rest from places over 30 kms away. All cases were from places below 2300 meters above sea level, 47 of the cases (65.3%) were from rural areas, and 25 (34.7%) from urban. A higher proportion of cases from urban areas died and this may be explained by the fact that more children came from urban communities where the fatality rate was 77 percent.

All cases were prone to one type of trauma because of the nature of their activity and as a result of ignorance and poverty (nearly all of them wore no shoes). Children staying at home, farmers, housewives and pupils constituted a high proportion of the cases (Table 2).

Seasonal variation: Forty-nine cases (68%) were admitted during the dry season, and the rest (32%) during the wet season.

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TABLE 1: Tetanus in Gondar Public Health Hospital: Age

AGE	Male Total Case	Male % of total	Male % of case fatality	Female Total case	Female % of total	Female % of case fatality	Total No.	Total Case fatality
Neonatals (<29 days)	7	87.50	85.71	1	12.50	100.00	8	87.50
29 days- 9 yrs	13	20.31	61.54	9	14.06	55.56	22	63.64
10 yrs-19 yrs	8	12.50	37.50	7	10.93	85.71	15	60.00
20 yrs-39 yrs	11	17.19	54.44	7	10.93	28.57	18	44.44
40 yrs +	5	7.81	80.00	4	6.25	50.00	9	66.67
Total (Non-neonatal)	37	57.81	59.46	27	42.19	55.50	64	57.81

TABLE 2: Occupation of 72 tetanus cases

Occupation	Number	% Total
Stay at home (children)	27	37.50
Farmer	15	20.83
House wife	12	16.67
Student	8	11.10
Daily labourer	2	2.78
Tella seller	2	2.78
Weaver	1	1.39
Servant	1	1.39
Merchant	1	1.39
Unknown	3	4.17
Total	72	100.00

This seasonal variation is statistically significant ($0.005 < P < 0.001$). There has been controversy about the seasonal variation in the incidence of tetanus in Africa. Tompkins (15), Baker (16), Adeuja (17) and Sènècal (18) reported that tetanus is common during the dry season. On the other hand Massawe (14) found no significant monthly variation. There is a communication problem in this administrative region which is reflected in lower patient attendance in the hospital during the wet season. However, of the 40 cases from Gondar town and its vicinity, where transport facility is available all the year, 30 were admitted during the

dry season. This may support the argument that tetanus is commoner during the warm and dry season. Detailed studies (19) from various countries have shown that, in areas with cool and temperate climates, cases of tetanus occur during the warm season but in tropical areas the seasonal variation of the incidence is less pronounced.

Portals of entry of infections: Table 3 shows the incidence of various modes of infection and their relative mortality. The commonest portal of entry was trauma in 45.8 percent, thorn-prick to foot and other foot injuries being the commonest. Other causes of trauma were car accident, bullet injury with retention of foreign material in the dry tissues, burn and dog bite. Ten cases had tetanus related to home delivery, five of puerperal sepsis and five neonatal following umbilical sepsis. In 10 cases, mode of infection was other crude, traditional surgical practices, namely excision of uvula (in four, three were neonates), extraction of deciduous teeth and incision of gums in two, and in four others following jigger extraction, thorn removal and incision. Four were associated with otorrhea (one with foreign body in the ear), three cases with skin infection and one with a cold abscess. In 11 cases (15.3%) there was no information on the portal of entry.

Table 4 shows the suspected sites of injury. In 59 cases the site was known, the commonest site being lower limbs. Foot as site of injury accounted for 35.6 percent of the known sites and 29.2 percent of the total. Similar observations have been noted by Ayim (20) and Adeuja (17) and Vakil *et al* (21). Portal of entry was unknown in 11 cases (15.3%) and this is similar to a report with larger series (22), in contrast to observations by Braganza (23) and Cox (4) who reported over 50 percent.

Clinical picture: (Table 5). In this study the cases were classified as severe, moderate and mild, using criteria by Dastur *et al* (24). There were 56 (77.8%) severe (five were neonatals), 15 (21%) moderate (three were neonatals), and only one case of mild form of tetanus. All five severe and two out of three moderate neonatal tetanus cases died. Mortality is high in this series and also in other reports, ranging from 80 to 95 percent (22,25). Lower mortality however has been reported in rural Haiti, 47 percent (26), and India, 56.8 percent (27). In nonneonatal tetanus there were 51 cases of severe, 12 cases of moderate and mortality was 66.7 percent and 25 percent respectively; there was only one case of the mild form and this survived. There was no difference in severity or mortality in both sexes.

The incubation period could be determined in number of days (1-37) in 55 cases.

TABLE 3.

Mode of Infection	Number Admitted	% Total Admission	No. Died	Dead
A Trauma	33	45.83	17	51.52
B Umbilical and uterine sepsis (home delivery)	10	13.89	7	70.00
C Traditional practices (other than cutting umbilical cord)*	10	13.89	9	90.00
D Miscellaneous	8	11.11	4	50.00
E Unknown	11	15.28	7	63.64
Total	72	100.00	44	61.11

*Indigenous medical practices by laypeople in the community

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TABLE 4. Site of injury and case fatality of tetanus

Site of Injury	Neonatal			Non-Neonatal		
	Total cases	%of total	% Case fatality	Total cases	% of total	% case fatality
Head	3	37.50	10.00	8	12.50	62.50
Upper limb	—	—	—	6	9.38	66.67
Chest	—	—	—	5	7.81	80.00
Umbilicus	5	62.50	80.00	—	—	—
Birth canal	—	—	—	6	9.38	66.67
Lower limb	—	—	—	26	40.62	46.15
Unknown	—	—	—	13	20.31	61.54
Total	8	100.00	87.50	64	100.00	57.81

TABLE 5: Tetanus — Classification according to severity* and case fatality

	Total No.	Severe			Moderate			Mild		
		No.	Death	%Death	No.	Death	%Death	No.	Death	%Death
Neonatal	8	5	5	100.00	3	2	66.67	—	—	—
Non-neonatal	64	51	34	66.67	12	3	25.00	1	—	—
Total	72	56	39	69.64	15	5	33.33	1	—	—

*Scoring criteria (21) was used considering a) frequency of spasms, b) temperature above 38°C c) tachycardia ,d) rigidity (trismus, opistothonus, abdominal and limb rigidity).

There were 22 cases with incubation period less than seven days, 27 cases 7-15 days, and six cases above 15 days. The further the site of entry from the head, the longer the incubation period. The case fatality was lower in those with the longer incubation period, 33.5 percent with incubation period greater than 15 days, 50 percent 7-15 days, and greater than 80 percent in less than seven days in non-neonatals. All neonatal cases that died had an incubation period of less than seven days.

The onset was documented in 39 cases and it ranged between 24 hours to nine days. In 23 of these cases the onset was less than 24 hours. Eighty-seven percent of these cases died. Forty-four percent of those with onset greater than 24 hours died. None of the patients had received tetanus antitoxin or toxoid before admission.

Almost all patients had trismus and spasm, 71.7 percent of the cases had rigidity. Eighty-three percent of the cases were

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conscious. Over 80 percent of the patients had tachycardia, fever and opisthotonus. Dysphagia, neck-stiffness, and pain occurred in over 50 percent of cases. Less common presenting clinical pictures were refusal to feed, hypotension, convulsions, sweating, irritability, constipation, and difficulty in urination.

MANAGEMENT OF PATIENTS IN THE HOSPITAL

There is no special unit for tetanus patients in the hospital, though there is a 22 bed ward where there are three rooms for patients with tuberculosis and one room with three beds for cases of meningitis, hepatitis, tetanus, etc. There is a physician responsible for the patients and close supervision of assistants. However, the whole unit is run by one advanced health assistant and two practical health assistants during working hours and only one practical health assistant during off hours (evenings, nights and holidays). Over the study period, 49 non-neonatal tetanus cases were admitted to this unit and 15 non-neonatal tetanus to the other wards. Eight neonatal cases were admitted to the paediatrics ward. Case fatality in the non-neonatals admitted to this unit was 24/49 (49%), while 20/23 (86.9%) in other wards.

All adult patients were given crystalline penicillin 8 to 12 million units I.V. per 24 hours in divided doses for 10 days. In the absence of crystalline penicillin, procaine penicillin 800,000 I.U. I.M. b.i.d. was given for the same length of time. Neonatals and children were also given crystalline penicillin 1.2 to 4 million units I. V. per 24 hours in divided doses. When crystalline penicillin was not available, procaine penicillin 400,000 to 800,000 units I.M. twice per day was used. Twenty-five patients were given chloramphenicol in addition to penicillin for complications. All except two patients received tetanus antitoxin treatment. The reason why the two patients who were admitted during off hours did not receive the tetanus antitoxin was not clear. Adults were given 50,000 units of tetanus antitoxin (TAT) stat. and a second dose of 50,000 units after six hours. Then, depending on the severity of the case, a daily dose of 10,000 units for five days was given. On the other hand, neonatals and children were given tetanus antitoxin, 5,000 - 500,000 units over one to five days. There were two adult and one child tetanus cases who were sensitive to tetanus antitoxin and all were successfully desensitized. The cases were few to compare the different doses of TAT. Optimum dose of TAT or TIG (tetanus immune globulin), both equally effective, has not been made but the fact that serological therapy in tetanus is effective has been supported by various studies in humans (28) as well as in animals (29,30).

Various combinations of relaxants were used in this study. Neonatals and children were given phenobarbitone 2-3 mg/kg IM/24 hours, and chlorpromazine hydrochloride (largactil) 2 mg-kg IM/24 hours in divided doses alternating four to six hours. Diazepam (valium or stezolid) 1-2 mg/kg IV per dose was also used whenever there was severe spasm. Adults were also treated with chlorpromazine hydrochloride 50 mg IM alternating with diazepam 10 mg IV every four to six hours. Diazepam was often used on P.R.N. basis for severe spasms. There was no significant difference in the outcome using different combinations of relaxants. However, our general observation was that in many non-neonatal tetanus cases relaxants were used more on P.R.N. basis and this was more effective for severe and frequent spasms and this method has been supported in another report (31).

Other important methods for the management of tetanus included giving oxygen, surgical toilet of wounds and oropharyngeal suctioning, plus nursing care. Various problems have been encountered, namely lack of oxygen supply, suction machine not available in time and lack of continuous nursing care during off-hours.

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Outcome of tetanus management: Twenty-eight patients (39%) survived and the average period of hospitalization of the survivors was 26 days (range of 9-59 days), while 44 died (61%), ie 87.5 percent neontal death and 57.8 percent non-neonatal death and the average period of hospital stay was 5.4 days (range 1-23 days). Fifty percent of deaths occurred within four days of admission (all neonatal and 17 non-neonatal deaths), 39 percent between 5-10 days and 11 percent after 10 days of admission. In the under 9 year age group only two cases survived out of 28. The case fatality rate decreased in those patients above 10 years of age. Moreover, this study has revealed that the traditional medical practices and home delivery as modes of infection (Table 3) have resulted in higher mortality than trauma. The total estimated cost of care of 72 tetanus patients was 11,514.34 Birr (US$ 5,757.17). On the other hand the cost of tetanus toxoid would have been 138 Birr (US$ 69) only, if immunization had been done on these patients.

Cause of death in tetanus patients: Table 6 indicates the causes of death. The most frequent causes of death, accounting for 40 percent and 30 percent, were respiratory spasm and respiratory failure (secondary to aspiration and pneumonia) respectively. In three neonates cause of death was unknown. Causes of death unrelated to tetanus were sepsis in two patients and one due to hypertensive encephalopathy in a 66 year old man. Such high causes of mortality of respiratory origin have been reported in large series (21). These could have been avoided if proper and continuous nursing care, especially during off-hours, had been given, together with continuous supply of oxygen and suction machine.

Complications during the course of management occurred, urinary retention in 17, diarrhoea in seven, pneumonia in nine, nervous system complications (depression, cranial nerve palsy and foot drop) in three and serum sickness in one. These complications occurred in the first 10 days in those who died.

DISCUSSION

It is the investigators' belief that social and cultural factors, lack of an active immunization programme, along with very limited MCH activities and many home deliveries by untrained local midwives, must contribute significantly to the incidence of tetanus. Vaccination and frequent

TABLE 6: Causes of death in tetanus patients (both neonatal and non-neonatal)

Cause	Number	% Total death
1. Respiratory spasm	18	40.91
2. Respiratory failure (aspiration, pneumonia and lung abscess)	13	29.55
3. Circulatory failure	5	11.36
4. Hyperpyrexia	2	4.56
5. Unknown (neonatal)	3	6.81
6. Unrelated (sepsis, hypertensive encephalopathy)	3	6.81
Total	44	

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intramuscular injections by untrained personnel have not been observed in our study to be the cause of injury resulting in tetanus. It is interesting also to note that there were no tetanus cases in this study from amongst carpenters, mechanics and bricklayers, even though they are subject to frequent trauma. It is expected that incidence of neonatal tetanus is higher because of customs of cutting the cord with various unsterilized instruments, such as knife, blade, etc. and the practice of putting on the umbilical stump various dressings.

The cause of death by and large was associated with conditions that could have been prevented, ie adequate basic supplies and, what is more, by continuous nursing care especially during the critical period, namely the day of admission and subsequent four days. A special effort has been made to teach health assistants in the special ward where 49 non-neonatals were admitted the management of tetanus patients. Out of 25 admitted during regular hours when continuous nursing care was given, only six died (24%) while mortality was high in those admitted during off hours, 18 out of 24 (75%), and there is a strong statistional difference ($p \leq 001$). Such high mortality during off-hours had been due to lack of staff (only one practical health assistant on duty, not only for tetanus patients but for 20 other patients), and delay in early management. Modern methods of tetanus treatment as set out by Cole and Youngman (32) and Robles (10) including high level trained staff, use of currarization, tracheostomy, artifical respiration and hyperbaric oxygen, are impossible and far fetched to envisage in our setting for economic reasons and because of the lack of available experts. On the other hand, a modified intensive care unit has been recommended by Ayim (20) for use in developing countries. The writers strongly emphasise the need for a special unit which could be even more economical if trained health assistants were used to give the continuous nursing care. We also recommend intensive teaching of relatives taking care of patients. Simpler and cheaper would be to use nasogastric tube for giving relaxant as well as for feeding. This has shown good results (33).

The cost of treatment of one tetanus patient in this study was, on the average, 159.92 Birr (US $ 79.96). This did not take into account financial value on human life or work lost through the disease or cost of personnel. On the other hand, it would have cost only 139.8 Birr (US $ 69.9) or 1.2 Birr ($ 0.60) to 3 Birr (1.50) for each person to prevent tetanus in all 72 patients. Reports gathered by Cvjetanovic *et al* (34) from different parts of the world show that the cost of immunization ranges from $ 0.1 to $ 3.3, while that of treatment ranges from $ 50 to $ 900. This finding is in agreement with ours.

The clear message from this analysis is that prevention of tetanus by active immunization is very considerably cheaper than the management of clinical cases. The vital importance of routine immunization programmes to high risk groups of patients as in Maternal and Child Health Clinics and casualties needs to be emphasised in the strongest terms. Furthermore, the cultural and social factors related to tetanus must be considered not only in terms of active and widespread immunization programmes but also as a basic important part of all health education.

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A STUDY ON ONCHOCERCIASIS IN IMMATES OF GONDAR PRISON

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ABSTRACT. *Skin snips were taken from 747 inmates of Gondar prison and 34 were positive for* Onchocerca volvulus *microfilariae. Although prisoners came from all parts of Begemdir and Semen Province, only among those who had a history of travel to and residence in Metema-Humera and the Sudan did we find positive skin snips. The total absence of positive findings in a relatively larger population of the non Metema-Humera group supports the view that onchocerciasis is found only in the Metema-Humera area of this province.*

The existence of onchocerciasis in north-western Ethiopia was not known until very recently. Lester and Tsega (1), Mengesha and Jembere (2) reported some cases of onchocerciasis from the Metema-Humera region of Begemdir and Semen Province. The Sudan border was suspected to be an endemic focus, and it was postulated that agricultural development in the Metema-Humera lowlands with its attendant population migration to and from the Sudan might have been responsible for the introduction of this disease to the Begemdir and Semen Region. The objective of the present study was to identify the endemic areas of onchocerciasis in north-west Ethiopia.

PATIENTS AND METHODS

Gondar prison has about 800 inmates representative of the province. However, the prison population does not represent all demographic characteristics of the population of this province. All prison inmates were interviewed in detail and the following items of information were obtained:- birth place, travel, residence in and outside Ethiopia, with special reference to known endemic areas of onchocerciasis and location of work near rivers, age, sex and occupation before imprisonment, past and present medical history, with particular reference to pruritus and visual disturbances. A complete physical examination with special attention to signs of onchocerciasis was made. Nodules were carefully looked for and their absence was confirmed by careful palpation over the pelvic area. The eyes were checked for corneal opacities. Skin snips were taken from the left gluteal region in all cases. Mazzotte's test was done with 50 mg diethylcarbamazine on a randomly selected group among the negatives and on all skin snip positive cases. Diethylcarbamazine therapy for onchocerciasis followed the recommendations of Duke and Anderson (3).

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RESULTS

A total of 747 prison inmates were included in this study. Except for two cases, all were males. There were 600 persons in the 15 - 44 years age range, while the rest were over 45 years. Eighty-five per cent of the prison population were farmers by occupation; daily labourers, merchants and others made up the remaining 15 per cent. The duration of imprisonment varied from less than one year in 176 persons to 190 who were in prison for over seven

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years. The majority, 279, were in prison for less than three years. Travel history showed that 479 (64 percent) persons never left their birth-place prior to imprisonment, while 165 (22 percent) travelled within the province and 41 (5.5 percent) did travel outside the province, but within Ethiopia. Sixty-two (8.3 per cent) had immigrated to the province and some of these had come from the Sudan.



Figure 1 A case of onchocercal dermatitis and secondary infection of long standing

A medical history of pruritus, both at home and in the prison, was present in almost all cases. Out of 747 prisoners, only 51 had excoriations. Pigmentary changes were observed in 69 persons; hyperpigmentation of the pretibial area was more common than hypopigmentation. Secondary infection with onchocercal dermatitis was observed in a few (Figure 1). Only one case had disturbed visual acuity corneal opacity, generalized onchocerca dermatitis with diffuse skin oedema presenting with a "peau d'orange" appearance (Figure 2). This same case was the only one who had a single nodule over the face (Figure 3). Inguinal and femoral lymphadenopathy were seen in 26 cases.

Skin snips from 34 patients were positive for *Onchocerca volvulus*. A further analysis of history of travel and area of residence showed that a total of 175 persons had travelled and lived in the Metema-Humera lowland. Out of the 175 only 59 had travelled to the Sudan. All of the 34 patients with skin snip positive results



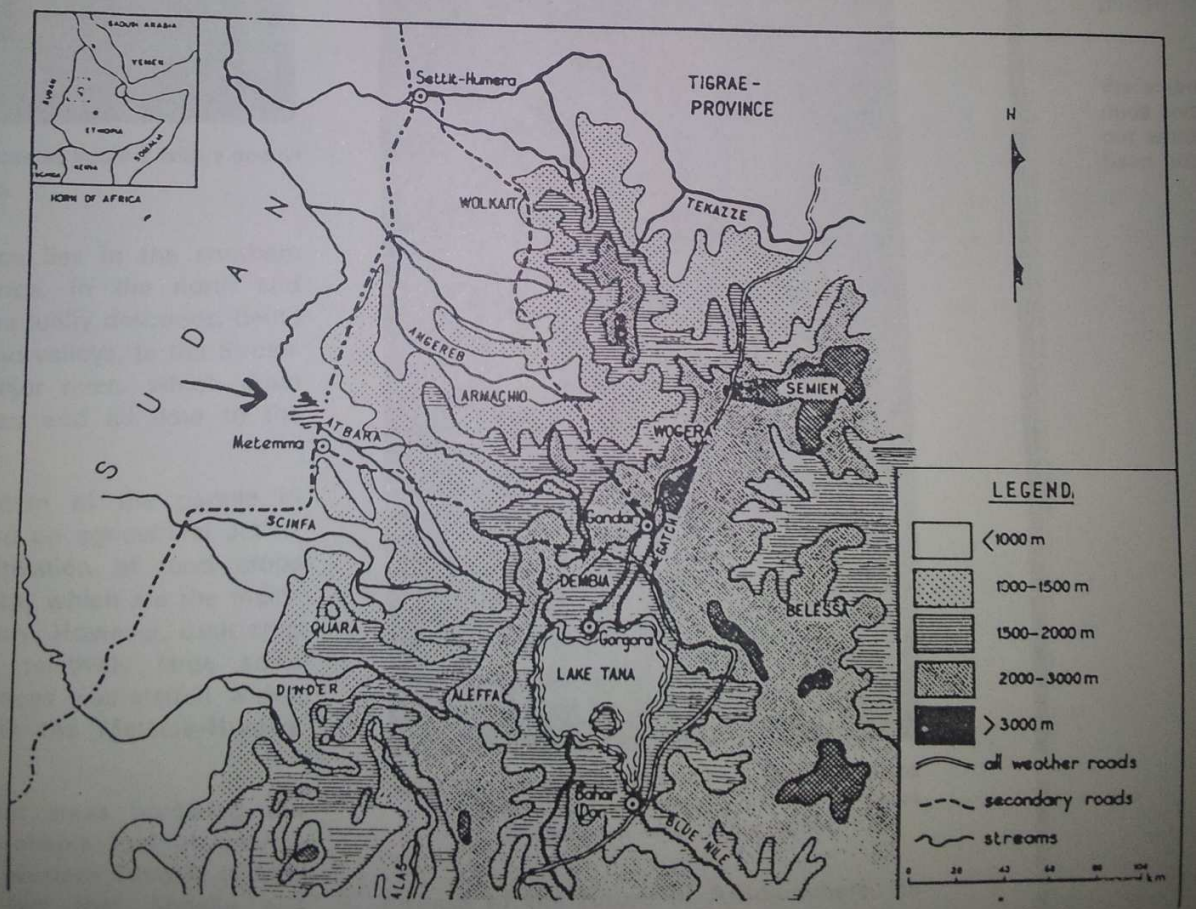
Figure 2 Generalized onchocercal dermatitis with "peau d' orange" ap-

had travelled and lived in the Metema-Humera area and 12 of these had also been to the Sudan. Five hundred and seventy-two prisoners who had no history of travel to, or residence in, Metema-Humera and the Sudan were all skin snip negative. Only one case out of this group was positive for Mazzotti's test and he was from Armachiho. Mazzotti's test was done on 202 persons and only 23 were positive. Except for the one case mentioned, all had a history of travel and residence in Metema-Humera and/or the Sudan.

Of the 34 patients with positive skin snips, 14 were in prison for less than one year and 13 were in prison from one to two years. One prisoner was skin snip positive after nine years of confinement.

DISCUSSION

The Begemdir and Semen Region of Ethiopia has an area of 74,600 sq.kms. It has an estimated population of 1,387,500 (4). The regional physical features are similar to most of highland Ethiopia, except along the Sudan border where the western plateau falls to the lowland of Metema-Humera. There is a central plateau which is surrounded by mountains forming the highest peaks of Ethiopia — Ras Dashen in the north and Guna in



Map of North-West Ethiopia

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Figure 3 The same case as figure 2 with a nodule on the face

the east. Lake Tana lies in the southern part of the province. In the north and west the plateau gradually descends, being broken by peaks and valleys, to the Sudan. There are four major rivers which drain the western plateau and all flow to the Sudan (see map).

The main occupation of the people in this region is based on agricultural activities, such as cultivation of food crops and raising livestock, which are the mainstay of the economy. However, cash crop production on a relatively large scale with modern practices was started within the last decade in the Metema-Humera lowlands.

The suspicion that areas bordering the Sudan are the probable foci of onchocerciasis in north-western Ethiopia is now cleared by the fact that Abdella and Abubaker (5) found a new focus of onchocerciasis in the Sudan along the upper Attbara River, close to the Ethiopian border. River Attbara is one of the four major rivers that flow to the Sudan from the western part of Begemdir and Semen Province (see map). Abdella believes that immigrants from northern Nigeria and Chad to upper Attbara, as a result of recent agricultural development in that area, might have imported the disease. The situation in Metema-Humera lowlands is similar in that it was developed relatively recently and people migrated from the highlands to work on the farms, which is mainly seasonal work. Some do cross over to the Sudan to work on agricultural projects.

The above findings, both in Ethiopia and the Sudan, prove the point that Duke (6) made about onchocerciasis as being the

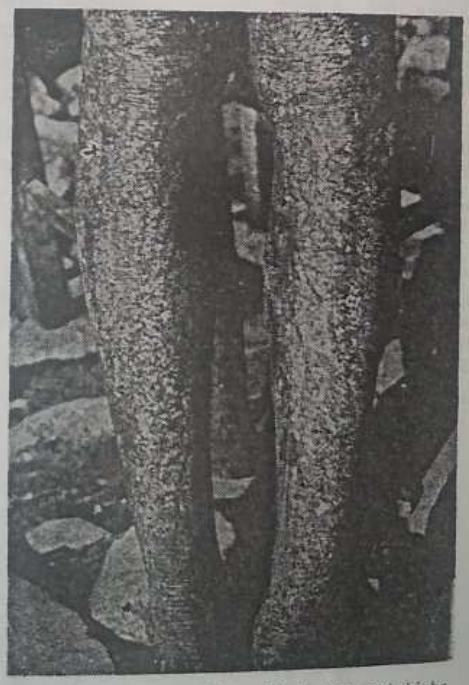


Figure 4 Depigmentation of both legs and thighs which is a common feature in cases of onchocerciasis in this region.

disease of the future in Africa where, he believes, agricultural development will lead to the disease becoming a major public health problem.

There is a similarity in the clinical picture to the Sudanese findings in that nodules were quite rare, except in one case. Nodules on the head are uncommon in known endemic areas of Ethiopia (7,8,9). Abdella and Abubaker (5) reported two nodules on the scalp in the upper Attbara survey. In our study visual impairment and corneal opacities were not common and we believe that either this is due to the disease being recently introduced or our cases did not live in the endemic area for long.

The common skin lesion was hyperpigmentation and hypopigmentation of the lower limbs, especially the shins and thigh (Figure 4). Secondary infection complicated the picture and some of these prisoners were treated as cases of scabies or impetigo in the past (Figure 1).

We extend our thanks to Gondar Prison authorities and dressers who were helpful and without whose cooperation this study would have been impossible.

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CASE REPORT

TYPHOID ENDOCARDITIS

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Endocarditis is a very rare complication of typhoid fever (Tillotson and Lerner, 1966). In salmonella infections, the incidence of endocarditis is about 0.5%, *Salmonella choleraesuis* being a common species identified (Saphra and Winter, 1957; Tillotson and Lerner, 1966). Twenty-three well documented cases of salmonella endocarditis were reported in the English literature between 1936 and 1966 (Tillotson and Lerner, 1966), and only one case of typhoid endocarditis has been reported from Africa during the past twenty-five years (Mokhobo, 1975).

The following are two case reports of salmonella endocarditis, one in a patient without valvular disease and the other in a known patient with mitral valve disease.

CASE REPORT

Case 1

L.T. was a 16 year-old Ethiopian boy admitted in September 1974 to St. Paul's Hospital with right upper quadrant swelling of the abdomen fever and night sweats for 5 months.

He was sick-looking, emaciated, and pale with a few petechiae on the trunk. Vital signs were normal. There was a grade 2/6 ejection systolic murmur maximal at the left sternal border between the second and fourth intercostal space. Lungs were clear. Liver was smooth, soft and tender with total vertical span of 15 cm. by percussion along the right mid-clavicular line. The spleen was firm, nontender and 7 cm. below the left costal margin. The rest of the examination was normal.

The tentative diagnosis at admission was cirrhosis of the liver.

Haemoglobin was 5.7 gm.%. WBC was 7,700/mm3 with a normal differential. The ESR was 149mm. per hour. Blood films were negative for haemoparasites. There was microscopic haematuria. The SGOT and SGPT were 72 and 82 W.U., respectively (normal 0-40). Serum alkaline phosphatase was 23 BLU (normal 0.5-3.1 BLU). Chest x-ray showed slight cardiomegaly. Electrocardiogram was normal. Percutaneous liver biopsy showed "subacute hepatitis".

The patient had profuse evening sweats, with temperature up to 38°C, and episodes of severe dyspnoea, orthopnoea and palpitation. Repeat chest x-ray showed marked cardiomegaly and pulmonary oedema. Furosemide and digoxin were administered after which he responded. The murmur noted at admission changed in intensity.

Four blood cultures, taken while the patient was afebrile on three consecutive days in the fourth hospital week grew *Salmonella typhi*. Widal titre was 1:320 against *S. typhi* OD and Hd.

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followed by 4 grammes daily of ampicillin for 3 more weeks.

[illegible] signs and symptoms of cardiac failure soon disappeared, and he was discharged from the eighth week having gained 4 kg.

Because of persistence of hepatomegaly, liver biopsy was repeated in December 1974: it showed a non-specific inflammatory process.

When last seen in September 1975, he was in excellent health, weighed 69 kg. (a further gain of 25 kg.) and had no symptoms of congestive heart failure. No murmur was heard. SGOT and SGPT were normal, and ESR was 26mm. per hour.

Case 2

S.A. was a 23 year-old Ethiopian male admitted in October 1975 to Black Lion Hospital because of anorexia, fever, cough and shortness of breath of one week duration. He had had five hospitalizations within the previous three years because of congestive heart failure due to mitral stenosis. Physical examination on admission revealed a sick-looking man who was toxic and apprehensive. The temperature was 39°C, the pulse 80 per minute and the respiratory rate 20 per minute. The blood pressure was 90/60 mm. Hg. There were fine crepitations at the lung bases. The peripheral pulse was irregular and reduced in volume. The jugular venous pressure was not raised. The point of maximum impulse was in the fifth intercostal space at the left mid-clavicular line. There was a prominent parasternal heave. The first heart sound over the apex and the second over the pulmonic area were accentuated but a diastolic murmur could not be heard. There was an apical systolic, grade 2/6 murmur radiating to the left axilla. The rest of the physical examination was essentially negative.

The urine showed 2+ protein and 1-2 erythrocytes per high power field. The haemoglobin was 14 gm. per 100 ml.; the white cell count was 6,000 per mm3 with a normal differential count. The erythrocyte sedimentation rate was 62 mm. per hour. Peripheral blood smear showed no haemoparasites. Chest x-ray showed a prominent pulmonary conus, left atrial enlargement and an enlarged right ventricle (Fig. 1). Electrocardiogram showed atrial fibrillation with evidence for right ventricular hypertrophy. A blood culture grew *Salmonella typhi* and Widal titre was 1:320 against both OD and Hd.

The patient was slowly redigitalized. Furosemide 40 mg. *b.i.d.* and Potasium chloride 750 mg. bid were started orally. Because of the positive blood culture, chloramphenicol 500 mg. *P.O.* 6 hourly was started. He responded well (Fig. 2) and chloramphenicol was stopped after two weeks. The heart failure improved too.

However, the atrial fibrillation persisted, fever recurred, haemoglobin dropped from 14 to 8.5 gm. per cent and the erythrocyte sedimentation rate rose to 137 mm. per hour. At this point, a clinical diagnosis of endocarditis was made, blood cultures were repeated and the patient was started

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on crystalline penicillin 2 million units every 4 hours and chloramphenicol 500 mg. every 6 hours intravenously. Procaineamide 250 mg. *t.i.d. P.O.* was also added. Inspite of therapy he remained febrile, his general condition deteriorated, and on November 18, he suddenly developed right-sided hemiplagia, aphasia and hypotension. He died on the same day.

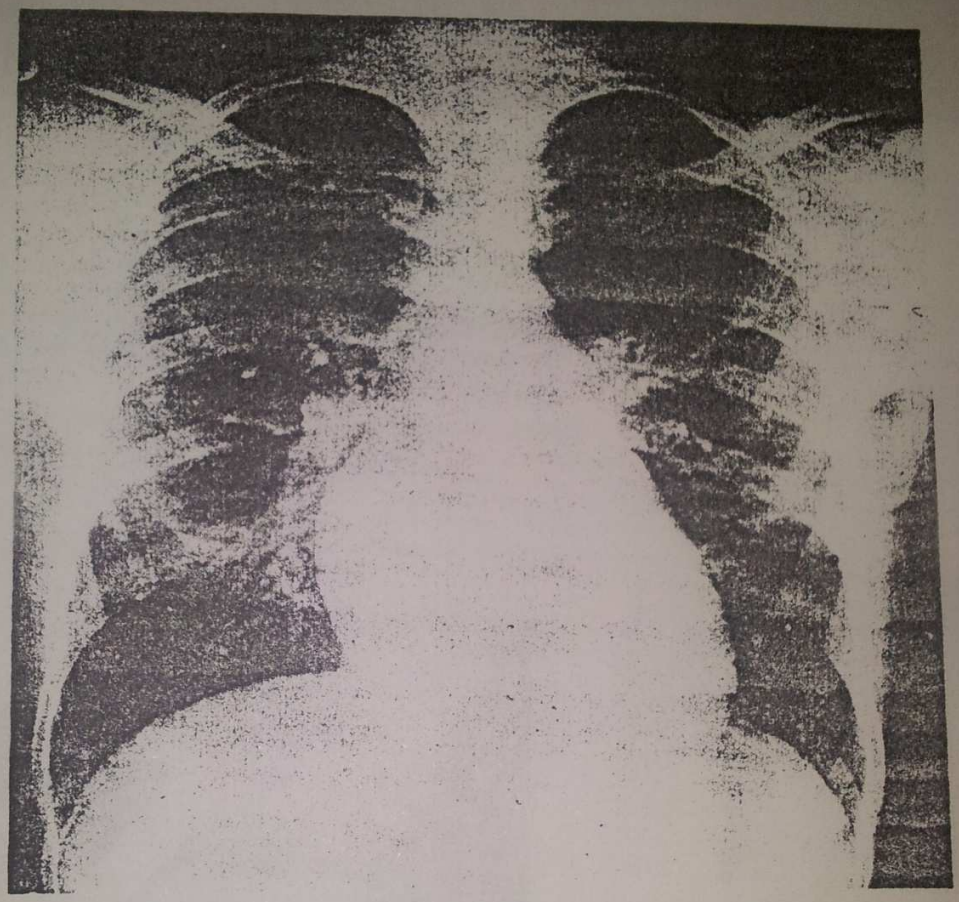


Figure 1a. Plane chest X-ray of Case 2 showing prominent pulmonary conus and cardiac sillouette.

One of the later blood cultures was reported, after his death, positive for *Salmonella typhi*.

Discussion

Endocarditis is a rare complication of typhoid fever. There were no cases of subacute bacterial endocarditis among the variety of complications seen in 98 cases in India (Gulati, *et al*, 1968) or among 1159 cases seen in Norway between 1912 and 1961 (Gadeholt and Madson, 1963). Huckstep (1962) who saw 1,300 cases of typhoid fever in Kenya and Uganda said "Pericarditis is rare, except in children, while endocarditis is probably always due to organisms other than typhoid."

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Figure 1b. Lateral chest X-ray of Case 2 showing left atrial and right ventricular enlargement.

Case 1 had no history of rheumatic fever and the murmur was absent a year later, and thus it is unlikely that he had pre-existing valvular disease. Mokhobo (1975) reported a 35 year-old woman, ill only three weeks, who died in congestive heart failure, with one of several blood cultures reported positive for *S. typhi* after death. She was found at autopsy to have fibrotic pericarditis and exuberant vegetations on the aortic valve, but all the cardiac valves were anatomically normal.

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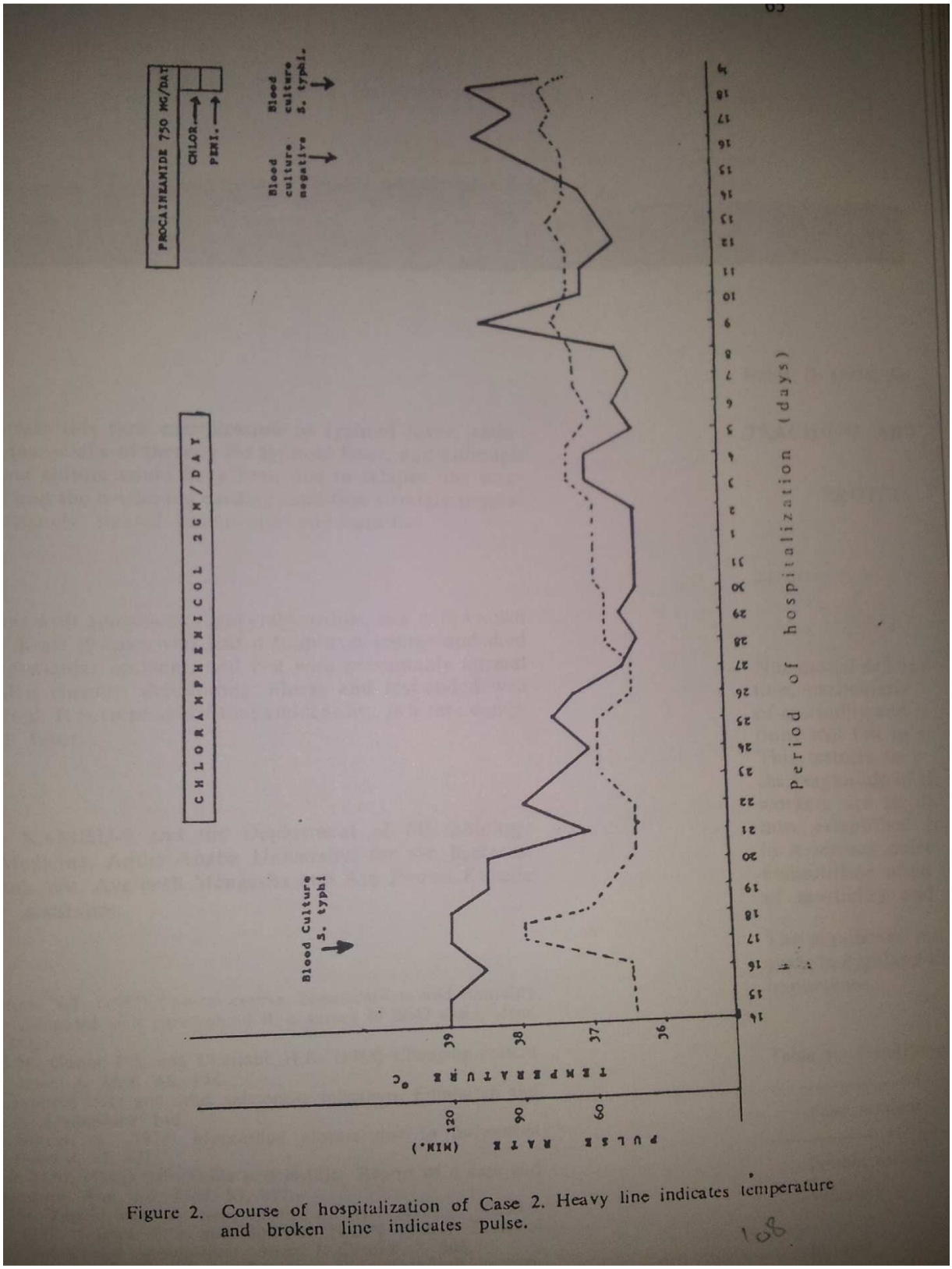


Figure 2. Course of hospitalization of Case 2. Heavy line indicates temperature and broken line indicates pulse.

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Our two cases illustrate this rare complication of typhoid fever, endocarditis. Case 2 had two weeks of therapy for typhoid fever, and although the last positive blood culture could have been due to relapse, the cerebrovascular accident and the worsening cardiac condition strongly suggest that he had inadequately treated salmonella endocarditis.

Summary

Two young Ethiopians with *Salmonella typhi* endocarditis, one with known pre-existing valvular heart disease who had a fulminant course and died after embolic cerebrovascular accident, and one with presumably normal valves who had had a chronic debilitating illness and responded well to therapy, are reported. It is emphasized that endocarditis is a rare complication of typhoid fever.

Acknowledgements

We are grateful to NAMRU-5 and the Department of Microbiology of the Faculty of Medicine, Addis Ababa University, for the bacteriology service. We thank Wo. Ayalnesh Mengesha and Ato Zewdu Kebede for their technical assistance.

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CHRONIC URTICARIA: ITS RELATIONSHIP TO INTESTINAL PARASITIC INFESTATION AND RESPONSE TO ANTHELMINTIC DRUGS

A Preliminary Study

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ABSTRACT. *Fourteen inmates of the Gondar prison who had chronic urticaria were closely followed to determine its relationship to intestinal parasitic infestation and response to anthelmintic drugs for four to five months. The urticaria in 11 of 14 patients had direct relationship to intestinal parasites particularly ascaris and was cured when the specific parasites were eliminated with anthelmintic drugs. The rest of the urticaria cases (three patients) had no parasites and responded to antihistaminic drugs. This preliminary study shows that there is an important association between chronic urticaria and intestinal parasites.*

Chronic urticaria or hives, is a fairly common skin disease characterized by sharply demarcated elevated wheals, accompanied by erythema and itching and recurring for months or years.

The incidence of chronic urticaria in the general population is unknown (1,2). However, various aetiologic factors have been implicated such as drugs (eg penicillin, aspirin); foods (eg egg, fish, chocolate, tomatoes); yeasts (*C. albicans*) and, rarely, infestations by parasites such as trichina, amoeba, pinworm, ascaris giardia strongyloides, schistosoma (3), larva currens strongyloides (4) and also filaria (5). Parasitic infestation as a cause of chronic urticaria has been reported less frequently. Though it has been claimed that even in heavily infested patients in the tropics urticaria is infrequent (6), we suspect parasites may play an important role in causing urticaria in the tropical areas.

The objectives of this study were: (a) to determine whether there is a relationship between urticaria and parasitic infestation; (b) to ascertain whether the elimination of parasites also cures possibly associated urticaria; and (c) to evaluate response to antihistaminic drugs in urticaria cases not associated with intestinal parasites.

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MATERIAL AND METHODS

Urticaria research has been carried out on the inmates of Gondar prison during the period January 1975 to May 1975. Fourteen cases among 800 inmates who complained of chronic or recurrent urticaria seen in the prison clinic were included in the study. Detailed information was acquired using a questionnaire on the following: age, sex, address, religion, previous occupation, duration and frequency of urticaria; period of stay in the prison; complaints at time of study, itching, sensation of pricking, stinging or burning, exacerbation and remissions and other associated symptoms; past medical history, family history for urticaria; history of allergy to drugs, foods, insect bites, chemicals or physical agents (cold, heat and light); passing of parasites in the stool; relationship to emotional disturbances.

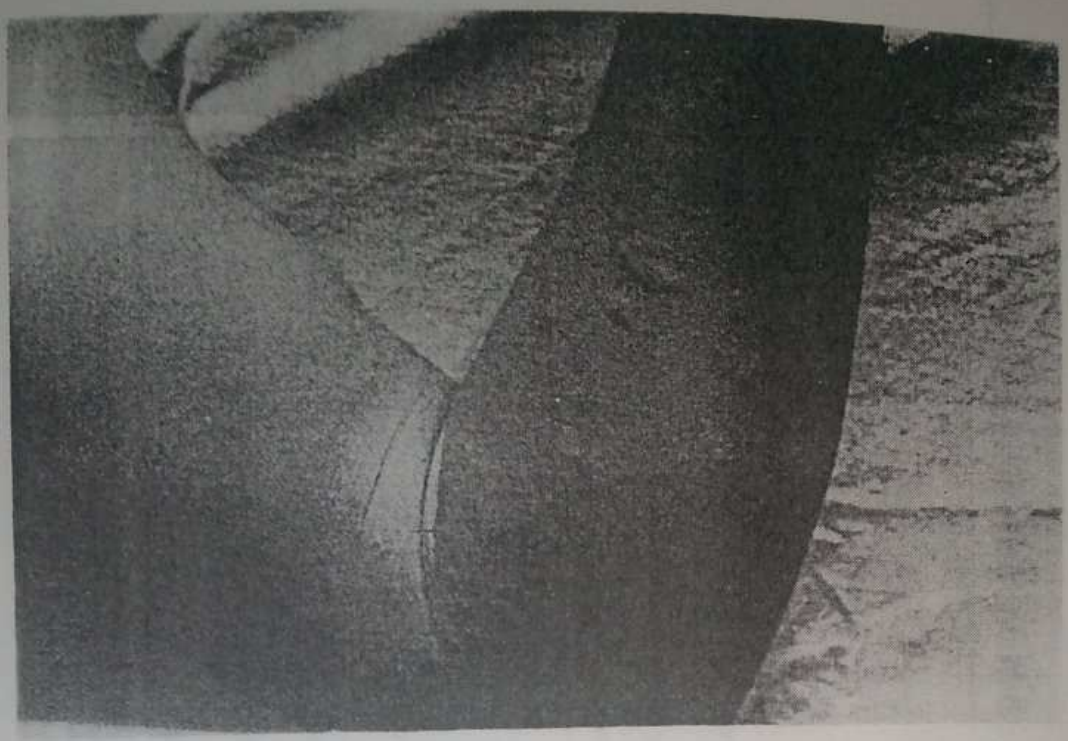


Figure 2. Localized urticaria.

Table 1 shows a summary of the relationship of urticaria to parasitic infestation both initially and during 4 - 5 months follow-up after treatment. Eleven of the cases had their urticaria related to parasitic infestation and were treated with anthelmintics and three which had no parasites were treated with antihistaminics and none had symptoms after treatment (Table 3). Urticarial lesions were absent except in one patient who had double infestation i.e. ascaris and hookworm (Table 2) but who showed improvement. A relationship between urticaria and parasite was established after the stool examination proved negative for specific parasites and at the same time and subsequently urticaria also disappeared. For example case 10, who had initially had ascaris and trichuris, was first cured of trichuris only and his urticaria also disappeared. Again after two months he had recurrences of both trichuris and urticaria and finally responded to both with anthelmintic drugs. Thus the patient's urticaria was related to trichuris.

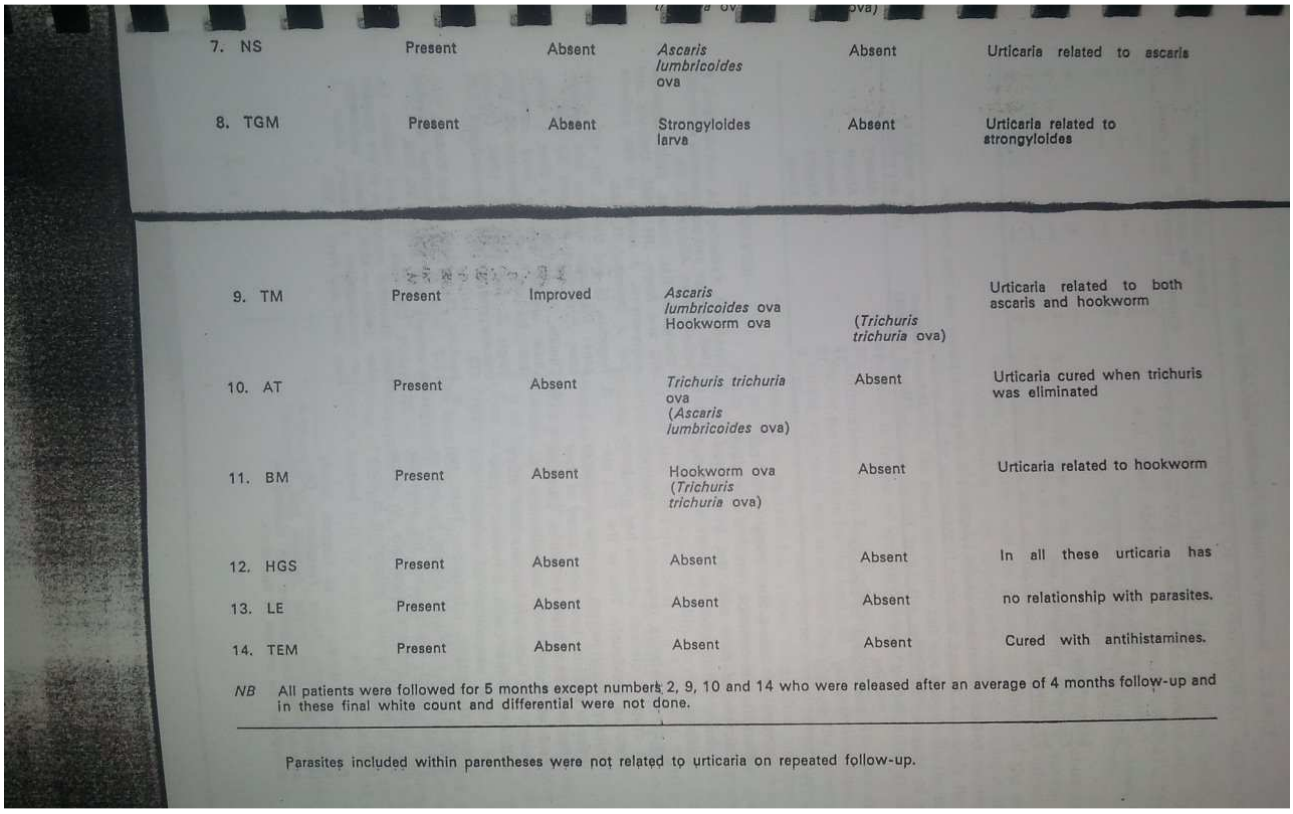
Due to the fact that four cases were released one to two weeks before the end of the study without having had final differential count and that the study did not involve any absolute eosinophil count, we cannot comment on the significance of eosinophilia before and after treatment. Table 2 summarizes the parasites that caused urticaria in 11 patients.

DISCUSSION

The importance of urticaria as a clinical problem should not be underestimated. At a later date when a survey of skin diseases in Gondar prison was done, out of 817 inmates, 158 had skin diseases and urticaria was the third commonest condition comprising 12 per cent of the skin diseases. Our study was conducted to find the relationship of chronic and recurrent urticaria to intestinal parasitic infestation as demonstrated by stool examination and not to larval penetration or migration. Because of the limited

TABLE 1. Urticaria and intestinal parasitic infestation before and after treatment

Patient	Urticaria		Intestinal Parasite		Comments
	Before treatment	After treatment	Before treatment	After treatment	
1. ZT	Present	Absent	*Ascaris lumbricoides* ova	Absent	Urticaria related to ascaris
2. AF	Present	Absent	*Enterobius vermicularis* ova	Absent	Urticaria related to oxyuris
3. GMT	Present	Absent	*Trichuris trichuria* ova (*Ascaris lumbricoides* ova)	Absent	Urticaria cured when trichuris was eliminated
4. TA	Present	Absent	*Ascaris lumbricoides* ova	(*Trichuris trichuria* ova)	Urticaria cured when ascaris was eliminated
5. GCH	Present	Absent	Hookworm ova (*Trichuris trichuria* ova)	Absent	Urticaria related to hookworm
6. GCH	Present	Absent	Hookworm ova (*Trichuris trichuria* ova)	(*Trichuris trichuria* ova)	Urticaria cured when hookworm was eliminated
7. NS	Present	Absent	*Ascaris lumbricoides* ova	Absent	Urticaria related to ascaris
8. TGM	Present	Absent	Strongyloides larva	Absent	Urticaria related to strongyloides



7. NS	Present	Absent	*Ascaris lumbricoides* ova	Absent	Urticaria related to ascaris
8. TGM	Present	Absent	Strongyloides larva	Absent	Urticaria related to strongyloides
9. TM	Present	Improved	*Ascaris lumbricoides* ova Hookworm ova	(*Trichuris trichuria* ova)	Urticaria related to both ascaris and hookworm
10. AT	Present	Absent	*Trichuris trichuria* ova (*Ascaris lumbricoides* ova)	Absent	Urticaria cured when trichuris was eliminated
11. BM	Present	Absent	Hookworm ova (*Trichuris trichuria* ova)	Absent	Urticaria related to hookworm
12. HGS	Present	Absent	Absent	Absent	In all these urticaria has
13. LE	Present	Absent	Absent	Absent	no relationship with parasites.
14. TEM	Present	Absent	Absent	Absent	Cured with antihistamines.

NB All patients were followed for 5 months except numbers 2, 9, 10 and 14 who were released after an average of 4 months follow-up and in these final white count and differential were not done.

Parasites included within parentheses were not related to urticaria on repeated follow-up.

TABLE 2. Summary of intestinal parasites associated with urticaria.

	Urticaria patients treated for parasites			Total
	Cured	Improved	Not cured	
Ascaris lumbricoides ova	3	—	—	3
Hookworm ova	3	—	—	3
Trichuris trichiura ova	2	—	—	2
Ascaris lumbricoides ova and hookworm ova	—	1	—	1
Strongyloides larva	1	—	—	1
Enterobius vermicularis ova	1	—	—	1
No parasites	3	—	—	3

TABLE 3. Urticaria-related symptoms in 14 patients before and after treatment.

Symptoms	Before treatment (No. of patients)	After treatment (No. of patients)
Itching	14	Absent
Pricking	12	Absent
Exacerbation of Urticaria	12	Absent
Burning	12	Absent
Stinging	6	Absent

number of cases this study does not elucidate the common parasites that cause urticaria or deal with the general prevalence of urticaria in heavily infested patients.

To our knowledge, response to anthelmintic drugs in chronic urticaria has not been reported previously. This is the first preliminary study where parasite-associated urticaria patients have been cured of their urticaria when their intestinal parasites were eliminated with anthelmintics. Although this was an uncontrolled study with only a few cases, it reveals a clear-cut clinical association of urticaria and intestinal parasitic infestation. Thus, we suggest that emphasis should be put on reliable stool examination for parasites in urticaria patients especially in areas where heavy parasitic infestation is common.

Our sincere thanks go to Captain Wolde Michael Mebratu, Major Fessehasion Okubagzhi, the Bata Prison dressers and the prisoners for their consent and cooperation throughout the process of this study.

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TEACHING ARTICLE

REVIEW OF ANTIMICROBIAL AGENTS:

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The rational use of antibiotics and chemotherapeutic agents requires a knowledge of the mechanism of action of those agents, their antibacterial spectrum as well as the identification of the infective agent, site of infection, sensitivity and the general condition of the patient necessitating consideration of the appropriate route of administration. Availability and cost are additional factors that need to be considered in the correct choice of the antibacterial agent or agents. Certainly the latest antibiotic is probably the most expensive but not necessarily the most effective one and clinicians should resist the seductive serenade of professional persuaders in favour of unbiased scientific evaluation at all times.

Antimicrobial drugs have "selective toxicity", i.e. they are far more toxic for the parasite than for the host cell. This selective action is due to certain unique structural and functional features of the parasite which make it different from the host cell. These antimicrobial agents are either bacteriostatic or bactericidal. Those drugs that are bacteriostatic prevent the growth of the organisms (e.g. tetracycline, chloramphenicol, erythromycin, novobiocin and lincomycin) while those that are bactericidal actively kill bacteria (e.g. penicillin, cephalosporin, streptomycin, kanamycin, cycloserine, etc.). In some cases this differentiation is a relative one since certain antibiotics (e.g. penicillin, erythomycin, etc.) are bacteriostatic at a low dose but bactericidal at a high dose. Further more, long term administration of bacteriostatic agents will result in elimination of organisms by the host.

Modes of Action of Antimicrobial Drugs

Unlike animal cells, bacteria have a rigid outer layer, a cell wall which maintains the unusually high osmotic pressure. Injury of the cell wall, such as by lysosomes, or inhibition of its synthesis by antibiotics, leads to lysis or death of the cell. The cell wall consists of polysaccharides and a highly cross-linked polypeptide.

The backbone of this mucopolysaccharide is formed by the alternating arrangement of N-acetylglucosamine and N-acetylmuranic acid, the latter is found only in bacteria (Fig. 1). To these amino-sugars are attached pentapeptide chains; the final rigidity of the cell wall is imparted by cross-linking of the peptide chains by a process known as "transpeptidation" which is carried out by enzymes. All penicillins and all cephalosporins

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act by inhibiting the activity of "transpeptidase" enzyme, i.e., the transpeptidation reaction, and thus arrest cell wall formation. The transpeptidation reaction involves the loss of a D-alanine from the pentapeptide. Cycloserine is an analogue of D-alanine. Thus it blocks the action of alanine racemase, an essential enzyme in the incorporation of D-alanine in the pentapeptide (Strominger and Tipper, 1965).

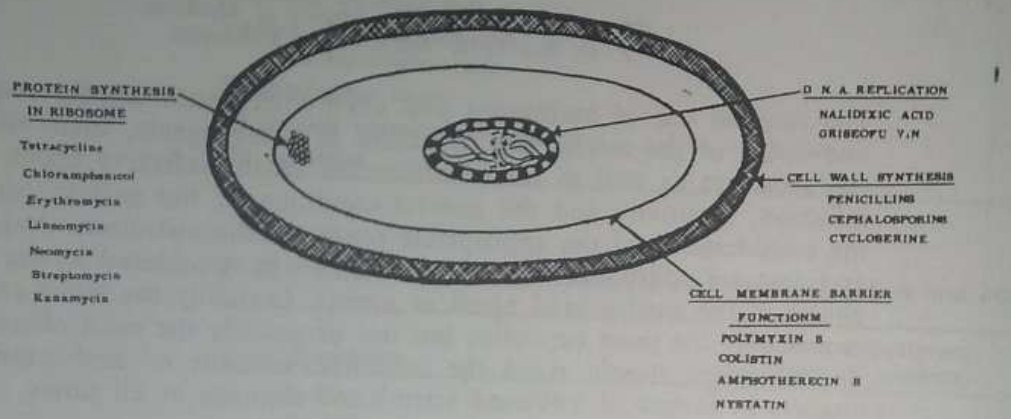


Figure 1. Bacterial cell wall composition.

The cytoplasm of all living cells is bounded by cytoplasmic membrane which serves as a selective permeability barrier and thus controls the internal compostion of the cell. If the functional integrity of the cell membrane is disrupted, purine and pyrimidine nucleotides and proteins escape from the cell and cells damage or death ensues. The cytoplasmic membrane of certain bacteria and fungi can be more readily disrupted by certain agents, thus, selective chemotherapy is possible. The polymyxins (polymyxin B and Colistin) act on gram-negative bacteria and the polyene antibiotics (nystatin, amphoterecine B, etc.) act on fungi. The former group have a detergent-like action on the cytoplasmic membrane by attaching to ionic binding sites. The latter are toxic only if they are bound to sterols present in the cell membrane. The polymyxins are inactive against fungi and polyenes are inactive against bacteria, i.e., sterols are absent in the bacterial membrane but are present in fungal cell membranes—a good example of cell individuality and of selective toxicity (Sanders and Cluff, 1968).

Several antibiotics act through inhibition of protein synthesis. Bacteria have 70s ribosomes whereas mammalian cells have 80s ribosomes in their cytoplasm. The sub-units of each ribosome are functionally specific and hence antibiotics act in bacteria but not in mammalian cell. Chloramphenicol attaches to the 50s sub-unit of bacterial ribosomes and interferes greatly with the binding of amino-acids to nascent peptide chains. The tetracyclines bind to the 30s sub-unit of bacterial ribosomes and inhibit protein synthesis by blocking the binding of charged aminoacyl-transfer RNA (tRNA) to the 30s sub-unit. Macrolides (erythromycins, oleandomycins) and lincomycins bind to the 50s sub-unit and probably compete with amino-acids for ribisomal binding sites. All aminoglyco-

sides (streptomycin, kanamycin, neomycin, gentamycin, etc.) bind to a surface protein on the 30s sub-unit of the bacterial ribosome and distort the recognition sites of the ribosome and cause a misreading of the mRNA message. This results in the insertion of the wrong amino-acids in the peptide chain and the synthesis of abnormal or nonfunctional proteins (Crofton, 1969; Meyers *et al*, 1974).

Drugs like nalidixic acid, griseofulvin, actinomycin, etc., interfere with DNA function and prevent synthesis of mRNA and hence, protein synthesis. However, the exact mechanism remains unknown. Figure 2 indicates the sites of action of different antibiotics.

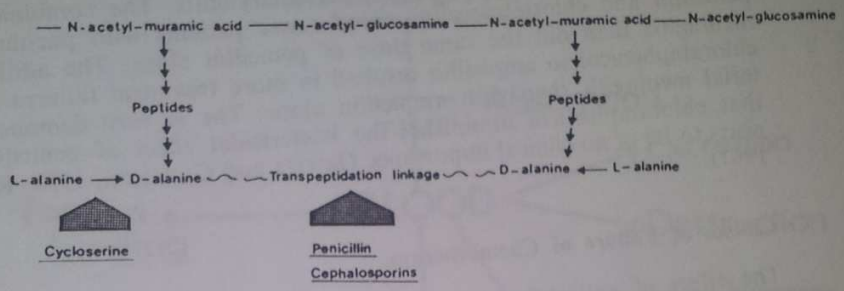
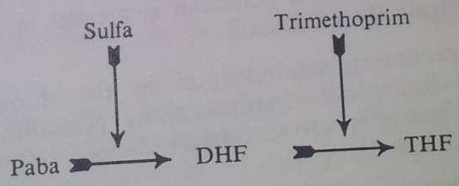


Figure 2. Sites of action of antibiotics.

Synergism and Antagonism

When the simultaneous action of two drugs results in an effect which is greater than that of one of them (given in a maximum dose) the action is said to be synergistic. Synergism may be due to blocking successive steps in a metabolic sequence (e.g. sulfamethoxazole and trimethoprim). Sulfonamides compete with para-aminobenzoic acid (PABA) which is required by some bacteria for the synthesis of dihydrofolate (DHF). Folate



antagonists such as trimethoprim inhibit the enzyme (dihydrofolate acid reductase) that reduces dihydrofolate to tetrahydrofolate (THF). Thus, the simultaneous administration of sulfonamide and trimethoprim results in a simultaneous block of sequential steps leading to the synthesis of purines and nucleic acid. A second type of synergism is when one drug inhibits an enzyme capable of destroying a second drug. Cloxacillin, methicillin or cephalosporins can bind beta-lactamases but remain resistant to their action. Concomitantly administered penicillin G or ampicillin susceptible to hydrolysis by beta-lactamases may thus be protected from destruction. A third but least known type of synergism is observed when the penetration of one drug through the bacterial cell wall is enhanced by the simul-

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taneous administration of a cell wall synthesis inhibitor. Thus, the penicillins enhance the penetration of the aminoglycosides, a true synergism apparent during the treatment of subacute bacterial endocarditis (SBE). In clinical practice, except in SBE, synergism may not be required provided that an adequate dose of a single drug is used and the organism is sensitive to it (Meyers *et al.*, 1974; Brumfitt and Percivol, 1971)

In clinical practice, there are few known examples of antibiotic antagonism (i.e. the reduction of the effectiveness of one antibiotic upon the addition of another). Antagonism has been shown for a tetracycline-penicillin combination and for an erythromycin-penicillin combination in Group A haemolytic streptococcal pharyngitis. The combination of penicillin and chlortetracycline cured fewer patients with pneumococcal meningitis than did the same dose of penicillin alone. The addition of chloramphenicol to ampicillin resulted in more treatment failures in bacterial meningitis than with ampicillin alone. The *in vitro* demonstration that chloramphenicol diminishes the bactericidal effect of penicillin appears to be of no clinical importance (Jawetz and Gunnison, 1953; Rogers, 1967).

Causes of Failure of Chemotherapy

The effect of antibiotics depend on their concentration in and around the tissue or lesion where the bacteria reside. This in turn is dependent on free or unbound antibiotic. The level of free antibiotic also depends on the serum level, destruction by the liver and excretion by the kindeys. The concentration decreases with distance from the blood vessels. Thus, it is important to maintain a high serum level until equilibrium is reached. This is important in relatively avascular lesions such as thick walled abscesses (Fig. 3) (Crofton, 1969). The best known membrane barrier is the blood-brain barrier (BBB) where only a small amount of penicillin penetrates into the CSF of normal people (but more does in meningitis). However, because of the low protein in the CSF, there is little protein-binding so that most of the penicillin is present in free form. Drugs like isoniazid penetrate the BBB well.

Penicillinease-producing staphylococci in the throat may prevent the elimination of haemolytic streptococci by penicillin during prophylaxis treatment of rhuematic valvular heart disease. However, this is not a frequent phenomenon.

Individuals with poor defence mechanisms are likely to fail to respond to antibiotics. Poor defence mechanisms may be due to congenital abnormalities in cell mediated or humoral immunity, chemotherapy (cancer chemotherapy or steroids), diabetes, malignancies such as lymphoma or sarcoma, poor drainage of an organ (e.g. bronchial obstruction).

Bacterial persistence, i.e. sensitive bacteria surviving when the great majority of the bacterial population die, has clinical significance in that they may be responsible for relapse. Such persisters emerge under conditions that favour old bacterial population, presence of poor drainage (e.g.. Brodie's abscess), presence of foreign body and induction of L-forms (unlikely to be affected by antibiotics that act on cell wall). The duration

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of chemotherapy also may result in the development of bacterial persistence. The best example is pulmonary tuberculosis. Tubercle bacilli can be killed in test tubes within a few days, but if there is a large bacterial population it may take 18 months to eliminate a clinical pulmonary infection. This may be due to slow metabolism of the bacteria or they remain dormant for a while and start to metabolize at which time they are dealt with by the drug(s). Other examples include SBE, chronic bronchitis and chronic genitourinary infections (Yow, 1966).

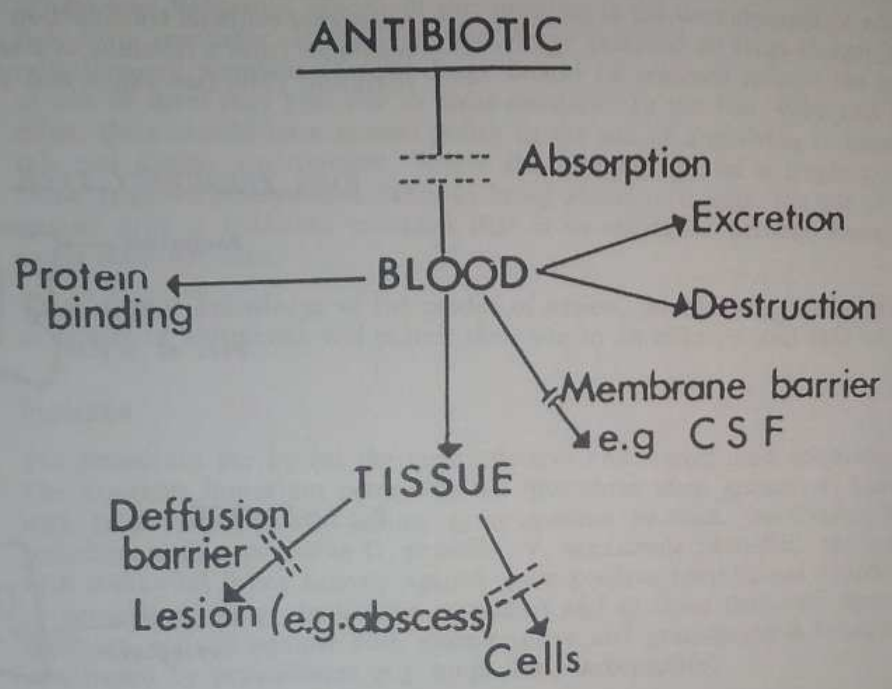


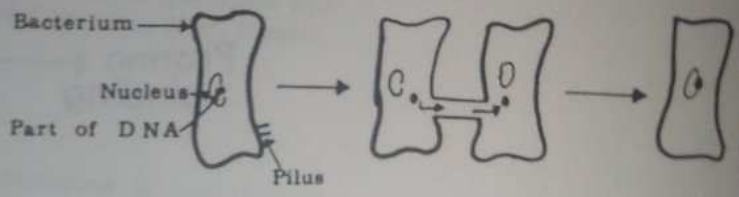
Figure 3. Factors influencing the effect of antibiotics (after Crofton, 1969).

In any clinical situation where anticipated response to antibiotics fails, drug resistance must be considered in the differential diagnosis. There are 3 major groups of resistance: 1) natural drug resistance which occurs in organisms never exposed to drugs before, 2) acquired drug resistance which occurs on exposure to drugs while the patient is on treatment, and 3) transferred ("infectious") drug resistance in which genetic material conferring resistance is transferred from a resistant to a sensitive strain of organisms. Natural drug resistance may occur in bacteria that lack the metabolic process which is affected by the drug in question (e.g. resistance to sulfonamides by producing PABA) or the absence of cell wall as in mycoplasma or L-forms (resistant to penicillins) or by producing enzymes which destroy the drug (e.g. penicillinase by staphylococci). Acquired resistance is usually due to genetically determined mutation. Since this is clinically significant, physicians should be aware of those drugs to which resistance may be readily acquired. Streptomycin, erythromycin, novo-

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biocin and lincomycin belong to a high risk group of drugs that develo acquired resistance readily. On the other hand, penicillin, tetracycline, chloramphenicol, colistin, polymyxin B, gentamycin and cycloserine (in the order listed) belong to a low risk group. Resistance is rapidly acquired to almost all antituberculous drugs when used alone. Transferred resistance is brought about by 3 different mechanisms: transformation, (transfer of parts of the DNA of the chromosome which become recombined within the host bacterial cell — the genes are released into the medium), conjugation (transfer of cytoplasmic genetic material by contact through a cytoplasmic bridge or by a "pilus" — the second cell can transfer it to another cell) and transduction (transfer of genetic material conferring resistance from a resistant to a sensitive strain by means of bacteriophage) (Crofton, 1969) (see Fig. 4 and Fig. 5).

A HIGH FREQUENCY TYPE:



B. R-FACTOR:

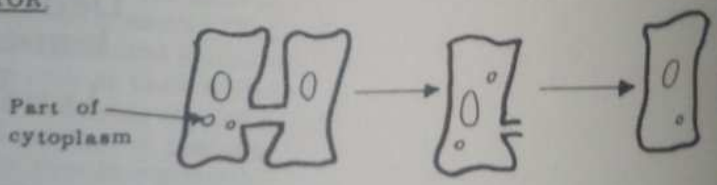


Figure 4. Transfer of drug resistance by conjugation.

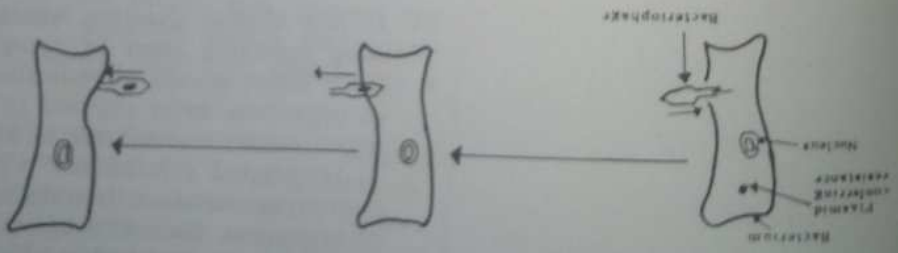


Figure 5. Transfer of drug resistance by transduction.

Some strains of organisms that are resistant to one drug may be resistant to another. Such cross-resistance exists between tetracyclines and it is useless to change one tetracycline to another. There is a relatively common occurrence of cross-resistance among erythromycin, oleandomycin, linco-

mycin, carbomycin and spiromycin. Also there is a risk of cross-resistance between cloxacillin, methicillin and cephaloridine, being complete between methicillin and cloxacillin.

Organisms likely to acquire transferred resistance include those causing typhoid fever, cholera, urinary infections, dysentery, plague, *Klebsiella* species and staphylococci. If antibiotics are used widely and indiscriminately, non-pathogenic organisms may acquire transfer resistance to pathogenic strains as in the case of antibiotic feeding to animals. One of the most dangerous aspects of this problem is the development of multiple drug resistance. If there are few drugs reserved to treat dangerous infections, all members of such drugs should be reserved in case the use of one of them may give rise to cross-resistance to the rest. With this in mind, there should be a general policy in the use of antibiotics in hospitals and similar environment. Where the frequent use of a single antibiotic (e.g. streptomycin) is likely to bring about resistance, the use of a second drug is indicated provided that cross-resistance between these 2 drugs does not exist.

Thus, a clear knowledge of the modes of action, interactions, and causes of failure of antibiotics will permit their use in an effective and safe way.

Penicillin

The penicillins are by far the most effective and widely used antibiotics. The available important penicillins fall into three main groups: a) those with maximum activity against gram-positive bacteria, inactivated by penicillinase (e.g. penicillin G, penicillin V, benzathine penicillin), b) those with somewhat lower activity against gram-positive bacteria but resistant to penicillinase (e.g. methicillin, oxacillin) and c) those that have broad spectrum activity against both gram-positive and gram-negative bacteria, inactivated by penicillinase (e.g. ampicillin, carbenicillin).

The following infections are particularly amenable to penicillin when administered adequately.

Pyogenic meningitis: In paediatric age group, the commonest cause of meningitis is *H. influenzae* while in adults pneumococcal and meningococcal organisms account for most of the cases. In a rural setting, one is limited to CSF Gram stain examination. In the paediatric age group, crystalline penicillin G in a dosage of 500,000 I.U./Kg./24 hrs. at 3-hour interval given intravenously for 10 days along with chloramphenicol has been found to be more beneficial than previously known modes of therapy in Ethiopia (Hadgu and Tafari, 1973). The crystalline penicillin G dosage suggested in the literature is 25-30 million I.U./24hrs. for pneumococcal meningitis and 10-15 million I.U./24hrs. for meningococcal meningitis, intravenously. However, experience has shwon that crystalline penicillin G given in a dose of 2 million I.U. intravenously every 3 hours for 10 days is effective in both types of meningitis.

Pneumonia: The commonest cause of penumonia in Ethiopia is *D. pneumoniae*. A predominance of this organism in a sputum Gran's stain suggests the diagnosis. Controlled studies have shown that procaine peni-

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cillin 600,000 units given twice per day by the intramuscular route is as effective as crystalline penicillin G 20 million units given intravenously for the same duration (Brewin, *et al.*, 1974). Thus the use of the former is easier and cheaper in a rural practice in present Ethiopia.

Gonorrhoea: Penicillin is still highly effective in gonococcal infections of all types. However, one should be aware of a continued trend toward penicillin resistance to *N. gonorrhoea* in Ethiopia (Wright *et al.*, 1970; Dodge and Wallace, 1975). Male patients should receive 2.4 mega units of procaine penicillin I.M. together with 1 Gm. (2 tablets) of probenecid by mouth. Penicillin sensitive patients can be given tetracycline 1.5 Gm. initially followed by 0.5 Gm. four times per day for four days (total dosage 9.5 Gm.). Patients with systemic gonorrhoea infections (arthritis, hepatitis, etc.) should receive procaine penicillin as above for at least 7 days. Persisting urethritis is treated with 4.8 mega units of procaine penicillin with probenecid. Female patients, because of poor defusion of penicillin into the vagina and rectum, require higher levels of penicillin for cure. Procaine penicillin 4.8 mega units I.M. together with 1 Gm. of probenecid by mouth is adequate. Those with pelvic sepsis need daily treatment with procaine penicillin for a longer period. Some infants may still have gonococcal ophthalmitis even after application of silver nitrate. These infants should be given penicillin drops every 4 hours for 5 days.

Syphilis: Primary and secondary syphilis in males is treated with 2.4 mega units of benzathine penicillin G intramuscularly in a single dose. Procaine penicillin 600,000 units I.M. every other day for 8-10 doses or penicillin aluminium monostearate (PAM) in a total dosage of 2.4 mega untis in two divided doses 3 or 4 days apart can also be used. The VDRL titre shows a decrease when measured 6 weeks to 3 months after treatment. However, a rising VDRL titre usually means that the patient has been reinfected and needs to be treated again as above. The treatment for females is the same as above. Infants born of mothers with a positive VDRL serology should receive benzathine penicillin G 50,000 units/Kg. I.M. in a single dose. Infants born with clinical signs of syphilis should receive crystalline penicillin G, in a total dose of 100,000 units/Kg., given in divided I.M. doses over a period of 10 days. Those with latent syphilis without cerebrospinal fluid (CSF) VDRL positivity are treated as primary and secondary syphilis. On the other hand, when the VDRL in the CSF is positive, prolonged treatment with parenteral procaine penicillin G in a total dose of 40-60 mega units in divided doses is indicated (Perine, 1975, unpublished data).

Rheumatic fever: For eradication of streptococcal infection, adults should get 600,000 units of procaine penicillin, b.i.d. for 10 days as prophylaxis, however, benzathine penicillin 2.4 mega units I.M. monthly is the ideal choice.

Subacute bacterial endocarditis: The optimal therapy for endocarditis due to *S. viridans* (or *S. faecalis*) is combined penicillin and streptomycin. This combination has synergistic effect (see introduction) and yields less relapse than penicillin alone (Wolfe and Johnson, 1974). Since follow-up is difficult in a rural health centre, subacute bacterial endocarditis is best

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Clamydia: Acute cases of lymphogranuloma venereum are treated with tetracycline hydrochloride 2 Gm. daily by mouth for 3-4 weeks. When chronic, the duration of treatment is extended to 1-2 months. Psittacosis requires a dose of 2 Gm. daily for 12-14 days while trachomas is treated with either ointment or drops applied 4 times per day for 4 weeks (in severe infections, sulfa may be added).

Bacillary infection: Acute cases of brucellosis are treated with tetracycline 250 mg. every 6 hours by mouth for 3-4 weeks. In severely ill patients the additon of streptomycin 1 Gm. daily I.M. is indicated. Severely ill patients with bacillary dysentery are given tetracycline 250 mg. every 6 hours by mouth for 5-7 days.

One capsule (250 mg.) of tetracycline usually clears the blood of *Borrelia recurrentis* within 4 hours in those who suffer from louse-borne relapsing fever. However, relapse may be prevented by administering tetracycline 250 mg. every 6 hours by mouth for 3 days. While this mode of treatment is easier in a rural health practice, other types of treatment should be also known (Knaack, *et al.*, 1972). There is a preliminary report that suggests a single dose of doxycyline is effective in the treatment and prophylaxis of typhus.

Chloramphenicol

Chloramphenicol possesses a fairly wide spectrum of antimicrobial activity — it is rapidly absorbed from the gastro-intestinal tract, significant plasma concentrations are obtained within 30 minutes and peak values are reached in approximately 2 hours. The drug is inactivated primarily in the liver but about 10% is biologically active before it is eliminated by glomerular filtration. It is poorly absorbed by the intramuscular route.

In rural health practice, where the serological and bacteriological services are inadequate, the use of chloramphenicol which is cheap, readily available and with a wide antimicrobial activity is highly recommended. A febrile patient who is observed over a period of 7 days and investigated with the available laboratory procedures during this period should be given a trial of chloramphenicol 500 mg. every 6 hours orally (or I.V., when indicated) for a complete period of 14 days. Chloramphenicol remains the drug of choice in typhoid fever and *H. influenza* meningitis. There is unpublished data to indicate that combined chloramphenicol and penicillin are effective in pelvic sepsis and gram-negative septicaemia (Duncan, unpublished observation).

The Aminoglycosides

The main aminoglycosides are streptomycin, kanamycin, gentamycin and neomycin. As their name implies they contain amino-sugars in glycosidic linkage and are products of specific species of soil actinomycetes. The characteristics described below pertain to this class of antibiotics as a whole except neomycin which is not used parenterally.

The aminoglycosides are generally effective against gram negative organisms but when used alone resistant strains tend to emerge quickly,

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(Plorde *et al.*, 1970) and this fact as well as their toxicity to the host have limited their clinical use.

They are poorly absorbed from the gastrointestinal tract and have to be given parenterally usually by deep intramuscular injection or less often intravenously unless sterilization of the bowel is required preoperatively or in the treatment of hepatic failure when they are administered orally. They may also be given subcutaneously, intrathecally or intrapleurally. They penetrate into body and fluids satisfactorily but concentration in the cerebrospinal fluid may not reach adequate therapeutic levels in conditions such as *H. influenzae* meningitis when intrathecal administration may be required. But since this route of administration may lead to complications special precautions (indicated in the section on streptomycin) have to be taken.

The aminoglycosides are mainly excreted unchanged through the kidneys. Therefore, adequate renal function has to be ascertained before administering these drugs in the usual therapeutic doses. If the specificity and sensitivity of the infective organism necessitates administration of any of these drugs in the presence of impairment of renal function reduction of the dose in accordance with the degree of impairment is imperative. Passage of these antibiotics in to the foetal circulation in the third trimester of pregnancy warrants the use of safer alternatives in this situation.

Renal toxicity and vestibular damage are the main complications of high dosage and prolonged therapy. Allergic reactions involving the skin, haemopoietic or connective tissue may occur and cross-reactions among drugs in this group is the rule but such reactions generally occur in less than 1% of cases. Prolonged use may also favour super-infection by pathogens resistant to the aminoglycosides due to alteration of the normal flora specially in the gastrointestinal and respiratory tracts.

Specific Aminoglycosides

Streptomicin in the form of the sulphate salt is the oldest aminoglycoside and has been used extensively in the treatment of tuberculosis in combination with other agents and for a large number of other infections in a fixed combination with penicillin.

Streptomycin has been superseded by other antibiotics in the treatment of most infections because of the ease with which organisms acquire resistance to it. But streptomycin is still used in the treatment of tuberculosis in combination with other agents and in bacterial endocarditis due to S. viridans and entrococcus where its combination with penicillin has proven of synergistic value. But the use of fixed combinations of penicilln and streptomycin for general use in pyogenic infections should be condemned because they offer no added advantage over penicillin alone and may lead to the emergence of strains resistant to streptomycin in undetected tuberculosis. Other indications are severe brucellosis in combination with tetracycline and peritonitis due to a ruptured viscus in combination with penicillin. In reference to the last condition it must be borne in mind that in our environment ruptured viscus may be due to typhoid fever which does not respond to streptomycin. 124

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Dosage *Subacute bacterial endocarditis* due to *S. viridans* and enterococci 1 Gm. I.M. daily for 2 weeks (see under penicillin).

Peritonitis due to ruptured viscus (see above): 2 Gm. I.M. daily in 2 divided doses with 20 to 40 million units of penicillin G given parenterally with surgical management as indicated.

Brucellosis: (see above under tetracycline)

Granuloma inguinale and *chancroid*: 2 Gm. in 2 divided doses for 7 to 10 days.

Contraindications: Allergy and renal insufficiency. Intraperitoneal administration may lead to respiratory arrest.

Gentamicin: is expensive and should not be used except where culture and sensitivity has revealed resistance to safer drugs and sensitivity to this agent or where a life threatening gram negative infection is strongly suspected. It is especially useful in *Pseudomonas*, *E. coli*, *Klebsiella* and *Enterobacter* infections. Gentamycin may cause gastrointestinal irritation, skin reactions and disturbance of liver and renal function. But its main toxicity is in the vestibular system especially in the presence of renal insufficincy which is a relative contraindication to its use in the absence of facilities for determination of the serum concentration. Gentamicin is contraindicated in pregnancy. Dosage: Gentamicin sulphate 3-5 mg./Kg. body wt. per day in divided doses every 12 hours for 5-7 days.

Kanamycin has a range of antibacterial activity similar to that of gentamicin but it is ineffective against *Pseudonomas* while it is more effective against *Staph. aureus*. It has marked ototoxicity as well as nephrotoxicity and the restricted indications for its use are similar to those for gentamicin.

Neomycin and Paramomycin tend to cause nerve deafness and renal damage rather more frequently than the other aminoglycosides and are not recommended for parenteral administration. Neomycin, which is a broad spectrum antibiotic, is used in skin infections and, orally, for preoperative bowel preparation and in hepatic coma in a dose of 3 to 8 Gm. daily. Malabsorption or superinfection may complicate its oral use. Paramomycin is mainly used in the treatment of intestinal amoebiasis Both drugs are very expensive and the clinician should only use them when cheaper agents are found ineffective. For instance, ampicillin (see above under ampicillin) can give satisfactory results in the treatment of hepatic coma.

Miscellaneous Antibacterial Agents

Only erythromycin will be discussed at some length under this heading. The other antibiotics, though useful under specific circumstances, are last resort drugs to be employed when bacteriologic tests or the patient's critical condition warrant their use regardless of cost or toxicity.

Erythromycin is a macrolide antibiotic which is bactericidal or bacteriostatic for gram positive organisms, *Treponema pallidum* and mycoplasma. It is prepared in the form of salts such as estolate, stearate and ethylsuc-

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estate for oral administration and is readily absorbed when given by this route. It diffuses readily into tissues and body davities and fluids including the cerebrospinal fluid in meningitis. While a small portion is excreted by the kidneys, the main portion is concentrated in the liver and goes into the bile. Hypersensitivity may occur and the estolate salt may cause cholestatic hepatitis.

Ethromyicin is mainly used as an alternative to penicillin when allergy occurs against the latter. Dose: 250 to 500 mg. 6 hourly for 10 days, orally.

Nitrofurantoin is used in the treatment of urinary tract infections. It is readily absorbed from the gastrointestinal tract and concentrated in the urine. Gastrointestinal irritation may occur especially when the drug is taken on an empty stomach and hypersensitivity reactions, which may involve the skin, haemopoietic system, liver, lungs and neurological system may develop. The dose is 5 to 10 mg./Kg. per day in four divided doses. This drug is contraindicated in renal insufficiency, pregnancy and infancy below 3 months of age.

Nalidixic acid has similar antibacterial properties to nitrofurantoin in the urinary tract. It is readily absorbed from the gastrointeatinal tract but may cause irritation as well as allergic manifestations in other systems. The adult dose is 1 Gm. four times daily for 1 to 2 weeks or 45 mg./Kg. body wt. The drug is not recomended for use in early infancy.

Sulfonamides

Sulfonamides were the first effective chemotherapeutic agents against microorganisms. Sulfonamides are cheap, stable and have a broad spectrum of bacteriostatic activity but resistant strains tend to emerge quickly. The presence of pus, because of the high content of PABA, reduces the efficacy of sulfonamides.

They are easily absorbed from the gastriontestinal tract and subcutaneous sites and diffuse into tissues and body cavities. Sulfonamides are excreted by the kidney while some are oxidized and acetylated in the liver.

A variety of allergic manifestations including fixed drug eruption, vascular lesions, drug fever, serum sickness, and hepatitis may occur during treatment with this class of drugs. Crystalluria and haematuria may occur leading to renal damage particularly when urine volume is reduced or when the pH is low. The use of newer preparations with higher solubility and combinations of sulfonamides taking advantage of the independent solubility of each has successfully circumvented the problems of crystalluria and haematuria. Representative preparations are sulfadiazine, sulfisoxazole, sulfamethopyridazine and succinyl-sulfathiazole. Sulfadiazine and sulfisoxazole are abosorbed and excreted rapidly, sulfamethoxypyridazine is rapidly absorbed but excreted slowly while the last preparation is poorly absorbed from the gastro-intestinal tract.

The sulfonamides are mainly indicated for the treatment of bacillary dysentery and urinary tract infections. The dose of sulfisoxazole is 2 Gm.

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initially followed by 1 Gm. every 4 to 6 hours or 150 mg. per Kg. ...
of which is given as a loading dose and the remainder in divided doses. The duration of treatment for urinary tract infection should not be less than 14 days. Triple sulfa consisting of sulfadiazine, sulfamerazine and sulfamethazine or sulfacetamide may be used in similar doses. The use of sulfa in conjunction with penicillin for the treament of meningococcal meningitis is no longer advocated because of the emergence of strains resistant to sulfa (Wright *et al.*, 1970).

Trimethoprim-Sulfamethoxazole: This combination of 2 agents was designed to prevent the emergence of bacterial resistance. The combination consists of 80 mg. trimethoprim to 400 mg. of sulfamethoxazole giving a serum concentration of 1:20 ug per ml.

The use of the drugs my be followed by skin reactions or blood dyscrasias.

This combination has a wide variety of uses but is mainly indicated for the treatment of urinary tract infections with organisms such as *E. coli* and *P. mrabilis*. The usual dose for adults is 2 tablets every 12 hours for 7 — 10 days.

It is contraindicated in severe renal diseases and the high cost of most brands would limit justification of their use to those infections that are life threatening or resistant to cheaper preparations.

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A PRELIMINARY REPORT ON ONCHOCERCIASIS IN NORTH WESTERN ETHIOPIA

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It is well known that human onchocerciasis occurs in Africa in a zone which stretches from Senegal and Angola in the west to Ethiopia and Tanzania in the east. The 15°N latitude is said to be roughly the northern limit (WHO, 1966; Duke and Anderson, 1972). While the distribution of this disease in Africa is fairly determined, isolated foci had been reported in northern Sudan (Kirk *et al.*, 1959) and Yemen (WHO, 1962). Begemdir and Simen (the north-western province of Ethiopia) borders the Sudan where, according to reports by Haseeb and co-workers (1962) and Abdela (1974), onchocerciasis is known to be endemic; however, to the best of our knowledge, onchocerciasis had never been reported from this Ethiopian province. In Ethiopia, onchocerciasis has been reported by Oomen (1967, 1968) and Iwamoto *et al.*, (1975) in Kaffa and Illubabor provinces respectively. Onchocerciasis constitutes one of the major causes of morbidity in Wollega Province. (Wollega Health Department Report, 1972).

Metema-Humera lowland is an area which borders the Sudan between Shinfa on the south and Tekeze river on the north and is within the onchocerciasis belt. It is a semi-arid acacia country with average altitude of 600 metres and day time temperature of 45°C. Within the last 10 years, a fairly extensive agricultural development has taken place in this region and has attracted a large migrant labour force from the neighbouring provinces of Wollo, Gojjam, Tigre and Eritrea (Belcher *et al.*, 1969). Most of these migrant labourers cross the border and work on agricultural projects in the Sudan during some part of the year. Presumably as a result of such major population movement and its concentration on the western strip of this province, (Figure 1), Gondar Hospital staff has witnessed significant change in the pattern of diseases within the last few years. To the best of our knowledge, onchocerciasis had never been reported from Begemdir and Simen Province in general and Gondar Hospital in particular.

Background

During 1967 and 1968, two senior Health Officer students made a survey of onchocerciasis in patients of the Gondar Hospital and neighbouring health centres. The survey included all patients from the different districts of the province; the sample size was 616 patients that had skin snips. They did not find a single positive skin snip; Mazzotti's test was not performed. In July 1973, two biopsy specimens from the surgical department of the hospital were reported positive for onchocerciasis. In October 1973, a patient with the chief complaints of intense pruritus, skin lesions and nodules compatible with onchocerciasis was admitted to the hospital from the Sudan border. A provisional diagnosis of onchocerciasis was made, however, the patient left the hospital against medical advice before a definitive microscopic diagnosis was established. Early during 1974, Dr. Eyassu

Habte-Gabr, saw labourers with skin lesions suspicious of onchocerciasis in Metema-Humera.

Accordingly, the present investigation was carried out to explore the possible occurrence of onchocerciasis in Begemdir and Simen.

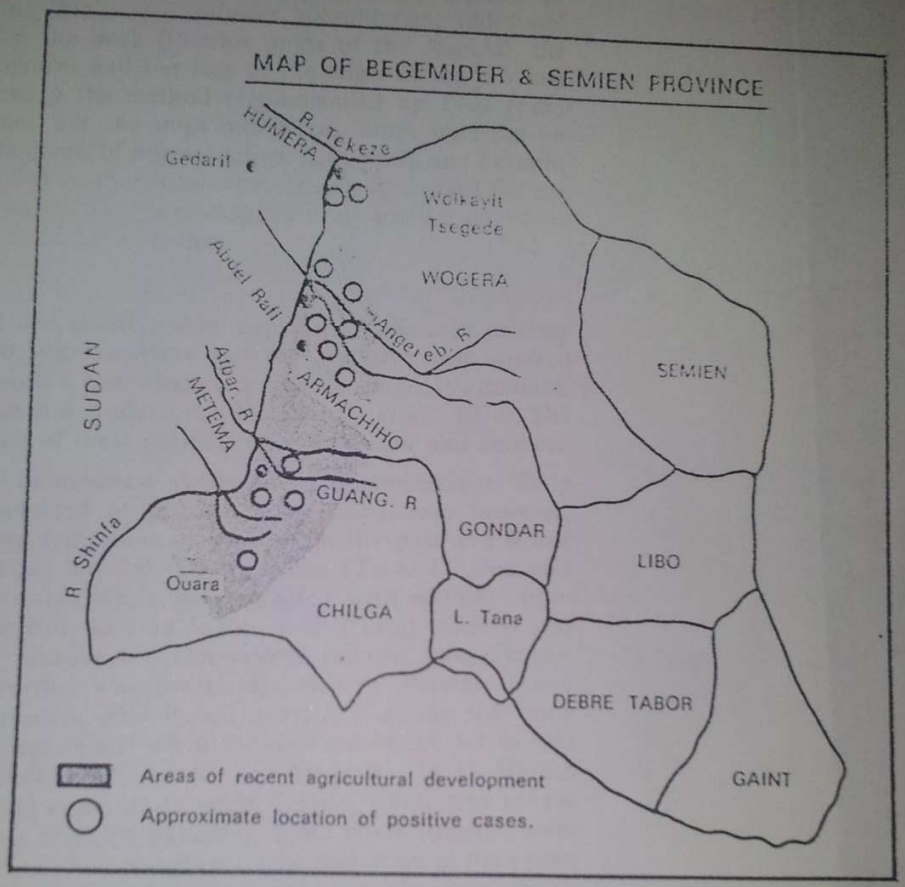


Figure 1

Patients and methods

Assuming that the most likely endemic foci is Metema-Humera, all patients who came from this region directly or gave history of residence, for at least some months, or worked on the farms in this area were studied. They were predominantly labour migrants within the 20-39 years age range and all were males. The study included both medical and surgical patients of Gondar Hospital. Since patients coming from Metema-Humera are few in number, all such patients presenting during the study period (April — July 1974) were included. A complete medical history, as well as history of travel to Metema-Humera, the Sudan and other places, were obtained.

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A history of pruritus, the time of insect bites, nature of occupation and presence of rivers near dwelling and work places were recorded. A complete physical examination and routine laboratory tests were performed upon all patients. A total of 19 patients were studied. Mazzotti's test was performed upon most patients with 50 mg. of diethylcarbamazine citrate. Patients who had positive skin snips with signs and symptoms intending not to go back to the Metema-Humera lowlands were given a seven-day course of treatment with diethylcarbamazine according to the schedule recommended by Duke and Anderson (1972).

Three skin snips were taken from each patient. A 3-4 mm. diameter skin snip was taken according to Duke and Anderson (1972). The snips were taken from the pelvic girdle, the thigh and the leg (pretibial region). In those that were positive for *Onchocerca volvulus* microfilariae, additional skin snips were taken from the back (inferior angle of the scapula), the dorsal aspect of middle forearm and the face at the angle of the jaw just below the ear lobe. Following the method recommended by Tada *et al.*, (1973), we neither tested nor cut the snips into pieces. Snips were put on separate labelled slides with drops of normal saline, kept warm and examined over 20-30 minutes. It was further incubated, dried and stained for examination under the microscope for morphological study and for quantifying the number of microfilariae per skin snip.

Results

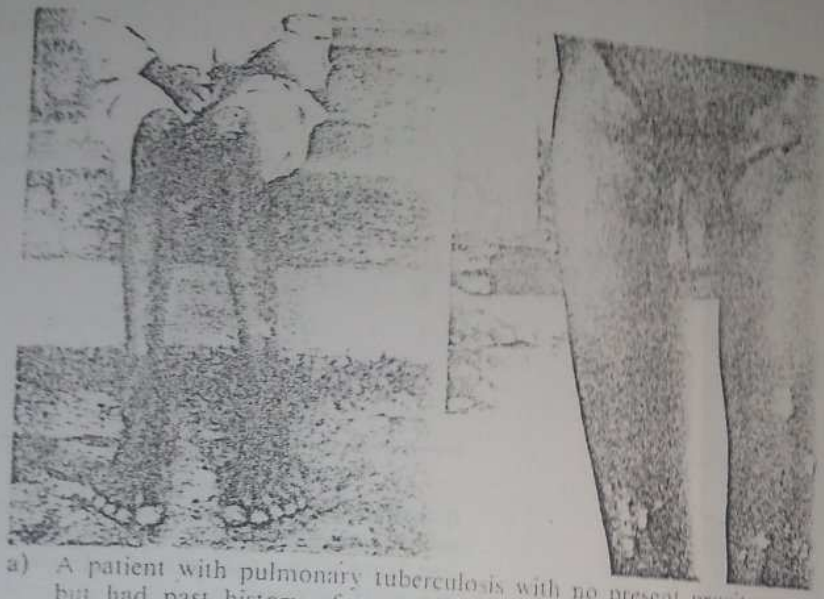
Out of the 19 patients, 12 had positive skin snips for *Onchocerca volvulus* microfilariae. All the skin snip positives and one negative case showed positive reactions to Mazzotti's test which is a reliable diagnostic method. (Manson Bahr, 1966; Duke and Anderson, 1972; Martin *et al.*, 1974). The main reasons for admission of these patients were kala-azar and beriberi.

Pruritus is purported the commonest symptom in onchocerciasis. Only two of our patients complained of pruritus upon admission; however, 19 patients admitted having symptoms of pruritus in the past and 6 had itching during hospitalization, but did not complain. (Table 1). One case of kala-azar developed pruritus while being treated with sodium stibogluconate (Pentostam). He had no skin lesions and a drug reaction was suspected. Skin snip was positive for *Onchocerca volvulus* microfilariae. Community history of pruritus was invariably positive. Patients stated that there were many labourers who itched especially during the rainy season (July, August and September) when the daytime insect bite is said to be very annoying (Horsfall, 1962; Adams and Magraith, 1971). Sixteen patients had worked near and swam in Angereb, Guang, Shinfa and Tekeze rivers. Most of the positive cases (8 patients), came from Angereb river basin (Figure 1). Seven patients had travelled to the Sudan more than once coming back to Ethiopia during the rainy season when employment opportunity on the farm is available and going to the Sudan during the dry season from January onwards. Many positive cases showed thickened, hyperpigmented and excoriated skin mainly on the legs.

Depigmentation is not common and in those that had, it was noted upon pretibial area. (Figure 2). Nodules were small in size and required careful palpation. Two patients had barely palpable nodules over the iliac crests bilaterally and two others over the sacrum in the midline. Only two men had inguinal and femoral lymphadenopathy. One of these had severe pyogenic

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Figure 2



a) A patient with pulmonary tuberculosis with no present pruritus now but had past history of severe itching on the legs, thigh and buttocks three years ago. He has pretibial depigmentation but no nodules.
b) A patient showing inguinal and femoral lymphadenopathy. He had super-infected skin lesions on the legs and thighs.



c) This is the on'y patient who came with the chief complaint of pruritus He had papules, macules, excoriated skin all over the body, including the face. Duration of symptoms is six months.
d) The same case as in (c.) showing vesicular and papular lesions developing on the forehead after Mazzotti's test. He had acute conjunctivitis which was controlled with Prednisone.

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TABLE 1: Frequency of certain histories, symptoms and signs in the 19 patients.

Residence in Metema-Humera	19
Daytime insect bites	19
Pruritus (past or present)	16
Community history of pruritus	16
Work near river	14
Travel to the Sudan	7
Excoriation, thickened and hyperpigmented skin with maculopapular lesions	9
Depigmentation	4
Nodules	4
Lymphadenopathy	2
Lymphoedema	0
Eye lesions	0

skin lesions which cleared with procaine penicillin, but left hyperpigmented areas. (Figure 2). Two patients had complaints of night blindness and one of these had Bitot spots. Visual acuity during the day was normal and fundiscopy did not reveal any abnormality in the eye grounds. However, four patients had acute conjunctivitis and oedema of eyelids following administration of 50 mg. diethylcarbamazine.

Discussion

Twelve positive (63%) of 19 patients, is a relatively high percentage for onchocerciasis in a population not indigenous to an endemic region.

A comparison of the clinical manifestations between our patients and those that Oomen (1967, 1968) described in Kaffa, revealed quite different presentations. The absence of scrotal elephantiasis, adenolymphocele and rare nodules or onchocercomata is probably due to either mild infection with a limited transmission season or short residence of our patients in Metema-Humera. Anderson *et al.*, (1974) found differences in clinical signs in rain-forest and Sudan-Savanna in the United Cameroon Republic. Metema-Humera is typical of Sudan-Savanna with transmission being limited to the short rainy season. The labour migrants reside in this region for not more than six months.

Most workers take skin snips from the buttocks in surveys for onchocerciasis. Although the size of our population is small, our findings (Table 2) do not support this procedure because skin snips from the leg and thigh yielded a greater number of positive snips and microfilariae per skin snip.

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Whether onchocerciasis is limited to Metema-Humera in Begemdir and Simen is doubtful and requires further study. Onchocerciasis, however, is present on the Sudan border of north-western province of Begemdir and Simen and might have been introduced recently as a result of extensive agricultural projects and population movement in this region.

TABLE 2: Density of microfilariae on different sites of the body, number of microfilariae per skin snip

Case No.	Leg	Thigh	Pelvic Girdle	Back	Forearm	Face
1	5	3	2	—	—	—
2	2	1	1	—	—	—
3	1	0	—	—	—	—
4	2	1	0	0	0	0
5	0	1	0	0	0	0
6	20	25	3	2	1	1
7	1	1	0	0	0	0
8	5	6	10	8	1	1
9	17	7	2	2	3	1
10	2	2	1	4	1	0
11	0	0	2	2	4	0
12	0	0	2	0	0	0
Average No. of Microfilariae per Skin Snip	5.3	4.8	2.2	2	1.1	0.3

Slides were broken; calculation is based upon cases 4 through 12.

Summary

From 19 patients who came from Metema-Humera lowlands, 12 were positive for *Onchocerca volvulus* microfilariae. Most positive cases were migrant labourers who worked on commercial farms in Metema-Humera lowland; except for two, all had been working in river basins. From a community history of pruritus during the rainy season, one might conclude that there are probably thousands of cases of onchocerciasis on the western strip of this province.

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CASE REPORT

ACUTE ERYTHRAEMIC MYELOSIS (DI GUGLIELMO SYNDROME)

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INTRODUCTION

Acute erythraemic myelosis was described by Di Guglielmo in 1923. It is represented by a generalized proliferation of the erythropoietic cells of the bone marrow, analogous to the leucocytic proliferation of leukaemia. The blood contains erythroblasts in all stages of maturation but the most immature forms predominate. Atypical forms, and erythroblasts with multilobed nuclei and altered nucleocytoplasmic ratios, are also found. There is a slight leucopenia, and occasional myelocytes and metamyelocytes may be found in the blood smear (Wintrobe, 1961).

Erythraemic myelosis has been recognized in both acute and chronic forms (Schwartz and Critchlow, 1952; Dickenman *et al.*, 1957; Dameshek and Baldini, 1958; Roath and Israels, 1962; and Scott *et al.*, 1964) and has been the subject of long consideration by the late William Dameshek (Dameshek, 1951, 1969).

The case now reported is that of the Di Guglielmo syndrome in an Ethiopian, in whom the disease endured for approximately one year and terminated as an acute myelogenous leukaemia.

CASE REPORT

A twenty-one year old Kembata Ethiopian male was referred from Metahara Sugar Estate to Wonji Hospital on January 16, 1970, with a two-week history of tiredness, anorexia, and bloody diarrhoea. He was found to have anaemia (hæmoglobin 4.5 g.), amœbic dysentery and hookworm infestation; he had also a white cell count of 24,000 per c.mm., but this was overlooked. He was treated first with parenteral emetine, and thereafter with chlorphenoxamide, bephenium hydroxynaphthoate, and ferrous sulphate, and was discharged after two weeks of hospital stay.

He returned to the Hospital on February 25, complaining still of tiredness and anorexia. On examination he was puffy-eyed, poorly nourished, and looked ill. He was pale but not jaundiced. There were a few small but palpable cervical glands and moderate hepatosplenomegaly, and no other significant findings. The haemoglobin was now 3.8 g. per cent, despite continued ferrous sulphate therapy, and the white cell count (WBC) was 34,100 per c.mm. with 77 per cent segmented, 17 per cent lymphocytes, 4 per cent monocytes, and 2 per cent eosinophils. The blood smear showed

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a normochromic anaemia with nucleated red cells and 5 per cent reticulocytosis: the white cell morphology was thought to be normal. There were no malaria parasites in the blood, the erythrocyte sedimentation rate was 100 mm. in the first hour, and the blood urea nitrogen was 40 mg. per cent. The urine showed consistently protein, granular casts, and pus cells. The stools still showed hookworm ova (approximately 10 per coverslip). A chest x-ray showed enlargement or prominence of the hilar shadow. At this stage he was thought to be suffering from nephritis and hookworm disease, and he was managed on penicillin, bephenium hydroxynaphthoate, parenteral iron (Jectofer), and a diet rich in protein and without added salt. On this regime his anaemia improved slightly, whereas his general condition deteriorated at an alarming rate. Although there was no clear indication for doing so, he was given also folic acid and parenteral vitamin B_{12}.

On March 27 the investigations were repeated and reviewed. The haemoglobin was now slightly higher at 5.5 g. per cent, the WBC 26,800. The Coombs test was negative, both direct and indirect. A bone-marrow smear was found to be rich in cells and the erythropoietic cells heavily predominated and were megaloblastic in type; iron staining of a marrow smear suggested that the iron content was normal. The plasma albumin : globulin ratio was 1.5 : 1. The urine showed granular and hyaline casts and much protein although not of the Bruce-Jones type. X-rays of the long bones and skull showed a generalized osteoporosis. The patient was still deteriorating, with an abcess now in the right foot, a fever, and a noticeable increase of the hepatosplenomegaly; incision and drainage of the abscess yielded pus which showed Gram-positive cocci. Treatment was also reviewed and doxycycline (Vibramycin) and prednisone (45 mg. daily) both prescribed.

In early June the patient was subjectively improved and the abscess had healed, but the anaemia was unchanged. The haemoglobin was 5.2 g. per cent and the WBC 55,300 per c.mm., and the peripheral blood smear now showed a great number of erythroblasts in various maturation stages and cells with multilobed nuclei, together with immature myeloid cells. The diagnosis of Di Guglielmo syndrome was considered established. Six weeks later, on July 17, the blood picture had changed completely: the erythroid hyperplasia had disappeared, and was replaced by the features of acute myeloid leukaemia, with WBC 520,000 per c.mm., platelets 130,000 per c.mm., and numerous atypical myeloblasts and myelocytes. The patient developed generalized lymphadenopathy, suffered intercurrent infections, and despite treatment with busulfan, died in the middle of November, 1970. A postmortem wedge biopsy of the spleen confirmed the final diagnosis of myeloid leukaemia.

DISCUSSION

According to diagnostic criteria given by Ridell and Davidson (1968), the case presented here is most likely to have been acute erythraemic myelosis. The Di Guglielmo syndrome comprises all the leukaemias wherein the proliferation of nucleated red cells is a major feature. The syndrome

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includes acute erythraemic myelosis, in which immature erythroblasts dominate the picture of both marrow and peripheral blood; chronic erythraemic myelosis, wherein more mature nucleated red cells predominate; and erythroleukaemia, in which proliferation of nucleated red cells is accompanied by equally obvious proliferation of immature myeloid cells. All the types of initial presentation may transform terminally into a proliferation mainly of myeloid cells; the leukaemia thus observed may be almost entirely myeloblastic in appearance, or less acute and showing both myeloblasts and myelocytes in the peripheral blood smear.

Acute erythraemic myelosis has some haematological similarities to advanced pernicious anaemia which may lead to confusion with diagnosis, as in the present case. Normal to high levels of vitamin B_{12} have been found in chronic erythraemic myelosis (Spray and Witts, 1958; Baldini *et al.*, 1959).

It is possible that vitamin B_{12} therapy achieved a small rise in the haemoglobin of our patient, but further speculation on this point is not justified. The transition to myeloid leukaemia, observed in this case, has been well documented and expresses the relationship of the Di Guglielmo syndrome to other myeloproliferative disorders (Dameshek, 1951, 1969; Gunz, 1958).

There is no effective treatment for erythraemic myelosis and although blood transfusion may provide useful support, the prognosis is poor and survival measured in months. Busulfan is the drug of choice in the late manifestation of myeloid leukaemia.

SUMMARY

A case is reported of the Di Guglielmo syndrome in an adult Ethiopian male. Presenting initially with acute erythraemic myelosis, the patient later developed acute myeloid leukaemia.

RESUME

Un cas de Di Guglielmo syndrome a été reporté d'un Ethiopien adulte male. Presèntant au dèbut un myelosis erythraemique acute, par la suite le patient a developê une leukaemie myeloide acute.

ACKNOWLEDGMENTS

I should like to thank Professor Bjornesjo and acknowledge his advice on the marrow and peripheral blood smears. I am grateful also to Professors Leithead and Samuel for encouragement and for help with this paper, and to Ato Makonnen Yimam of the Wonji Hospital for his help in the laboratory investigation of the patient.

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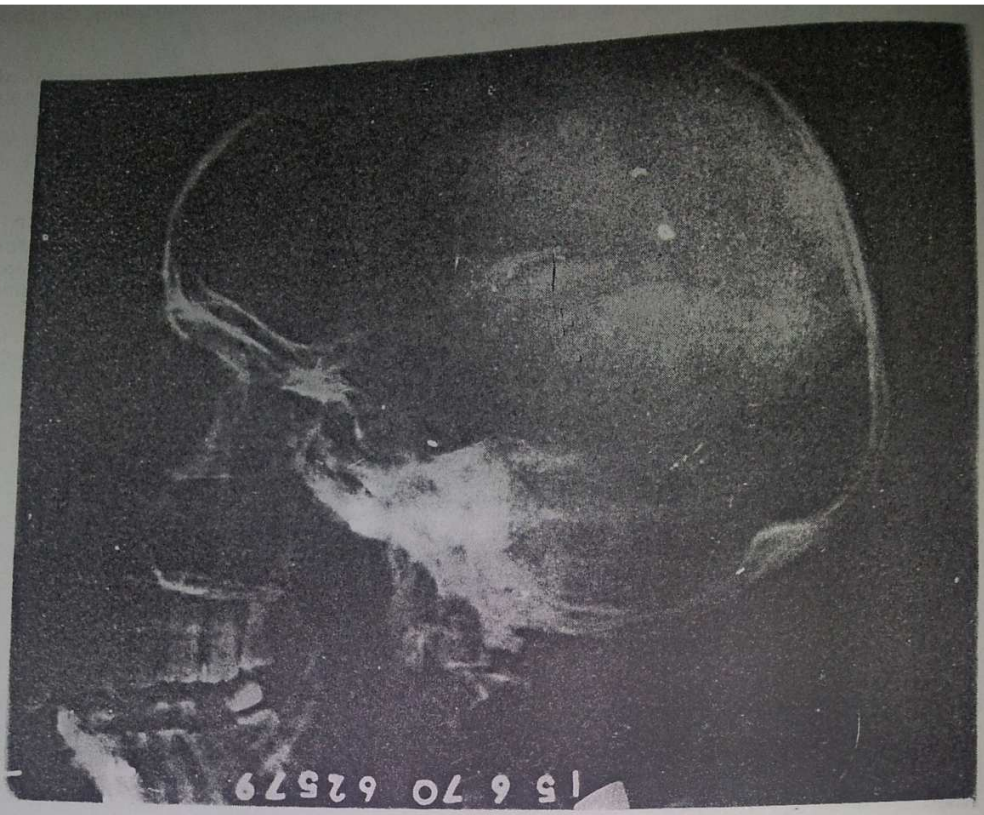


Figure 2: Skull X-ray of the case showing osteolytic lesions.

duction in the normal level of immunoglobulins and should be treated accordingly. Patients with hyperuricaemia or hypercalcaemia were effectively treated with allopurinol and corticosteroids, respectively (2,5). The objective behind specific therapy is to arrest the further proliferation of myeloma cells. The structural damage already made is irreversible. Many drugs have been tried in the treatment of myelomatosis. Stilbamidine, methotrexate, vinblastine and hydroxyurea were found to be ineffective (5). Other drugs such as urethane and corticosteroids produced subjective and objective improvements but did not prolong life (5). On the other hand, cyclophosphamide and melphalan have been shown to be effective in alleviating the pain and prolonging life in over 50 per cent of cases (1,3,6). These drugs may be given on a daily basis or intermittently. According to Malpas (5), the intermittent use of melphalan and corticosteroid gives better results than daily treatment and appears to be the currently preferred regimen (7). These cytotoxic drugs are contraindicated in patients with severe anaemia, leucopenia and thrombocytopenia. The patient, started on cyclophosphamide, left the hospital before the result of the treatment could be evaluated.

We wish to thank Ato Abdulkadir Ahmed and Wro. Mulunesh Zerihun for their technical assistance.

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Based on the clinical, laboratory and radiological findings, the diagnosis of multiple myeloma was made and oral cyclophosphamide 200 mg. daily was begun on 5-III-78. However, the patient was taken away by her relatives on 13-III-78 against medical advice.

DISCUSSION

In a country like Ethiopia where infectious diseases are prevalent, it is perhaps justified to think often in terms of these diseases. Nevertheless, the existence of rare diseases such as multiple myeloma should be considered. The main complaint in this patient was bone pain. Low backache, or bone pains have been reported as common presenting symptoms of myelomatosis (1,2). The presence of osteolytic lesions, typical bone marrow findings and an elevated erythrocyte sedimentation rate, as in this patient, are important diagnostic features. Patients with Bence Jones proteinuria are reported to have a poor prognosis (2,3,4). The serum protein electrophoresis showed a gamma spike in this patient as in almost half of Otieno and Ogada's patients (2). The therapeutic approach to myelomatosis includes both supportive and specific measures. Supportive therapy alleviates pain or treats complications. Deep X-ray therapy to a localized skeletal lesion gives rapid relief. Infections, especially chest infections, are common complications because of a re-

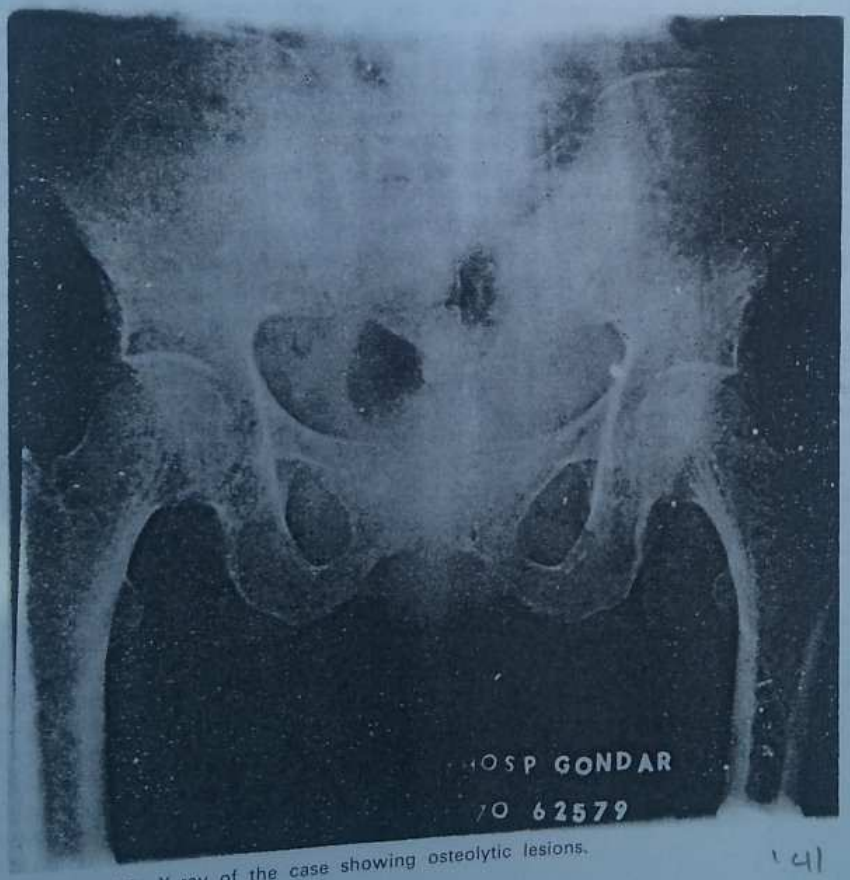


Figure 1: Pelvic X-ray of the case showing osteolytic lesions.

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MULTIPLE MYELOMA: A CASE REPORT AND REVIEW OF THE CURRENT THERAPY

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ABSTRACT: *A 50-year-old housewife presenting with weakness, anoroxia, weight loss, intermittent fever and severe bone pain is described. The elevated erythrocyte sedimentation rate, the homogeneous spike on serum electrophoresis, the osteolytic lesions, and the bone marrow findings confirmed the diagnosis of multiple myeloma in this patient. The currently available treatment is reviewed.*

Multiple myeloma is a malignant disease of plasma cells. It occurs usually in middle-aged and elderly people and is characterized by a proliferation of the plasma cells throughout the bone marrow. Sometimes it starts as an isolated tumour mass, but eventual dissemination is the rule. Bone marrow failure, bone destruction, increased susceptibility to infection, metabolic disturbances such as hypercalcaemia, hyperuricaemia, amyloidosis, uraemia and damage to other organs like the nervous system, the spleen and the liver, and rarely the lungs as well as other structures, are complications which may occur with the progress of the disease.

Like other malignant diseases, the incidence of this invariably fatal disease is unknown in Ethiopia. In this paper, a case of multiple myeloma seen at the Public Health College Hospital, Gondar, is presented and the current therapy is briefly reviewed.

CASE REPORT

D.T. (Hospital No. 62579), a 50-year-old housewife, was admitted to the Public Health College Hospital on 22—II—78, complaining of severe pain over the pelvic bones and the lumbar vertebrae, weakness, poor appetite and intermittent fever of 4 months' duration. The bone pain became progressively worse until finally she was immobilised. On examination, she appeared chronically ill and in pain. The vital signs were within normal limits. The mucous membranes were pale. There was no palpable lymph node or gland. The lungs were clear to percussion and auscultation. There was an apical grade 2-6 systolic murmur. There was no palpable organ or area of tenderness in the abdomen. There was no flank or costovertebral angle tenderness. She had exquisite tenderness over the lumbar vertebrae and the pelvic bones. The rest of the physical examination was unremarkable.

The white bloodcell count was 6,500/mm^3 with a normal differential. The erythrocyte sedimentation rate was 107mm in the first hour. The haemoglobin was 9gm%. The urinalysis showed proteinuria with a positive Bence Jones' protein. The total serum protein was 9.5gm%. The serum protein electrophoresis revealed 36% albumin (normal 50-60%) and 64% globulin of which 35.6% was gamma globulin (normal 13% to 23%), 8% $beta_2$, 7% $beta_1$ (normal 9.3% to 15%), 9.9 $alpha_2$ and 3.5% $alpha_1$ globulin (normal 4.2% to 7.2%). The serum calcium and phosphorus were normal. The serum uric acid and blood urea nitrogen were not tested. The VDRL was non-reactive. The bone marrow morphology showed 55% plasma cells, 19% neutrophils, 16% myelocytes, 7% eosinophils, 2% erythroblasts and 1% lymphocytes. The pelvic, skull and lumbosacral spine radiographs demonstrated multiple punched-out lesions (Figures 1 and 2)

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NON-TRAUMATIC ADHESIVE ARACHNOIDITIS AS A CAUSE OF SPINAL CORD SYNDROMES. INVESTIGATION ON 507 PATIENTS†

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Abstract. Epidemiology and pathogenesis of spinal cord syndromes due to adhesive arachnoiditis are discussed. The similarity of those syndromes with classical syringomyelias is pointed out. Two studies in Ethiopia indicate that in the majority of patients there is no benefit from treatment with antibiotics and steroids.

Key words: Non-traumatic adhesive arachnoiditis; Spinal cord syndromes; Syringomyelic sensory pattern; Radiculo-myelopathy.

Introduction

ADHESIVE spinal arachnoiditis, a rather rare condition in Europe, is a common problem in the developing world. Several earlier authorities from the numerous papers on the issue should be mentioned here (Charcot & Joffroy, 1869; Joffroy, 1873; Horsley, 1909; Elkington, 1936). Arachnoiditis after tuberculous meningitis was described by Brouwer (1931), Ransome and Montiero (1947), Arseni and Samitca (1960), Bawa and Wahi (1961), Jenkins (1963), Parsons and Pallis (1965), Wadia and Dastur (1969), Dastur and Wadia (1969), Tandon and Pathak (1973), Wadia (1973), Freilich and Swash (1979) and others.

In the course of 2 years in the newly established Neurological Unit of the Department of Medicine at the Black Lion Hospital, University of Addis Ababa, we saw 1305 new patients, including 507 patients with symptoms suggestive of arachnoiditis. We undertook a retrospective study of 154 patients seen between January and December 1976 and a prospective study of 353 seen between January and October 31, 1977, at which time the investigation had to be terminated.

Methods of assessment. In addition to a detailed neurological examination all patients of the prospective study had a full blood count, ESR and blood urea nitrogen determination. The VDRL test of serum was performed in all prospective study patients and the Mantoux test in 114 consecutive cases. The

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† Based on a preliminary report at the Fourth Annual Conference of Neurological Society of Kenya, Nairobi, 19 March 1977 as well as a further completed paper read at XIIIth Annual Medical Conference of the Ethiopian Medical Association, Addis Ababa, 26 May 1977.

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was performed in [illegible] patients.

Results

The patients came from all parts of Ethiopia. There were five 'foreigners'—three Europeans and two Asians. All the non-Ethiopians had lived in the country for at least 1–2 years before the onset of symptoms. Patients from all socio-economic groups were seen, although the majority came from the lowest.

Age and sex. Table I shows that the age ranged from 7–65 years (mean 31) and that men were more frequently affected than women (ratio 3 : 2).

TABLE I

Age and sex distribution

Age	Males	Females	Total	%
7–10 years	1	—	1	0·2
11–15 years	8	4	12	2·3
16–20 years	28	32	60	11·8
21–25 years	63	40	103	20·3
26–30 years	62	53	115	22·7
31–35 years	47	17	64	12·6
36–40 years	42	17	59	11·6
41–45 years	32	9	41	8·1
46–50 years	15	12	27	5·3
51–55 years	6	4	10	2·0
56–60 years	9	2	11	2·1
61–65 years	2	2	4	0·8
Total	315/62·1%	192/37·9%	507	100
Mean age	31·9 years	29·5 years	31·0 years	

Onset. Of 255 consecutive prospective study patients the onset was insidious in 160, i.e. 62·7 per cent. In 65 (25·5 per cent) the neurological symptoms began acutely or subacutely following a febrile illness characterised by malaise, nausea and sometimes stiff neck. In 30 patients (11·8 per cent) the neurological symptoms began subacutely without awareness of a preceding acute illness, (with the exception of patients with a history of gonorrhoea or syphilis occurring a year or more before).

Patients in the prospective series (255) presented the following complaints of dull pain in the lumbar region with sensory and motor symptoms in the legs, with or without sensory and motor symptoms and pain in the neck, shoulders and arms. Other patients complained of a burning sensation in the head and frequently of headache. Sphincter disturbances (20 per cent) and decreased sexual potency (31 per cent) were relatively common. Finally, symptoms of intracranial disorders were sometimes encountered—dizziness and loss of balance (13 per cent), impairment of hearing (18·5 per cent), epilepsy (5 per cent) and some with memory impairment.

Course—duration of symptoms

Progression of the symptoms was usually gradual with even long periods of relative stabilisation. At one extreme there were patients who had had symptoms for 10 to 20 years with relatively little disability. At the other end there were occasional patients with an abrupt onset of symptoms which progressed to severe paraparesis or even paraplegia within a few weeks or months.

Physical examination (Table II)

Full details of the physical signs were available in 200 patients in the prospective group. They are shown in Table II. The outstanding feature was a dissociated sensory decrease or a loss of syringo-myelic type, present in 180 (90 per cent). There was maximum impairment of pain and diminution of temperature sensation in the area C4/5 down to T5/6(7/8) distribution and L1–L4(5) (occasionally down to S2/3) segments. This sensory decrease or loss was usually bilateral, more or less symmetrical (unilateral in 9·5 per cent). This was combined with a similarly dissociated sensory loss of 'onion peel' type in the trigeminal distribution of the face (88 per cent) with variable sparing of the nose and its vicinity. Only a few patients were (except 1–2 'peels' at the nose) almost completely 'dull', that is insensitive to strong pinching and pricking down to S5.

All patients showed either a tendency for or positive pyramidal signs in the upper and lower extremities, more often in the latter. The upper limb tendon jerks were diminished in 47 patients (23·5 per cent), atrophies of arm and hand muscles occurred in 27 (13·5 per cent), and of leg muscles in 23 (11·5 per cent). In 12 patients the signs were restricted to a single localised spinal cord region, mimicking tumour or transverse myelitis with deficiencies of all sensory modalities and severe paraparesis or paraplegia.

TABLE II

Physical signs in 200 consecutive prospective study patients

Symptoms	Number	%
Dissociated sensory decrease—loss of syringomyelic type	180	90
—included nuclear trigeminal involvement of 'onion peel' type	176	88
Spastic signs, more marked in the lower limbs	200	100
Exaggerated jaw jerk	152	76
Sucking reflex	35	17·5
Tendon jerks diminished in the upper limbs	47	23·5
Muscular wasting in the arms and hands	27	13·5
in the legs	23	11·5
Argyll Robertson pupils	48	24
Nystagmus on conjugate lateral gaze	52	26
Decrease of hearing	37	18·5
of deafness	2	1
Diplopia, internuclear ophthalmoplegia, peripheral facial palsy,	12	6
bulbar symptoms	5	2·5
Papilloedema		
Slight to moderate diminution of postural sensibility and vibration sense	70	35

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Investigations

Apart from a tendency towards a relative lymphocytosis in the blood, routine *laboratory investigations* were within normal limits except in those patients with other concomitant illnesses.

Cerebrospinal fluid (CSF)

In most patients the cell count was normal. In a small number examined during a sub-acute phase there was a pleocytosis of 20–118 mm^3. Glucose levels were normal. The protein concentration was normal except in patients with obstruction in the spinal subarachnoid space in whom levels of 60–80 mg per cent were found.

Bacteriological and virological examination (in 40 and eight cases respectively) revealed no abnormality. Tuberculous bacilli culture and guinea-pig inoculation in 19 consecutive patients were negative. None of the patients admitted for lumbar puncture was in a highly acute phase.

Serology

In the prospective series (Table III) the VDRL test on serum was positive in 15 per cent (53 of 353 patients), as compared to 11 per cent for the population of Addis Ababa (Friedmann, 1976). Yaws does not occur in Addis Ababa and its surrounding provinces. The FTA test was done in many patients with a positive VDRL and always confirmed the VDRL reaction. Positive VDRL or FTA was never found in CSF.

Mantoux Test (1 : 5000)

This test was positive in 104 (92 per cent) out of 114 consecutive cases, as compared to a positive rate of 64 per cent in the general population in Addis Ababa and surrounding areas (Teklu, 1975).

Radiological examination of the spine

This was carried out in most of the cases in the prospective series, amounting to over 60 per cent of the overall number of patients. Apart from plain X-ray changes, found in association with e.g. rudimentary cervical ribs, old compression fractures of the vertebral bodies, fluorosis of the spine or suspected disc prolapse (excluded from the study), no significant abnormalities were found in the remainder.

Myelography

Myelography with oil was performed in 105 patients with spinal cord syndromes. Evidence of arachnoiditis without other abnormalities was found in 95 out of 105 patients. The most common findings (similar to those of Lombardi *et al.*, 1962; Shaw *et al.*, 1978) were adhesions (the finest of them could be seen rupturing when the table was tilted rapidly), filling defects, narrowing of one or more segments or sometimes complete obstruction of the subarachnoid space, fixity of previously inserted oil contrast medium, obliteration of the nerve root sleeves and pseudocyst formation. In 80 patients the changes were diffuse, usually predominant in the C7–T8 segments, but frequently extending up to the high cervical

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region and thereby reducing or preventing the flow of the contrast medium in the cisternal spaces in the *supine myelogram*. Adhesions in the lumbar region were less common. (Illustrative myelograms, Figures 1 to 5).

Pneumo-encephalography

Pneumo-encephalography was performed on 35 patients, particularly in those with headache and cranial nerve deficiencies. In ten patients the air did not enter the ventricles. In three of these patients hydrocephalus was indirectly demonstrated by carotid angiography.

Treatment

A randomised trial of anti-tuberculous chemotherapy, with or without steroids by mouth and intrathecally, was initiated but had to be abandoned after 10 months. There were four groups of patients, each comprised of 15 patients: patients with chemotherapy (group 1); patients with chemotherapy and steroids



FIG. 1

Marked narrowing and irregularity of the contrast medium flow T8 up to C6 on the right side with maximum on T3–C6, cervical section slightly widened. In the upright position of the patient the oily medium was observed dropping down only by slight coughing manoeuvres. Fixity signs were also observed in the region.

by mouth (group 2); patients with chemotherapy and steroids by mouth and intrathecally (group 3); untreated control group (four). No obvious differences between the four groups have emerged. However, the follow-up period has been too short to draw any definite conclusions.

The 53 VDRL positive patients were initially treated with Penicillin and/or Tetracycline. Later, steroids by mouth and/or intrathecally were given. No benefit was observed, but again the follow-up period was too short.

Laminectomy with opening of the dura and freeing of adhesions (adhesiolysis) was performed in five cases. In two patients cystic cavitations of spinal cord were observed, combined with atrophic changes. Two patients with cervical laminectomy showed moderate improvement. Three patients with circumscribed lower thoracic adhesions and partial or complete paraplegia did not benefit from surgery. In another patient, surgical freeing of massive adhesions at the cerebellopontine angle and local application of cortisone led to satisfactory improvement of symptoms which pre-operatively mimicked acoustic neurinoma (microsurgery performed by Prof. R. Ruberti, Nairobi).

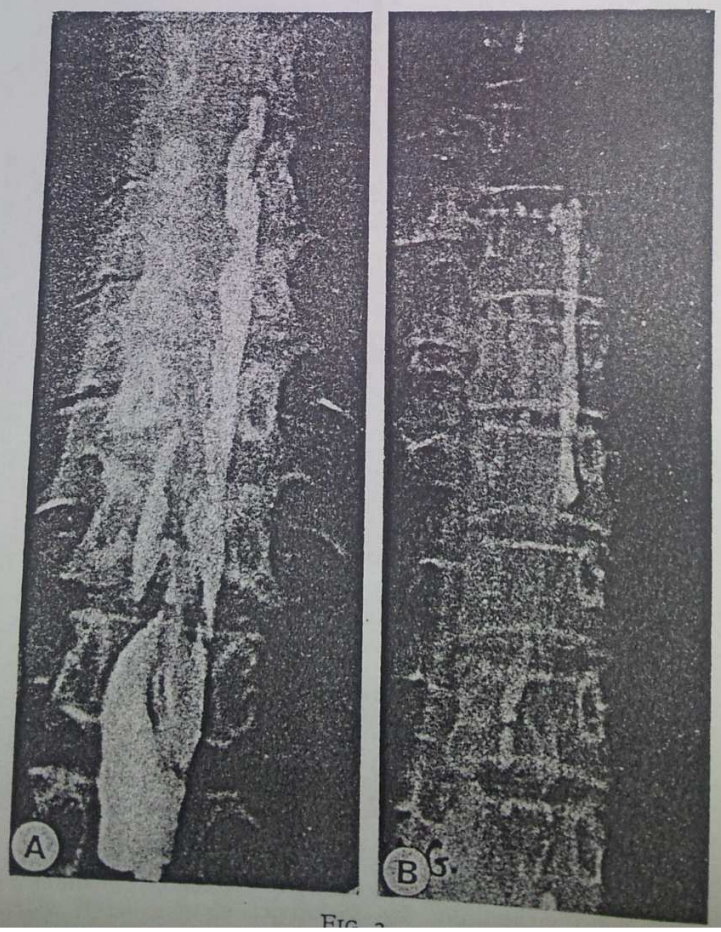


FIG.

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Discussion

Adhesive spinal arachnoiditis unrelated to trauma has not been described previously in Ethiopia. Our investigation shows that the disorder is a common source of neurological complaints and disabilities. A similar syndrome has been reported from widely separated tropical regions, including India (Dastur & Wadia, 1969; Wadia & Dastur, 1969; Mani, 1973), Singapore (Ransome & Montiero, 1947), Malaysia (Selby, 1973) and Jamaica (Rodgers & Cruickshank, 1962; Cruickshank, 1973).

Series of cases have been reported from other African countries, Kenya (Ojiambo, 1966; Harries, 1973), Nigeria (Ojikutu, 1971; Osuntokun, 1973), Uganda (Shaper & Shaper, 1958; Murphy & Hardikar, 1968; Billinghurst, 1970 and 1973), Rhodesia (Levy & Axton, 1973), Ghana (Haddock, 1973), Senegal (Collomb *et al.*, 1973) and South Africa (Cosnett, 1973, 1973*a*). Leigh (1976) presented ten cases of Tanzanians with paraplegia and complete myelographic obstruction of the middle or lower thoracic space in whom only arachnoiditis was surgically proved.

We wonder how many patients with 'obscure myelopathy' and 'other spinal cord syndromes' (Osuntokun, 1973), sensory ataxia—optic atrophy syndrome'

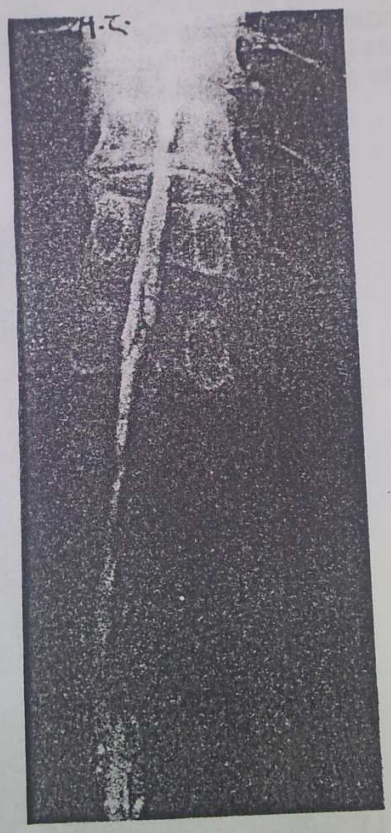


FIG. 3

An impressively slow and filiform passage of oil contrast throughout the entire T–C arachnoidal space.

(Wadia, 1973), or 'tropical spastic paraplegia', 'paraplegia: type unknown', 'spastic myelopathy' (all by Mani, 1973, Cosnett, 1973 and others) were in fact suffering from chronic leptomeningitis, *i.e.* adhesive arachnoiditis. The similarities of almost all clinical criteria in our patients and those patients of Mani (1973) in South India with, *e.g.* 'tropical spastic paraplegia' are evident.

The question of 'negative myelography' is a difficult one, especially in cases with mild adhesions where so much depends on experience. Sometimes where advanced changes would be expected only slight spinal adhesions are found, not corresponding to the clinical picture. In such cases one should also examine the upper cervical region and the passage into the posterior fossa (cisterna magna cerebello-medullaris).

In the majority of the previous reports the presence of the dissociated sensory loss (syringomyelic sensory type), so characteristic of the patients in the present investigation has either not been mentioned or, the possible relationship between adhesive arachnoiditis and spinal cord cavitation (Nagpal *et al.*, 1975) has been neglected. There is insufficient information in other African series to determine the nature of the sensory impairment. In all four cases of tuberculous meningitis of Ransome and Montiero (1947), 'sensory loss was most marked to pin-prick; hot and cold, postural sensibility, vibration sense and touch were little affected'. The clinical features in the Indian cases were described (Wadia & Dastur, 1969) in detail and it is clear that such a pattern was not present. Reporting on South Indian patients suffering from the so-called 'tropical spastic paraplegia', Mani

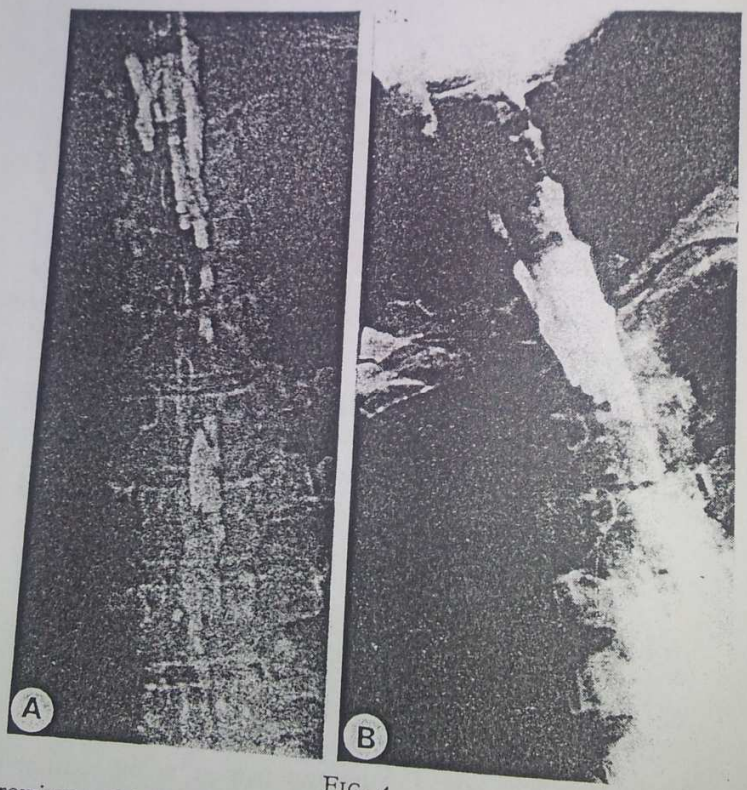


FIG. 4

Marked narrowing and irregularities particularly in thoracic (A), and less in the cervical section (B). Contrast medium was passing poorly.

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(1973) describes a 'diminution of appreciation of touch, pain and temperature . . . far from impressive'. Rodgers and Cruickshank (1962) found the following signs in their 20 Jamaican patients: 'The pyramidal tracts were invariably the most severely affected, but posterior column and, more frequently spinothalamic sensation were also involved' (features almost identical with those of our patients).

The *pathogenetic mechanism* of the sensory dissociation in our cases is uncertain. There are numerous earlier reports of an association between 'adhesive pachymeningitis' (arachnoiditis) and cavitation of the spinal cord (Charcot & Joffroy, 1869; Schwarz, 1897; Holmes & Kennedy, 1908; Martin, 1925; Lubin, 1940; Nielsen, 1953). In cases of cavitation with underlying adhesive arachnoiditis a circulatory impairment of the spinal cord was considered as a possible pathogenetic mechanism. A greater role than that of thickening of the vessel walls causing diminution of the blood supply (Tauber & Langworthy, 1935; Lubin, 1940; McLaurin *et al.*, 1954), may be played by impaired venous drainage (venostasis) from the cord with resulting ischaemia (Stevenson, cited by Nelson, 1943).

Appleby *et al.* (1969) postulated an association between hydromyelia and adhesive arachnoiditis around the outflow foramina of the 4th ventricle and generally at the foramen magnum to be caused by Gardner's (1965) hydrodynamic mechanism (pulsatile CSF pressure from the ventricular system into central canal —communicating syringomyelia).

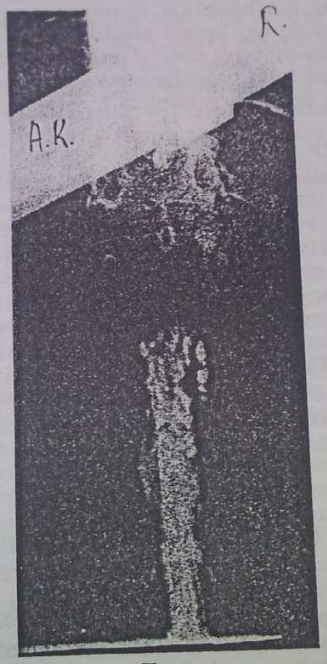


FIG. 5

Full blockage of oil contrast flow at the level L1–2 with typical 'candle-guttering'.

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We have been unable to determine whether cavitations of the spinal cord (distension of central canal more probable) were present in our patients since post-mortem was not permitted. Myelography at cervical space has rarely shown a significant enlargement of the cervical spinal cord as indirect evidence of hydromyelia. This, however, would not appear to be evidence enough against a hydrodynamic disorder (Foster & Hudgson, 1973) as it depends on the position of the body during myelography (Heinz *et al.*, 1966). Williams (1970, 1970*a*, 1974, 1976, 1977, 1977*a*, 1978) and Barnett (1973, 1976) have extensively dealt with the problem of syringomyelia caused by arachnoiditis. Williams has not been satisfied by a simplified hydrodynamic principle as a cause of syringomyelias. The blockage of the subarachnoid space at the foramen magnum, causing differences in 'venous' pressure between the head and the spine (1970*a*), 'is more likely to cause filling of the syrinx than funnelling of the "arterial" pulsations within the CSF pathways . . . incriminated by Gardner' (Williams, 1978). The 'cranio-spinal pressure dissociation' of Williams originates 'from a valve-like action at the foramen magnum which causes a difference in pressure consequent upon the shifts of CSF caused by the imposition of energy from the venous system' (Williams, 1978).

The results of our study of 507 cases of spinal cord syndromes of the syringomyelic type revealed a close association with non-traumatic postinflammatory spinal and/or cisternal arachnoiditis. We agree with Barnett (1973) who postulated two pathogenetic aspects of syringomyelia due to arachnoiditis: (*a*) Adhesive cisternal arachnoiditis (foramen magnum level) alone is causing syringomyelic syndromes; (*b*) Spinal arachnoiditis, causing local adhesions at any level, can by itself present with clinical features resembling classical syringomyelia. In addition, partial or total vascular obstruction may cause painful radiculopathies and myelopathies, reaching complete transverse spinal cord lesion.

Aetiology

While the aetiology of the spinal arachnoiditis syndrome in Ethiopia must remain uncertain because of the absence of post-mortem examinations, there is indirect evidence to suggest that infections are involved in a significant number of patients. Arachnoiditis followed classical bacterial meningitis in seven patients. In the remainder, two specific infections, tuberculosis and syphilis, warrant particular attention.

There is good evidence that arachnoiditis in Asia is commonly a sequel of tuberculosis (India: Wadia & Dastur, 1969; Udani *et al.*, 1971; Thailand: Vejjajiva, 1974). Tuberculosis is widespread in Ethiopia (Susteric, 1976), and the Mantoux test was positive in 92 per cent of our patients. A causative connection between tuberculous infection and arachnoiditis is probable in some of our cases and the syndrome followed tuberculous meningitis in two patients. In another, wasting of the hands and syringomyelic pattern of sensory loss developed 18 months after the patient presented with thoracic spinal tuberculous caries. In the majority of our patients, however, there was no evidence of active tuberculous infection.

It is of particular interest that Emond *et al.* (1973) have shown that *tuberculosis* can produce a *transient aseptic meningitis* and, in one of his five patients with discrete meningeal symptoms, the CSF contained normal protein and glucose levels without pleocytosis. Nevertheless, guinea-pig inoculation revealed tuberculosis. This patient recovered without therapy. The transient febrile illness which preceded the onset of neurological symptoms in many of our patients would be compatible with an episode of tuberculous meningeal infection of this

type. The CSF for tuberculous-culture or guinea-pig inoculation should have been taken immediately at the onset of fever.

Earlier authorities considered syphilis to be a causative agent of adhesive arachnoiditis in many cases. Horsley (1909) suggested that not only syphilis but also gonorrhoea were responsible for his 'Chronic Spinal Meningitis' patients. In fact, all the authors from Asia and Africa dealing with the problem do accept syphilis as a cause of the meningovascular changes, luetic meningitis and arachnoiditis. Doing so they refer to a rather high incidence of VDRL positive serum (mostly negative in CSF), and emphasise that the 'diagnosis (of neurosyphilis) must frequently be based on positive blood serology alone' (Cosnett, 1973).

However, the role of syphilis seems to us even less clear and certain than the role of tuberculosis. Apart from the fact that there is no difference in the clinical findings in VDRL positive patients and those with VDRL negative reactions and a convincingly negative history for syphilis, the overall incidence of a positive VDRL test in the blood was 15 per cent (Table III), as compared with the 8 to 11 per cent of the general population in Addis Ababa and surrounding areas (Friedmann, 1976). The test was negative in the CSF in all examined patients, even in those ten serum positive patients who had a lumbar puncture prior to any treatment with antibiotics. It is probable, however, that the true incidence of syphilis was higher, since 8 per cent of the VDRL negative patients had Argyll Robertson pupils and approximately 50 per cent of the whole series, retrospective and prospective, had been treated for gonorrhoea at least once, commonly without prior VDRL test. It is interesting that one of our three European patients, a 60-year-old male, acquired syphilis 3 years before he insidiously developed the clinical and radiological patterns or arachnoiditis which we have described in the Ethiopians. At the time he acquired syphilis he felt a general malaise. VDRL repeatedly confirmed the diagnosis. Ten days after luetic contagion Penicillin and another antibiotic (probably Tetracycline) were introduced. After 3 weeks of treatment he felt well again.

We conclude that it is likely that a percentage of cases of arachnoiditis in Ethiopia are due to syphilis.

What of the future?

It is unlikely that progress in understanding the aetiology of the disease in Ethiopia will be made before post-mortem becomes acceptable. The evidence that syphilis and particularly tuberculosis are a significant cause for this common disorder is nevertheless good enough to urge that patients acquiring syphilis or tuberculosis should receive vigorous treatment by antibiotics and chemotherapeutics respectively at the earliest stage of infection. Assuming that syphilis is a cause of arachnoiditis the immediate treatment is decisive in preventing the later sequelae. After contagion with treponema pallidum treatment must be started within the next few days. In our experience, therapeutic efforts that are only

TABLE III

Evidence of syphilis in the prospective series

	Total	Male	Female
All patients	353/100%	218/61·8%	135/38·2%
VDRL positive	53/ 15%	42/19·2%	11/ 8·1%
Argyll Robertson pupils on VDRL negat. patients	30/ 8·4%	20/ 9·1%	10/ 7·4%

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begun 7 to 10 days post-contagion are unlikely to prevent the patients from developing vascular and/or arachnoidal luetic lesions.

Differential diagnosis of tuberculous or syphilitic leptomeningitis (arachnoiditis) should be considered in patients presenting with diminution of vision, diplopia, facial palsy, vertigo and decreased hearing and other cranial nerve lesions. On the other hand, in patients with a spinal cord lesion at any level a myelogram should be performed to exclude a surgically curable compression such as tumours, disc prolapses and other conditions.

Although there have been some reports of satisfactory results after surgical treatment of arachnoiditis (Teng & Papatheodorou, 1967; Jorgensen *et al.*, 1975; Tedeschi & Benini, 1976), our own experience and that of a number of other authors have been disappointing (Lombardi, *et al.*, 1962; Barnett, Foster & Hudgson, 1973; Leigh, 1976), except for secondary hydrocephalus which can be treated by shunting (Appleby *et al.*, 1969). Posterior fossa surgery has been critically re-evaluated (Williams, 1978) and will be limited for a very carefully selected group of patients.

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Summary

Spinal cord syndromes with a mainly syringomyelic pattern of sensory disorders, radiculopathies, mixed paresis of varying degrees (without any history of trauma), have been found in 507 out of 1305 new patients referred to our Clinic from January 1976 till 31 October 1977. In 105 randomised and unselected cases with these syndromes, myelographies have disclosed findings compatible with an adhesive spinal and/or cisternal arachnoiditis. A prospective study of the syndromes for evidence of infectious aetiology has been performed, in which tuberculosis, syphilis and other infections appear to be causative agents. A randomised therapeutic trial on a limited number of cases has been evaluated, as well as the results of specific therapy in a larger number of cases. Results of treatment have not been satisfactory. Operations were performed on only five patients and in no case was an autopsy obtained. Spinal cord syndromes due to non-traumatic adhesive arachnoiditis are discussed. The possible pathogenetic mechanisms of the predominantly syringomyelic sensory deficits in those syndromes are briefly mentioned.

Résumé

Les syndromes de la moelle épinière, avec un ensemble principalement syringomyélique de désordres sensoriels, de radiculopathies, de paralysies conjointes de divers degrés, sans aucune origine traumatique, ont été observés dans 507 cas des 1305 patients confiés à notre Clinique, etre le mois de janvier 1976 et le 31 octobre 1977.

Dans 105 cas pris au hasard et non-sélectionnés présentant ces syndromes, les myélographies ont révélé des résultats compatibles avec une arachnoïdite spinale ou citernale. On a fait une étude éventuelle des syndromes pour déceler l'évidence d'une étiologie infectieuse et il semble, en effet, que la tuberculose, la syphilis et d'autres maladies infectieuses soient à l'origine de ces cas. Un essai thérapeutique fait au hasard sur un nombre limité de cas aussi bien que le résultat d'une thérapeutique spécifique sur un plus grand nombre de malades n'ont pas donné de résultats satisfaisants. Seuls cinq patients ont subi une

opération. Aucun cas ne nous a donné un résultat d'autopsie. Les syndromes p inflammatories de la moelle épinière et la pathogénèse de la syringomyélie qui y est associ à la suite d'une arachnoïdite adhésive sont brièvement discutés.

ZUSAMMENFASSUNG

Rüchenmarkssyndrome mit überwiegend syringomyelischen Sensibilitätsausfällen, Radikulopathien, gemischten Paresen wechselnden Grades, ohne Unfallanamnese, wurden bei 507 von 1305 Patienten gefunden, welche von Januar 1976–31. Oktober 1977 an unsere Klinik überwiesen wurden. Die Myelographie deckte bei 105 randomisierten und unselektierten Fällen mit diesen Syndromen Befunde auf, die mit adhesiver spinaler und/oder cisternaler Arachnoiditis vereinbar sind. Es wurde eine prospektive Studie zum Nachweis einer infektiösen Aetiologie durchgeführt. Aus dieser geht hervor, daß Tuberkulose, Syphilis und andere Infektionen als ursächliche Faktoren erscheinen. Bei einer begrenzten Anzahl von Patienten wurde ein therapeutischer Versuch und bei einer größeren Gruppe die Resultate der spezifischen Therapie ausgewertet. Die Resultate der Therapie waren unbefriedigend. Nur fünf Patienten wurden operiert. Es wurde keine Autopsie durchgeführt. Rückenmarkssyndrome verursacht durch nicht-traumatische adhesive Arachnoiditis werden diskutiert. Die möglichen pathogenetischen Mechanismen der überwiegend syringomyelischen Sensibilitätsausfälle bei diesen Syndromen werden erwähnt.

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Thus the objective of this paper is firstly to document 6 cases of "reactive" renal amyloidosis diagnosed in Ethiopian patients at the Black Lion Hospital in Addis Ababa, and secondly to create an awareness of the existence of this disease.

PATIENTS AND METHODS

Between April 1980 and January 1981, percutaneous kidney biopsies were performed on 38 patients with glomerular diseases, using a Menghini needle. Laboratory tests, which included white blood cell count, haemoglobin, erythrocyte sedimentation rate, quantitative and qualitative urine analysis, Bence Jones protein, urine culture, Venereal Diseases Research Laboratory (VDRL), Rose Waaler, blood urea nitrogen, creatinine, total serum protein, serum protein electrophoresis and immunoelectrophoresis, as well as a chest X-ray, were performed on most patients.

RESULTS

Of the 38 patients, 28 had primary and 10 had secondary glomerular diseases. Out of the 10 secondary glomerular disease cases, 6 patients (15.8%) had renal amyloidosis. Of these 6 cases, 4 had proven tuberculosis (3 pulmonary, 1 tuberculosis of the lymph node); 1 had leprosy; and the sixth patient, with endemic goitre, probably had a past chronic lung disease. The pertinent clinical data are shown in Table 1. All patients but one came from the northern part of Ethiopia. The mean age was 29.8 years. Only 1 patient had a transient macroscopic haematuria; 2 patients had chylous ascites.

Laboratory tests (Table 2) showed that 4 patients were anaemic, and 3 were in renal failure of various degree. Only 1 patient had a normal erythrocyte sedimentation rate. The bone marrow tested in 2 patients was normal. The serum protein was low in all 4 cases on whom this was examined, and 1 patient had a high serum alkaline phosphatase level. Urine tests (Table 3) showed all with heavy proteinuria, and, of 5 patients, 4 had a 24-hour urine protein of over 3g%. Only 1 case had urinary infection due to *Klebsiella* species; 1 patient had mild microscopic haematuria, and pyuria was present in 5 patients. The serum and urine protein results in 4 patients (Table 4) indicated that all had hypoalbuminaemia. The $alpha_2$ globulin was elevated in all patients, and the gammaglobulin in two. The I_gG was reduced in 3, I_gA in 2, and I_gM in 1 patient.

DISCUSSION

The deposition of amyloid in various tissues and organs is believed to be a result of a prolonged antigenic stimulation (7,12). In Ethiopia, chronic infections like tuberculosis and leprosy are very prevalent. Besides, the incidence of amyloid-related serum protein (protein ASC) in apparently healthy Ethiopians is high (22%) compared to that in healthy Norwegians (2.9%) (18). It is thus probable that "reactive amyloidosis" is not rare in Ethiopia. The diagnosis of amyloidosis depends on the demonstration of deposits of amyloid material in tissues stained with appropriate stains like Congo red and methyl violet. The green birefringence under polarized light is quite specific for amyloid, but electron microscopy and X-ray diffraction are the most specific histological methods of diagnosing amyloidosis, and can detect even early cases (2,14). The demonstration of amyloid fibrils in the urinary sediment may also be diagnostic (2). In our non-selected group of patients, the prevalence of amyloidosis compares very well with that in selected cases from Iran (15) but sharply contrasts with that in Uganda (9). The 6 patients in this study had normal blood pressure.

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TABLE 1. Clinical data of 6 renal amyloidosis cases.

Case	Age (years)	Sex	Address	Duration of illness	Symptoms	Signs	Weight (kg)	Blood pressure (mmHg)	Aetiologic factor
1*	30	F	Assab	3 years	Cough, right side chest pain, fever, sweating, swelling of abdomen and legs. No loin pain or haematuria.	Slight pallor, dullness and reduced air entry at the bases; ascites and leg oedema.	56	100/60	Tuberculosis
2*	40	F	Tigray	1 month	Haematuria, swelling of abdomen and legs, weight loss. No loin pain.	Slight pallor, ascites and leg oedema.	38	120/90	Tuberculosis
3	18	M	Gojjam	3 years	Swelling of body, cough and loin pain. No haematuria.	Slight pallor, goitre and ankle oedema.	49	120/80	?Goitre ?Tuberculosis
4	18	F	Tigray	1 year	Swelling of body, loin pain but no haematuria. Was treated for tuberculosis a year before.	No pallor, but slight puffiness of the face, palpable spleen and leg oedema.	50	120/70	Tuberculosis
5	45	M	Assab	1 year	Diarrhoea, cough, fever, sweating, weight loss; also swelling of legs but no loin pain or haematuria.	Pallor, emaciation, lymphadenopathy, enlarged thyroid gland and leg oedema.	39	100/60	Tuberculosis
6	28	M	Shoa	23 years	Swelling of body, but no haematuria or loin pain.	Pallor and leg oedema.	49.5	100/50	Lepromatous leprosy

*had chylous ascites

TABLE 2. Haematological, biochemical, serological, radiological and stool test data of 6 renal amyloidosis cases

Case	Haemo-globin	Leucocyte count (per mm^3)	Erythrocyte sedimentation rate (mm/hr)	Platelet count (per mm^3)	Blood urea nitrogen (mg%)	Serum protein (g%)	Choles-terol (mg%)	Rose Waaler	VDRL	Stool for ova and parasites	Chest radiograph
1	9.7	8900	120	206,000	9.2	-	-	-	-	Giardia	Tuberculosis
2	11.7	5600	95	367,000	37.0	5.5	225	Negative	-	Negative	Tuberculosis
3*	11.4	8800	105	150,000	13.0	4.8	-	Negative	Negative	Ascaris	Pleuro-pericardial adhesion
4*	14.3	5100	3	122,000	9.6	4.6	230	Negative	Negative	Negative	Normal
5**	7.0	9000	140	120,000	86.0	4.3	-	Negative	Negative	Negative	Tuberculosis
6	13.0	9800	120	400,000	61.0	-	-	-	-	Negative	-

*had normal bone marrow
**had a high alkaline phosphatase level in serum

TABLE 3. Data on urine tests of 6 renal amyloidosis cases

Case	Protein (qualitative)	24 hrs urine protein (g)	Bence-Jones protein	Red blood cells per high-power field	Leucocytes per high-power field	Urine culture
1	+++	6.7	-	5-6	Plenty	Klebsiella sp.
2	++++	-	Negative	3-4	10-15	Negative
3	++++	3.7	Negative	15-16	Plenty	Negative
4	++++	8.8	Negative	5-6	Plenty	Negative
5	+++	1.9	Negative	1-2	30-35	Negative
6	+++	10.0	-	2-3	0-1	Negative

TABLE 4. Serum and urinary proteins in 4 renal amyloidosis cases

Case	Total serum protein (g)	Albumin (%)	α_1-globulin (%)	α_2-globulin (%)	β-globulin (%)	γ-globulin (%)	IgG	IgA	IgM	24 hrs urine protein (g)
2	5.5	36.90	5.0	19.30	15.10	23.50	36.9	155.0	101.9	-
3	4.8	32.50	7.5	15.00	7.50	27.50	280.0	49.4	67.3	3.7
4	4.6	46.00	5.5	18.20	16.60	13.40	280.0	43.4	36.9	8.8
5	4.3	37.38	5.6	15.88	10.28	30.04	-	-	-	1.9

Brandt *et al.* (8) reported that 76% of their cases had normal blood pressure, as did 50% of the cases in the series reported by Triger *et al.* (14).

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BRIEF COMMUNICATION

MASS MINIATURE RADIOGRAPHY AT THE TUBERCULOSIS DEMONSTRATION AND TRAINING CENTRE, ADDIS ABABA

Bayu Teklu,[1] MD, FACP, and Kinde Kassegn,[2] MD

ABSTRACT. *Mass miniature radiography (MMR) 70mm chest films have been used for some time in mass screening for tuberculosis. The Tuberculosis Centre in Addis Ababa, Ethiopia, takes daily MMR on all who come to the Centre for consultations. From January to December 1980, all the chest films taken on one and the same day of the week were studied. There was a total of 8,298 films, with a study-day average of 180 films, and, of these, 1,240 (14.9%) were of known cases of tuberculosis coming on follow-up. Of the remaining 7,058 patients presenting at the Centre for the first time, 5,143 (73%) had normal X-rays. Four hundred and thirty-two patients (6.1%) had cavitary pulmonary disease, and cardiac diseases were present in 260 (3.7%); but the largest group – 13.4% – comprised pulmonary cases of apparently non-tuberculous origin. The study emphasises the need for more selective use of MMR, and further illustrates the utility of the method in screening for a wide variety of cardio-pulmonary diseases.*

Mass miniature radiography (MMR), employing 70mm chest films, has long been used in mobile mass screening for tuberculosis, and it was considered that this method was cheap and technically simple enough to be applicable in Ethiopia (1). In more recent years, the practice has been abandoned because of the extra funds and skilled manpower required (2). Although MMR is used as a screening procedure in tuberculosis surveillance, there is no typical picutre of tuberculosis on MMR (3). On the other hand, MMR has been employed in detecting cardiac diseases among Ethiopians (4).

The purpose of the present prospective study is to document the chest pathology seen in MMR taken at the Tuberculosis Demonstration and Training Centre in Addis Ababa on a selected day of the week over a period of one year.

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PATIENTS AND METHODS

The patients were drawn from those who came to the Centre seeking medical care for chest symptoms, and from those seeking check-up. Each patient had only one 70mm chest film.

All 70mm films taken on one and the same day of the week between January and December 1980 were read by each of the authors, one with experience in tuberculosis and the other specializing in chest diseases. Although there was an inter-observer variability of 10% to 15% on random assessment, the differences were generally minor. Moreover, the investigators discussed all differences, and agreement was reached in each case.

RESULTS

There were 8,298 films available for study, taken on 46 days corresponding to 48 weeks, with an average of 180 films per day. Of these, 1,240 films were those of follow-up cases of tuberculosis. Excluding these, there were 7,058 films of new cases, of which 72.9% were considered normal (Table). Cavitary disease, not always necessarily tubercular, was seen in 6.1%. Other forms of pulmonary tuberculosis were rare. Non-tuberculous lung pathology was the most common abnormal finding, comprising 944 cases (13.4%). Cardiomegaly with or without abnormal pulmonary shadows was seen in 3.7% of the films. Sixty-three (0.9%) films were not interpreted because of the poor technical quality of the radiographs.

TABLE. Chest X-ray findings, Tuberculosis Training and Demonstration Centre in Addis Ababa, in 46 days over a period of a year

X-ray finding	*No.*	*%*
1. Normal	5143	72.86
2. Cavitary disease	432	6.10
3. Cardiomegaly ± abnormal lung shadows	260	3.68
4. Hilar lymphadenopathy ± lung and/or pleural disease	113	1.60
5. Pleural effusion ± lung shadows	45	0.60
6. Bone pathology only	19	0.30
8. Miliary pattern (lung)	5	0.07
9. Hydropneumothorax	4	0.06
10. Lung pathology other than the above (pneumonias, cysts, nodules, fibrosis, etc.)	2	0.03
11. Miscellaneous (widened mediastinum, aortic aneurism, etc.)	944	13.40
12. Technically poor X-ray	28	0.40
Total films	63	0.90
	7058	100.00

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DISCUSSION

Chest X-rays taken once a week throughout a year may well be representative of that year's activity with regard to pathology and load of work at the Tuberculosis Centre. If only one or two months were to be taken consecutively, however, the findings would not be representative of one year, for two major reasons. First, the load may vary from one month to another, since, for example, a smaller number of patients may come from the countryside during the rainy season and harvest time. Second, the pattern of respiratory diseases changes during the year; for example, July to September is the asthma season, while May and June show peaks for pneumonia (5,6).

We are aware of the significant intra-observer and inter-observer variability in reading chest X-rays, as noted among chest physicians, tuberculosis specialists and radiologists (7, 8). In a very large study, there was a 28% disagreement in reading cavitary disease, and an 80% disagreement in detecting lymph node abnormalities (8). Nevertheless, even allowing for a certain degree of inter-observer variability, the finding of 5,143 (73%) of normal chest X-rays among patients presenting themselves at the Tuberculosis Centre for the first time is quite high (Table). The finding that 260 cases (greater than 3%) of all newcomers had gross cardiac disease is not to be underestimated, and could justify the employment of a full-time cardiologist. There was a large group of various pulmonary pathologies in which tuberculosis could not easily be ruled out. This group comprised 944 patients, or 13.4% of all new cases, and would require the services of more than one full-time chest specialist to deal with them. Not all the 432 patients – 6% of new cases – with cavitary disease necessarily had tuberculosis; they might have necrotising pneumonias, other granulomatous diseases, or even malignancies. This group would also be of great interest to the chest physician. The 45 cases of pleural effusion, an average of one a day, presented striking diagnostic problems. The paucity of miliary tuberculosis and hydropneumothorax, in a country where tuberculosis is highly prevalent, is remarkable. The number of cases of primary childhood tuberculosis is small, partly because the Centre discourages the taking of films on children under 4 years of age.

The readings of the MMR and the findings of the special weekly Chest Clinic at the Centre both demonstrate that a variety of pulmonary and cardiac disease is found. Although it is desirable for the Centre to reduce drastically the number of X-rays which prove to be normal, and to cut costs by using simple screening procedures, it is evident that there is a potential clinical wealth for cardiologists, and even for the "phthisiologists" of days gone by.

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TUBERCULIN CONVERSION AFTER BCG VACCINATION IN INFANCY AND EARLY CHILDHOOD

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ABSTRACT. *Response to BCG vaccination was studied in 217 apparently healthy Ethiopian children. Forty-five per cent of the well-nourished and 50% of the malnourished children had a positive reaction to Mantoux test; but the percentage positivity in these two groups does not show significant difference ($P < 0.90$). The over-all conversion rate was 45%, and it did not appear to be influenced by malnutrition. The percentage of positive Mantoux was greater in those children with a BCG scar. Complications of BCG vaccine were observed in 4 children (1.8%). Our study suggests that the usual practice of giving BCG vaccine to non-immune individuals in Ethiopia should be continued, as conversion rates after BCG, hence protection against tuberculosis, is relatively high.*

Bacillus of Calmette and Guérin (BCG) vaccination has been for many years and remains a subject of controversy, since the protection rate observed in community studies varies from zero to 80% (1,2,3). A controlled clinical trial in humans reported recently from South India showed that BCG did not protect against development of pulmonary tuberculosis. This was thought to be due to high infection rate, nonspecific sensitization and other epidemiological factors in that community (2). However, the study covered a mainly adult population and did not provide any evidence, one way or the other, regarding the protective effect of BCG against tuberculosis in infancy and early childhood.

Assuming that Mantoux positivity has a relevance to protection in tuberculosis in endemic areas, we designed this study to determine tuberculin conversion in Ethiopian infants and children after BCG vaccination, and whether or not nutrition had any infleunce on the conversion rate.

PATIENTS AND METHODS

Two hundred and seventeen healthy Ethiopian children who had received BCG vaccinations and came for other vaccinations to Lidetta Clinic, Gulele Clinic and the Ethio-Swedish Pediatric Clinic (ESPC) in different areas of Addis Ababa were tuberculin-tested. Their ages ranged from 1 month to 5 years, and they came from different socio-economic backgrounds. Each child received 0.1ml of Glaxo freeze-dried BCG vaccine intradermally over the deltoid.

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A history of intercurrent infection, concurrent immunization, steriod therapy and contact with tuberculous adults was taken for each child examined, and they were checked for BCG scar and enlarged axillary and cervical glands. The weight was recorded and the nutritional status assessed, using the Wellcome classification (4). The children were divided into 2 groups: above and below 80% of the Harvard standard, Groups 1 and 2 respectively.

The method of tuberculin testing used was the Mantoux test. A test dose of 0.1ml of PPD RT-23 with Tween 80 containing 2 tuberculin units (TU) was injected intradermally on the volar surface of the left forearm. Seventy-two hours later, the largest transverse diameter of induration was measured in millimetres.

A reaction of less than 5mm induration was considered negative, 5 to 9mm doubtful, and 10mm or greater positive. Children with 15mm or more induration were referred to the ESPC for further evaluation, as reactions of this magnitude suggested clinical infection (5). The stock solution of PPD RT-23 was prepared by Statens Seruminstitut, Copenhagen, Denmark, and is the WHO-recommended antigen used for skin testing. This stock solution is reconstituted at the Central Laboratory and Research Institute, Addis Ababa.

All except 2 children were tuberculin-tested at 8 weeks after BCG vaccine. These remaining 2 children were tested, however, at 4 and 5 weeks. All the tests were done by one experienced nurse, trained in the technique of Mantoux test.

The Chi-square (χ^2) test was used to determine statistical significance.

RESULTS

Table 1 shows the age and sex distribution of the 217 children at the time of test.

The ratio of male-to-female was 1 : 1.2. The ages ranged from 1 month to 5 years. Seventy-five per cent of the children were below 6 months, and 94% below 1 year.

Mantoux test results according to weight are given in Table 2. In Group 1, 90 (44.8%) had positive Mantoux. Eight of 16 children (50%) in Group 2 had positive tuberculin reaction. These percentage positivities in the 2 groups do not show statistically significant differences at $P < 0.90$. The overall tuberculin reaction in both groups, however, revealed induration of zero millimetres in 68 (31.3%) children, 4 to 9mm in 51 (23.5%) and 10mm or more in 98 children (45.2%).

BCG scar and Mantoux results showed an interesting relationship. Forty-two per cent of children with BCG scar and 3% without BCG scar showed positive reaction. This is statistically highly significant, at $P < 0.0005$.

Table 3 gives the percentage conversion rate in the different age groups, which was 45% overall. This Table shows an increase in the rate of conversion as the age increased.

Nine children gave a history of contact with tuberculous adults, and 6 with chronically coughing persons. Six of the former and 5 of the latter had positive Mantoux test.

There were 7 children who received measles vaccine and tuberculin test simultaneously. Of these, 4 had positive reaction and 3 had negative reactions.

Complication of BCG vaccine occurred in 4 children (1.8%). One child had an abscess at the vaccination site, and the other 3 had axillary lymphadenitis.

DISCUSSION

A positive tuberculin reaction indicates sensitivity to the antigens of the tubercle bacillus. Thus, it indicates either a past

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TABLE 1. Age and sex distribution of 217 children at the time of Mantoux test

Age (months)	Male	Female	Total No.	Total %
1 - 3	42	61	103	47.47
4 - 6	31	31	62	28.58
7 - 9	16	11	27	12.44
10 - 12	4	9	13	5.99
13 - 15	3	1	4	1.84
16 - 18	1	1	2	0.92
19 - 21	0	2	2	0.92
22 - 24	2	1	3	1.38
24+	1	0	1	0.46
	100	117	217	100.00

TABLE 2. Mantoux test results according to weight

Weight-for-age % of Harvard Standard	Size of No reaction	Mantoux reaction 1-4mm	5-9mm	10-14mm	15mm	Total
80 (Group 1)	64 (29.5)*	6 (2.8)	41 (18.9)	77 (35.5)	13 (6.0)	201 (92.6)
80 (Group 2)	4 (1.8)		4 (1.8)	7 (3.2)	1 (0.5)	16 (11)
Total	68 (31.3)	6 (2.8)	45 (20.7)	84 (38.7)	14 (6.5)	217 (100)

*Figures in parentheses denote percentages.

TABLE 3. Conversion rate in the different vaccinated age groups

Age (months)	Children tested	Children with positive Mantoux	Rate of conversion: %
1 - 3	103	45	44
4 - 6	62	27	44
7 - 9	27	15	56
10 - 12	12	5	38
13 - 15	4	2	50
16 - 18	2	1	50
19 - 21	2	1	50
22 - 24	3	1	33
24+	1	1	150
	217	98	45

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present tuberculous infection or immunization with BCG vaccine. But false negative reactions may result from (a) an intercurrent disease like measles; (b) viral vaccines; (c) corticosteroids and immunosuppressive agents; (d) severe malnutrition; (e) an overwhelming infection such as miliary tuberculosis; (f) faulty technique, and (g) use of impotent testing materials (6,7).

Measles was not encountered in this study, because three-fourths of the children were below six months of age; we know that passive transplacental immunity after measles is usually complete for the first 6 months of life, and disappears at varying rates later. However, a history of measles was obtained from 4 children. Three had positive Mantoux and the fourth negative. Measles makes a child non-reactive to tuberculin for some weeks after infection (8).

Of the 7 children who had simultaneous measles vaccination and Mantoux test, 4 had a positive reaction. Our figures were too small to allow any meaningful conclusion on the influence of vaccinations on tuberculin conversion. However, others have found that measles and polio vaccines do not totally depress tuberculin conversion (9).

None of the children had received corticosteroid or immunosuppressive agents or had miliary or meningeal tuberculosis.

The percentage positivity in the well-nourished (Group 1) and malnourished (Group 2) was not statistically significant. Although this is contrary to the findings of Lloyd and Harland (10, 11), it is in complete agreement with the findings of other authors (1,7,12), that nutritional status does not have any significant influence on the development of sensitivity after BCG vaccination.

BCG reaction is age-related: as age increases, Mantoux test positivity increases. For instance, it is much less in a newborn than in older children (12, 13), who have a fully developed immune system, and more chance of exposure. The overall conversion to 10mm or more induration in our study was 45% (Table 3). Franziss and Dale-Lace (14) and Cartwright from South Africa (13) obtained a conversion rate of 60% to 80%, but others have reported a lower figure (15).

Fifty-two per cent of children with BCG scar and 15% without it had positive Mantoux. Moreover, there was no tuberculin reaction in 57% of children without the BCG scar, and reaction occurred in only 20% with BCG scar. Thus the presence of BCG scar can be of use as an indicator of immunity (16).

BCG has been associated with adverse reactions which include prolonged severe ulceration at the vaccination site, lymphadenitis, lupoid reactions, disseminated BCG infections and death (17, 18). BCG osteomyelitis has also been reported recently from the Scandinavian countries (17, 19). But all these complications are rare. In the USSR, BCG complications were observed in only 0.01% (16). Lehmann *et al.* (20) reported lymph node enlargement, whereby more than 1% of all vaccinations progressed to lymphadenitis with abscess formation. Cartwright (13) found no serious side-effects; only small abscesses were observed in a few babies. Our finding of one abscess and 3 cases of axillary lymphadenitis (1.8%) is in complete accord with the above authors.

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NEPHROTIC SYNDROME IN ADULT ETHIOPIANS

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ABSTRACT. *The clinical, laboratory and histopathological data and outcome of treatment are described in 36 adult Ethiopian patients with nephrotic syndrome, admitted to the Black Lion Hospital in Addis Ababa over a 14-month period (April 1980 to July 1981). There were 20 males and 16 females; the mean age was 34.7 years. During the study period, nephrotic syndrome accounted for 2.1% of medical admissions. The aetiology of the nephrotic syndrome was known in 12 of the cases. The commonest histological finding was proliferative glomerulonephritis, of which membranoproliferative and mesangial proliferation accounted for over 52% of the total and of 73% of the primary glomerular diseases. There was no case of minimal lesion glomerulonephritis in this study.*

The prevalence of renal diseases in general, and of nephrotic syndrome in particular, in adult Ethiopians is unknown. Analyses of hospital admissions from different parts of Ethiopia indicate that renal diseases account for 1.2% — 2.8% of the total admissions (1-7). Nephrotic syndrome has been mentioned only in 4 reports (6-9). The syndrome has, however, been reported as a common condition in Kenyatta National Hospital, Nairobi (10); Nigeria (11); in Mulago Hospital in Uganda (12); and in the South African Bantu (13).

Except for the recent report by Alfonzo *et al.* (9), in which renal biopsy was performed, the diagnosis of renal diseases in previous reports (1-8) has been made on the basis of clinical and laboratory findings. This paper describes the clinical, laboratory and histopathological reports and outcome of treatment in 36 adults with nephrotic syndrome who were admitted to the Black Lion Hospital, Addis Ababa.

PATIENTS AND METHODS

After the development of the nephrology unit in Black Lion Hospital, in early 1980, kidney biopsy became a routine procedure whenever indicated and when patients consented to the procedure.

During a 14-month period (April 1980 to July 1981), there were 36 adults with nephrotic syndrome who had renal biopsy; these patients were studied prospectively, using a prepared protocol. In addition to a carefully taken history and physical examination, in order to elucidate the aetiology of the syndrome, the following investigations were made: urine for protein and sugar, microscopic examination of urine sediments, 24 hours' urine protein, urine culture;

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complete blood count, serum protein and electrophoresis, cholesterol, creatinine, blood urea nitrogen (BUN); chest X-ray; stool examination for ova and parasites; and serological test for syphilis. The assay of the antistreptolysin O titre was not possible. All the patients had a percutaneous kidney biopsy, with the Menghini needle. The kidney tissue was fixed in 10% formalin. Thin paraffin sections of the tissue were then stained with periodic acid Schiff (PAS), Congo Red and haematoxylin-eosin. The slides were then examined only under light microscopy, since fluorescence microscopy was not available.

The criteria for the diagnosis of nephrotic syndrome included the presence of oedema, hypoproteinaemia of less than 6g%, and a significant proteinuria (24-hour protein of more than 2.5g per litre, or proteinuria of 2.5mg per minute or 50mg per kg body-weight).

Treatment and response. The treatment given was one of the following:

A. *Standard steroid.* Standard steroid treatment was given in a dosage of 2mg per kg body-weight on alternate days up to a maximum dose of 100mg per day for 6 to 8 weeks, and then gradually tapered off and discontinued after one month.

B. *"Steroid pulse".* "Steroid pulse" treatment was given in a dosage of 10mg per kg body-weight intravenously on alternate days for 3 doses.

C. *Symptomatic.* Diuretics and/or indomethacin were used.

The response to treatment is described as improved if the urine was continuously free of protein and the BUN or creatinine was equal to or less than the initial value after 8 weeks of treatment maintained up to the last examination (which in some cases was after a year). The outcome of those patients with persistent proteinuria and a BUN or creatinine greater than or equal to the value before treatment is described as unchanged.

RESULTS

During the study period, 903 males and 827 females (total 1,730) were admitted to the 83-bed medical department of the Black Lion Hospital. Of these, 20 males and 16 females had nephrotic syndrome; there were 24 other cases, making an incidence of 3.5% renal admissions and 2.1% nephrotic syndrome.

Clinical data. The mean age was 34.7 years (range 16 to 62 years). There were 9 cases above the age of 40 years, while the remaining 27 were below 40 years. None of the patients had malaria or skin lesions. There were 2 patients who had a history of sore throat, but there was no history of insect bite, vaccination, drug intake or use of cosmetics. The duration of illness was less than 1 year in 20 cases, 2 to 5 years in 12, and above 5 years in 4 patients. About two-thirds of the cases had no pallor or macroscopic haematuria. Most of the patients had oedema of both the face and legs, and some had ascites in addition. Eighteen patients had hypertension (diastolic blood pressure $\geq$ 95mmHg).

Laboratory data. The haematological, urinary, stool and biochemical results are given in Table 1. The mean 24-hour urine protein was 6.4g per litre (range 2.5g to 14.4g per litre). There was pyuria, haematuria, and hyaline and granular casts in varying degrees in the majority of the cases. The BUN and cholesterol levels were elevated in almost a third of the patients. The serum protein electrophoresis, tested in 15 cases, showed hypoalbuminaemia of less than 2.5g% in all, and elevation of the alpha-2 globulin fraction in 14 patients.

TABLE 1. Haematological, urinary, stool and biochemical data of 36 nephrotic syndrome cases

Type of test	*Total tests*	*No. of patients*
Haemoglobin	36	
below 13g%		24
above 13g%		12
Erythrocyte sedimentation rate	36	
above 10mm/hr		34
below 10mm/hr		2
24-hour urine protein	36	
2.5 to 5g/l		20
6g/l and above		16
Urine sediment	36	
pyuria		29
haematuria		28
casts		33
Urine culture	28	
positive		2
(1 *Klebsiella*, 1 *Enterobacter*)		
negative		26
Stool examination	34	
positive for ova and parasites		15
negative for ova and parasites		19
Blood urea nitrogen	36	
abnormal (> 25mg%)		13
normal		23
Creatinine	25	
abnormal (> 2.3mg%)		9
normal		16
Cholesterol	36	
abnormal (> 250mg%)		13
normal		23

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The serological reaction for syphilis carried out in 10 cases was negative. Chest X-ray, performed on 33 patients, showed no abnormality in 26, fibrosis in 2, infiltration of the apices compatible with tuberculosis in 3, and pleural effusion in 2 patients. Stool examination was made in 34 patients, and of these 15 were positive for ova or parasites (ascaris in 5; hookworm in 2; giardia in 2; *Taenia saginata* in 2; *Strongyloides* larvae in 3; *Trichuris trichiura* in 1; and *Entamoeba histolytica* cysts in 1).

The histopathological classification as well as the type and outcome of treatment are summarized in Table 2. Twenty-six patients had primary glomerulonephritis (membranoproliferative 12; mesangial 7; post-infective 2; focal 2; idiopathic membranous 2; and rapidly progressive 1). There was no case of minimal lesion nephrotic syndrome. There were 10 cases of secondary glomerular diseases, of which 7 were amyloidosis. Six patients received standard steroid therapy, 11 "steroid pulse" and 14 symptomatic treatment. Five patients were not started on any treatment. Seven of the 11 "steroid pulse", 3 of the 6 standard steroid, and 3 of the 14 symptomatic treatment patients showed improvement. Eleven patients (2 from the standard steroid, 1 from the "steroid pulse" and 8 from symptomatic treatment) were lost to follow-up, and 7 patients (1 from the standard steroid, and 3 each from "steroid pulse" and symptomatic treatment) remained in the same condition.

DISCUSSION

The patients came from various parts of Ethiopia. It is of interest to note that the 2.1% frequency of nephrotic syndrome in this series compares very well with the 2.4% from Ibadan Hospital in Nigeria (11), and the 2.0% from Mulago Hospital in Uganda (12), but is considerably higher than that of North America (quoted in 12). Our finding appears to be in agreement with the generally-held view that nephrotic syndrome is more common in the tropics than in temperate climates (10). The aetiology of nephrotic syndrome was known in 12 (33%) of our cases. Although quartan malaria has been reported to be the cause of African nephrotic syndrome (12), this type of malaria is extremely rare in Ethiopia. Schistosomiasis has also been reported as a cause of nephrotic syndrome (14), but this was not specifically looked for in this study.

The commonest histological finding was proliferative glomerulonephritis, of which membranoproliferative and mesangial proliferation accounted for over 52% of the total, and for 73% of the primary glomerular diseases. Unlike the situation in other reports (11-13, 15, 16), minimal change lesion was not seen in our series. Amyloidosis accounted for slightly over 19% of our cases.

Ten of the 17 patients who were treated with steroid showed improvement (3 from standard treatment, and 7 from "steroid pulse"). However, it is difficult to draw definitive conclusions from these results, since the number of patients is small, and the follow-up period is short. Further studies, using a larger group and a longer follow-up period, should be undertaken.

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TABLE 2. Histological classification, type and outcome of treatment of 36 nephrotic syndrome cases

TYPE OF LESION	No. of patients	% Total	TYPE OF TREATMENT AND OUTCOME									
			Standard steroid				"Steroid pulse"				Symptomatic			
			Total	Improved	Same	Lost to follow-up	Total	Improved	Same	Lost to follow-up	Total	Improved	Same	Lost to follow-up
Primary Glomerular diseases	26	72.2	6	3	1	2	11	7	3	1	5	2	1	2
Membrano-proliferative glomerulonephritis	12	33.3	3	1	1	1	6	3	2	1	2	-	1	1
Mesangial proliferation	7	19.4	3	2	-	1	2	1	1	-	1	-	-	1
Post-infective glomerulonephritis	2	5.5	-	-	-	-	2	2	-	-	-	-	-	-
Idiopathic membranous	2	5.5	-	-	-	-	-	-	-	-	1	1	-	-
Focal glomerulonephritis	2	5.5	-	-	-	-	1	1	-	-	-	-	-	-
Rapidly progressive glomerulonephritis	1	2.8	-	-	-	-	-	-	-	-	1	1	-	-
Secondary Glomerular Diseases	10	27.8	-	-	-	-	-	-	-	-	9	1	2	6
Amyloidosis	7	19.4	-	-	-	-	-	-	-	-	6	1	2	3
Diabetes	3	8.9	-	-	-	-	-	-	-	-	3	-	-	3

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CASE REPORT

FATAL LIVER TOXICITY DUE TO HYCANTHONE (ETRENOL) IN A PATIENT WITH PRE-EXISTING LIVER DISEASE: A CASE REPORT

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ABSTRACT. *A 30-year-old female patient who developed a fatal acute hepatic necrosis after an injection of hycanthone (Etrenol) is presented. The precautions to be taken while using the drug are stressed, and the literature is briefly reviewed.*

Eternol (Winthrop) is a brand of hycanthone mesylate which is used as a schistosomicidal agent. Its effectiveness against *Schistosoma* was experimentally demonstrated in animals some 15 years ago by different authors (1, 2, 3), and in 1968 and 1969 the drug was tried in humans suffering from schistosomiasis and found to be effective (4, 5). Subsequent studies by other workers also confirmed the effectiveness of the drug in humans (6-9).

The drug is increasingly used in Ethiopia, as in other parts of the world (10), both on out-patients and in-patients, and is associated with side-effects which may be minor or major, depending on the dosage administered. The minor side-effects, which include anorexia, nausea, abdominal pain, dizziness, and pain at the injection site, cease within 24 hours after the injection (8). Serious side-effects, leading to a fatal outcome in some, result from the administration of an overdose of the drug (8, 9), and/or when used in patients with absolute contraindications, namely confirmed, suspected or recent hepatic disease; hepatic tenderness; clinically significant febrile bacterial infections; and the concurrent use of potentially hepatotoxic drugs such as antituberculosis drugs and the phenothiazines (10). In Ethiopia, the drug seems to be quite effective and is not associated with serious side-effects (11). In this paper, the case of a patient with proven *Schistosoma mansoni* is presented; she was admitted to the Black Lion Hospital, Addis Ababa, because of toxicity after an injection with Etrenol.

CASE REPORT

A 30-year-old female patient was admitted to the hospital because of vomiting and jaundice. The patient was apparently healthy until 5 months before admission, at which time she developed occasional abdominal cramps not associated with diarrhoea nor with vomiting. A stool

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examination showed *Schistosoma mansoni* eggs. As evidenced by transaminases and alkaline phosphatase, her liver function tests were then normal, and she was given 200mg Etrenol intramuscularly. A few hours after the injection, she developed persistent vomiting of ingested and bilious material. She received Baralgin (Hoechst), of which a major component is dipyrone, intramuscularly, but this was not of any help at all. Three days later, she was jaundiced. On the sixth day following the administration of Etrenol, she was admitted to the hospital. She had no past history of jaundice, and stated that she never took any local or other form of drug before or after the Etrenol, except for the Baralgin. She occasionally drank the local mildly alcoholic beverage *tella*. She had no prodromal symptoms suggestive of a viral infection prior to the Etrenol.

On examination, the patient was well-nourished, fully conscious but rather depressed and lethargic. Her weight was about 55kg and her height 155cm. The vital signs were normal. The sclerae were jaundiced and the liver edge was tipped, the total span being 10cm along the right mid-clavicular line. The rest of the physical examination was unremarkable.

The white blood-cell count was 7000 per mm^3, erythrocyte sedimentation rate 15mm in the first hour, haemoglobin 14.1g%, and platelets 128,000 per mm^3. The blood film was negative for haemoparasites. The blood urea nitrogen was 4mg, glutamic-oxaloacetic transaminase 121 I.U. (normal 5-18), glutamic-pyruvic transaminase 126 I.U. (normal 6-21), alkaline phosphatase 74 I.U. (normal 60-170), and total serum bilirubin 12.7mg (direct 4.6mg). The serum sodium, potassium and chloride were within the normal limits.

The patient was started on intravenous fluid which contained glucose and vitamins. The jaundice became progressively worse and, on the eleventh day following the administration of Etrenol, she became drowsy and developed asterixis (involuntary flapping reactions). She was put on a standard pre-coma regimen. The following day she lapsed into unconsciousness. She started haemorrhage from the nose and from vein puncture sites, and a transfusion of 5 units of fresh blood was given; but her condition deteriorated, and she died in hepatic coma on the fourteenth day following the Etrenol injection. A post-mortem liver biopsy revealed acute liver cell necrosis with severe bile retention and minimal inflammation. There was also some fibrosis suggesting a preceding cirrhosis, probably of schistosomal aetiology.

DISCUSSION

To date, the mortality rate due to Etrenol is not clearly known. In one study there was less than one death in 20,000 patients treated with the drug, and in over 90% of these deaths there were already conditions predisposing to a possible hepatic insult (12).

This patient had no past history of jaundice nor use of hepatotoxic drugs nor prodromal symptoms suggestive of viral hepatitis. Moreover, the liver function tests just before the Etrenol injection were normal, although this does not rule out the possibility of an underlying liver disease. On the other hand, the patient developed vomiting a few hours after the Etrenol injection, and deteriorated quickly thereafter. This strongly suggests an association of the drug with her acute illness. A similar case was reported by Buchanan and co-workers from South Africa (10).

Vomiting is the commonest symptom of Etrenol toxicity when given in a dosage of 3mg per kg body-weight; a dose of 1.5mg to 2.0mg per kg is considered as effective as the 3mg-per-kg dose, and is more acceptable for

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a control programme because of the marked reduction in side-effects (8). This patient was inadvertently given about 3.5mg per kg, which is 2½ times the dose recommended in the package insert. Hence, even though fulminant viral hepatitis cannot be definitely excluded in the present case, the hepatic damage was most probably due to the overdose of the drug.

Although one Ethiopian study (11) shows Etrenol as both safe and effective, we do not know the incidence of serious side-effects leading to death, as in this patient. Certainly, the drug is of considerable practical importance, since it can be given as a single intramuscular injection, overcoming the problem of patient compliance. The drug is thus of considerable value in the treatment of schistosomiasis, if due consideration is given to dosage and contraindications such as liver disease or the concurrent use of potentially hepatotoxic agents. Our patient was given an injection of Baralgin; the role played by Baralgin the hepatotoxicity is unknown.

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CASE REPORT

FATAL LIVER TOXICITY DUE TO HYCANTHONE (ETRENOL) IN A PATIENT WITH PRE-EXISTING LIVER DISEASE: A CASE REPORT

Mulugetta Mengistu, MD

ABSTRACT. *A 30-year-old female patient who developed a fatal acute hepatic necrosis after an injection of hycanthone (Etrenol) is presented. The precautions to be taken while using the drug are stressed, and the literature is briefly reviewed.*

Eternol (Winthrop) is a brand of hycanthone mesylate which is used as a schistosomicidal agent. Its effectiveness against *Schistosoma* was experimentally demonstrated in animals some 15 years ago by different authors (1, 2, 3), and in 1968 and 1969 the drug was tried in humans suffering from schistosomiasis and found to be effective (4, 5). Subsequent studies by other workers also confirmed the effectiveness of the drug in humans (6-9).

The drug is increasingly used in Ethiopia, as in other parts of the world (10), both on out-patients and in-patients, and is associated with side-effects which may be minor or major, depending on the dosage administered. The minor side-effects, which include anorexia, nausea, abdominal pain, dizziness, and pain at the injection site, cease within 24 hours after the injection (8). Serious side-effects, leading to a fatal outcome in some, result from the administration of an overdose of the drug (8, 9), and/or when used in patients with absolute contraindications, namely confirmed, suspected or recent hepatic disease; hepatic tenderness; clinically significant febrile bacterial infections; and the concurrent use of potentially hepatotoxic drugs such as antituberculosis drugs and the phenothiazines (10). In Ethiopia, the drug seems to be quite effective and is not associated with serious side-effects (11). In this paper, the case of a patient with proven *Schistosoma mansoni* is presented; she was admitted to the Black Lion Hospital, Addis Ababa, because of toxicity after an injection with Etrenol.

CASE REPORT

A 30-year-old female patient was admitted to the hospital because of vomiting and jaundice. The patient was apparently healthy until 5 months before admission, at which time she developed occasional abdominal cramps not associated with diarrhoea nor with vomiting. A stool

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examination showed *Schistosoma mansoni* eggs. As evidenced by transaminases and alkaline phosphatase, her liver function tests were then normal, and she was given 200mg Etrenol intramuscularly. A few hours after the injection, she developed persistent vomiting of ingested and bilious material. She received Baralgin (Hoechst), of which a major component is dipyrone, intramuscularly, but this was not of any help at all. Three days later, she was jaundiced. On the sixth day following the administration of Etrenol, she was admitted to the hospital. She had no past history of jaundice, and stated that she never took any local or other form of drug before or after the Etrenol, except for the Baralgin. She occasionally drank the local mildly alcoholic beverage *tella*. She had no prodromal symptoms suggestive of a viral infection prior to the Etrenol.

On examination, the patient was well-nourished, fully conscious but rather depressed and lethargic. Her weight was about 55kg and her height 155cm. The vital signs were normal. The sclerae were jaundiced and the liver edge was tipped, the total span being 10cm along the right mid-clavicular line. The rest of the physical examination was unremarkable.

The white blood-cell count was 7000 per mm^3, erythrocyte sedimentation rate 15mm in the first hour, haemoglobin 14.1g%, and platelets 128,000 per mm^3. The blood film was negative for haemoparasites. The blood urea nitrogen was 4mg, glutamic-oxaloacetic transaminase 121 I.U. (normal 5-18), glutamic-pyruvic transaminase 126 I.U. (normal 6-21), alkaline phosphatase 74 I.U. (normal 60-170), and total serum bilirubin 12.7mg (direct 4.6mg). The serum sodium, potassium and chloride were within the normal limits.

The patient was started on intravenous fluid which contained glucose and vitamins. The jaundice became progressively worse and, on the eleventh day following the administration of Etrenol, she became drowsy and developed asterixis (involuntary flapping reactions). She was put on a standard pre-coma regimen. The following day she lapsed into unconsciousness. She started haemorrhage from the nose and from vein puncture sites, and a transfusion of 5 units of fresh blood was given; but her condition deteriorated, and she died in hepatic coma on the fourteenth day following the Etrenol injection. A post-mortem liver biopsy revealed acute liver cell necrosis with severe bile retention and minimal inflammation. There was also some fibrosis suggesting a preceding cirrhosis, probably of schistosomal aetiology.

DISCUSSION

To date, the mortality rate due to Etrenol is not clearly known. In one study there was less than one death in 20,000 patients treated with the drug, and in over 90% of these deaths there were already conditions predisposing to a possible hepatic insult (12).

This patient had no past history of jaundice nor use of hepatotoxic drugs nor prodromal symptoms suggestive of viral hepatitis. Moreover, the liver function tests just before the Etrenol injection were normal, although this does not rule out the possibility of an underlying liver disease. On the other hand, the patient developed vomiting a few hours after the Etrenol injection, and deteriorated quickly thereafter. This strongly suggests an association of the drug with her acute illness. A similar case was reported by Buchanan and co-workers from South Africa (10).

Vomiting is the commonest symptom of Etrenol toxicity when given in a dosage of 3mg per kg body-weight; a dose of 1.5mg to 2.0mg per kg is considered as effective as the 3mg-per-kg dose, and is more acceptable for

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BRIEF COMMUNICATION

GLOMERULONEPHRITIS: A PRELIMINARY CLINICO-PATHOLOGICAL REPORT ON 29 PATIENTS

J.P. Alfonzo,[1] MD, J.W. Landells,[2] BCh, MRCP, and Seifu Daniel,[1] MD

ABSTRACT. *Between March and December 1980, 29 patients with glomerular diseases were studied at the Black Lion Hospital, Addis Ababa. The pertinent clinical, laboratory and histopathological findings are described. Four of the renal biopsy speciments were of no use for histological interpretation, but the rest were adequate for study under the light microscope. Diffuse proliferative glomerulonephritis was the commonest finding. There were 4 secondary amyloidosis cases. There were 22 patients who presented as nephrotic syndrome, 5 as nephritic syndrome, 1 with proteinuria-haematuria, and 1 with isolated proteinuria.*

Seven patients with nephrotic syndrome received "steroid pulse" therapy, and 3 of these had improvement or total remission, while 3 of the 6 nephrotics treated with the standard steroid therapy responded well. Of the 29 patients, 14 had total remission or improvement, 9 showed no change, 5 were lost to follow-up, and 1 died.

We suggest further studies to determine the extent of the disease, as well as to know the type of the lesion, therapy and prognosis of glomerulonephritis in Ethiopia.

Glomerular disease is not a single pathological entity. It includes at least 8 identifiable primary diseases in addition to many other systemic diseases which also involve the kidney, mainly the glomeruli (1). These glomerular diseases, commonly referred to as glomerulonephritis, may be similar clinically, but they can be classified into different pathological entities on the basis of the pattern of aetiology, pathogenesis, prognosis and histology.

The frequency of renal disease in general in Ethiopia, and glomerulonephritis in particular, is not well known. Retrospective analyses of medical admissions from various hospitals (2-8), as indicated in Table 1, mention acute and chronic glomerulonephritis which were diagnosed on clinical and laboratory grounds. Recently, Berhanu Habte and Bayu Teklu (8) emphasized that glomerular diseases (chronic glomerulonephritis) were the main cause of chronic renal failure. Mesfin Afework *et al.* (9) also reported on glomerular diseases in children. In these reports, however, histological confirmation of the type of glomerular disease is lacking.

The purpose of this review is to focus attention on renal diseases and to emphasize the importance of histopathological studies in diagnosis, prognosis and treatment.

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TABLE 1. Morbidity of genito-urinary diseases due to acute and chronic glomerulonephritis: retrospective analysis of medical admissions from 1966 in Ethiopia

Authors, year and reference	Years of survey	City	Total no. of patients	Morbidity: genito-urinary system	Principal renal disease:	%
Molineaux, L, et al., 1966 (2)	1963-65	Gondar	3508	4.4	Acute glomerulonephritis Chronic glomerulonephritis	1.1 1.5
Teferra, A, and Abdulkadir, J, 1968 (3)	1966-67	Addis Ababa	1013	6.4	Chronic glomerulonephritis	2.9
Pavlica, D, 1970 (4)	1966-70	Addis Ababa	3922	2.8	Acute glomerulonephritis Chronic glomerulonephritis	0.5 0.8
Lainovic, D, 1974 (5)	1963-69	Dire Dawa	9330	7.8	Unspecified	
Habte-Gabr, E, et al., 1976 (6*)	1971-72	Gondar	3611	3.3	Acute glomerulonephritis Nephrotic syndrome	0.6 0.6
Lester, FT, and Tsega, E, 1976 (7)	1971-75	Addis Ababa	4640	6.0	Acute glomerulonephritis Chronic glomerulonephritis Acute renal failure	0.6 0.6 0.04
Berhanu Habte and Bayu Teklu, 1980 (8)	1975-79	Addis Ababa	3530	--	Chronic glomerulonephritis	1.3

*This paper includes children.

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PATIENTS AND METHODS

A prospective study was made of 29 consecutive adult patients with glomerular diseases, admitted over a nine-month period (March to December, 1980) to the Black Lion Hospital, Addis Ababa. Using a prepared protocol, the pertinent clinical, laboratory and histological data were documented for each patient. The laboratory investigations included a routine haematological examination, blood chemistry, total serum protein, serum electrophoresis, cholesterol, stool examination for ova and parasites, 24 hours' urine protein, quantitative urine sedimentation determination and urine culture, chest X-ray and an intravenous pyelogram. Patients with a serum creatinine of more than 5mg per decilitre (dl) were excluded, except those who had a recent onset of the disease without anaemia and with a normal-sized kidney. All patients suspected of advanced chronic renal failure were also excluded from this study.

A percutaneous renal biopsy was performed on 27 patients using a Menghini needle, while in 2 patients the renal biopsy was taken at exploratory lumbotomy. The renal tissue was fixed in 10% formalin. Thin paraffin sections were stained with haematoxylin-eosin and periodic acid Schiff (PAS), and some of them were also stained with silver methenamine, Masson's trichromic and Congo Red stains. These sections were examined by direct light microscopy by the nephrologist and pathologist. On the histopathological findings, the patients were grouped according to the WHO classification on Nomenclature of Renal Diseases (1).

All patients with a primary nephrotic syndrome received either a standard steroid therapy (2mg per kg body-weight on alternate days for 6 to 8 weeks, and then the steroid was tapered off and discontinued after a month) or a high dose of prednisolone (10mg per kg body-weight intravenously on alternate days for 3 doses), i.e. "Steroid Pulse". Those cases with secondary nephrotic syndrome were given either a symptomatic treatment alone or indomethacin. The patients with nephritic syndrome were treated with a combination of drugs (steroid plus indomethacin, or steroid indomethacin and heparin) or symptomatically. The response after 8 weeks of treatment, assessed by means of renal function tests, proteinuria and clinical improvement, was categorized as (a) total remission when the serum creatinine or blood urea nitrogen (BUN) was equal to or less than the value before treatment and without proteinuria; (b) improvement when serum creatinine or BUN was equal to or less than the value before treatment but with persistent, moderate proteinuria of less than 3gm per 24 hours; and (c) no change when there was an increase in serum creatinine or BUN from the initial value, with persistent and severe proteinuria of equal to or greater than 3gm per 24 hours.

RESULTS

There were 20 female and 9 male patients. The mean age was 33.4 years (range: 14 to 62 years). Nineteen patients had developed symptoms for the first time within the previous 6 months before their hospital admission, and most of these were nephritic and nephrotic syndrome cases. The aetiology of the nephropathy in 17 patients was unknown. Of the remaining 12 patients, 4 had "reactive amyloidosis"; 4 had previous throat or skin infections; 2 had diabetes mellitus; 1 was pregnant; and 1 had a suspected renal vein thrombosis.

Twenty-two of the patients presented as nephrotic syndrome (serum protein of less than 6gm per dl and a heavy proteinuria of more than 3gm in 24 hours' urine, or a

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persistent 3 to 4-plus proteinuria in the standard urine analysis); 5 cases had nephritic syndrome (hypertension, haematuria, oliguria and slight to moderate proteinuria); 1 had macroscopic haematuria and mild proteinuria; and 1 had an isolated proteinuria. The main complaints were macroscopic haematuria, described as tea-coloured urine, or gross haematuria as well as swelling of the legs and face. The main physical findings were hypertension and pallor. Of the nephrotic syndrome cases, 50% had reddish urine and hypertension, and both of these findings were considered as signs of poor prognosis in these patients. All patients with nephritic syndrome had severe hypertension (diastolic of over 110 mmHg), while macroscopic haematuria as well as slight to moderate oedema was noted in 4 out of 5 cases. Anaemia was present in 5 cases of longstanding nephrotic syndrome, with some degree of renal insufficiency (BUN greater than 25mg per dl), but was found in only 1 case of nephritic syndrome, even though these presented a higher level of BUN in the initial period of the disease.

Patients with proteinuria and haematuria or isolated proteinurea had no anaemia. Of the 29 patients, 11 had increased serum BUN at the time of renal biopsy, and, of these, 7 were nephrotic syndrome cases and 4 were nephritic syndrome cases. The urine showed a moderate to severe proteinuria of more than 1.5gm, or a qualitative urine test result of 3 to 4-plus. All cases of nephritic syndrome had microscopic haematuria, while 6 of the nephrotic syndrome cases had macroscopic haematuria at the beginning of their illness. Two patients had a positive urine culture for *Aerobacter* and *Klebsiella* organisms.

A total of 34 renal biopsies was performed in the 29 patients. Four of the biopsy specimens were useless, while the rest were adequate for histological study by light microscopy. There was no major complication from the procedure; some patients had transient haematuria and low-grade lumbar pain. The commonest histological finding was a diffuse cellular proliferative pattern, giving rise to the various forms of glomerular diseases. The clinicopathological correlation is summarized in Table 2. Twenty-three cases were primary glomerulonephritis, and 6 were secondary glomerulonephritis, of which 4 were reactive amyloidosis and 2 were diabetes nephropathy.

The results of treatment are indicated in Table 3. The overall result of treatment in the nephrotic syndrome group shows that 9 had total remission or improvement, 8 showed no change, and 5 were lost to follow-up. Of the 5 nephritie syndrome cases, 4 had total remission or improvement, and the fifth patient had a rapidly progressive glomerulonephritis with anuria for 23 days. He had exploratory lumbotomy for suspected obstructive anuria; on the ninth day after his operation he was put on heparin, but he developed retroperitoneal bleeding and died. Of the 2 cases with proteinuria-haematuria and isolated proteinuria respectively, treated symptomatically, there was remission in the first case, while no change was noticed in the second.

DISCUSSION

The morbidity and the type of primary glomerulonephritis in adult Ethiopians is not well known. There have been reports from Africa on nephrotic syndrome, mainly in children (9-13), which attempted to characterize the diseases from a clinical and pathological viewpoint (10), but such studies in adult Africans are few. The pathogenesis of renal lesions in Africans is also not well known, although *Plasmodium falciparum* and *P. malariae* as well as streptococcal

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TABLE 2. Histological studies from needle biopsies of the kidney in 29 patients with glomerular diseases

	Nephrotic syndrome	*Nephritic syndrome*	*Proteinuria and haematuria*	*Isolated proteinuria*
Mesangio-proliferative	4	-	-	-
Membrano-proliferative	4	2	-	-
Rapidly progressive	-	2	-	-
Amyloidosis	1	-	-	-
Focal	1	-	-	-
Minimal change	-	1	-	-
Diabetes nephropathy	1	-	-	1
Focal segmental sclerosis (hyalinosis)	1	-	-	-
Post-infectious	4	-	-	-
Membranous (idiopathic)	2	-	-	-
Unclassified	1	-	1	-
Total	22	5	1	1

TABLE 3. Treatment and results in 29 patients with glomerular diseases

	Total remission	*Improvement*	*No change*	*Lost to follow-up*	*Died*
Nephrotic syndrome (22 cases)					
Steroid, alternate days	1	2	1	2	-
Steroid pulse	2	1	3	1	-
Indomethacin	-	1	1	1	-
Symptomatic	1	1	3	1	-
Nephritic syndrome (5 cases)					
Steroid/indomethacin	-	1	-	-	1
Steroid/heparin/azathioprine	1	-	-	-	-
Symptomatic	1	1	-	-	-
Proteinuria and haematuria (1 case)					
Symptomatic	1	-	-	-	-
Isolated proteinuria (1 case)					
Symptomatic	-	-	1	-	-
Total	7	7	9	5	1

antigens are mentioned as the cause in some patients (10, 14).

It is hoped that the present study, the first of its nature, will act as a stimulus for further studies. The small number of patients and the short period of follow-up has made it difficult to draw any conclusion in terms of the extent of the problem, outcome of treatment and prognosis of the disease. However, we suggest that renal biopsy is a safe and important procedure which should be done routinely on patients with glomerular lesion, in order to learn the type of the disease, and so to be able to institute appropriate therapy and to determine response and prognosis.

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NEPHROTIC SYNDROME IN ADULT ETHIOPIANS

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ABSTRACT. *The clinical, laboratory and histopathological data and outcome of treatment are described in 36 adult Ethiopian patients with nephrotic syndrome, admitted to the Black Lion Hospital in Addis Ababa over a 14-month period (April 1980 to July 1981). There were 20 males and 16 females; the mean age was 34.7 years. During the study period, nephrotic syndrome accounted for 2.1% of medical admissions. The aetiology of the nephrotic syndrome was known in 12 of the cases. The commonest histological finding was proliferative glomerulonephritis, of which membranoproliferative and mesangial proliferation accounted for over 52% of the total and of 73% of the primary glomerular diseases. There was no case of minimal lesion glomerulonephritis in this study.*

The prevalence of renal diseases in general, and of nephrotic syndrome in particular, in adult Ethiopians is unknown. Analyses of hospital admissions from different parts of Ethiopia indicate that renal diseases account for 1.2% — 2.8% of the total admissions (1-7). Nephrotic syndrome has been mentioned only in 4 reports (6-9). The syndrome has, however, been reported as a common condition in Kenyatta National Hospital, Nairobi (10); Nigeria (11); in Mulago Hospital in Uganda (12); and in the South African Bantu (13).

Except for the recent report by Alfonzo *et al.* (9), in which renal biopsy was performed, the diagnosis of renal diseases in previous reports (1-8) has been made on the basis of clinical and laboratory findings. This paper describes the clinical, laboratory and histopathological reports and outcome of treatment in 36 adults with nephrotic syndrome who were admitted to the Black Lion Hospital, Addis Ababa.

PATIENTS AND METHODS

After the development of the nephrology unit in Black Lion Hospital, in early 1980, kidney biopsy became a routine procedure whenever indicated and when patients consented to the procedure.

During a 14-month period (April 1980 to July 1981), there were 36 adults with nephrotic syndrome who had renal biopsy; these patients were studied prospectively, using a prepared protocol. In addition to a carefully taken history and physical examination, in order to elucidate the aetiology of the syndrome, the following investigations were made: urine for protein and sugar, microscopic examination of urine sediments, 24 hours' urine protein, urine culture;

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complete blood count, serum protein and electrophoresis, cholesterol, creatinine, blood urea nitrogen (BUN); chest X-ray; stool examination for ova and parasites; and serological test for syphilis. The assay of the antistreptolysin 0 titre was not possible. All the patients had a percutaneous kidney biopsy, with the Menghini needle. The kidney tissue was fixed in 10% formalin. Thin paraffin sections of the tissue were then stained with periodic acid Schiff (PAS), Congo Red and haematoxylin-eosin. The slides were then examined only under light microscopy, since fluorescence microscopy was not available.

The criteria for the diagnosis of nephrotic syndrome included the presence of oedema, hypoproteinaemia of less than 6g%, and a significant proteinuria (24-hour protein of more than 2.5g per litre, or proteinuria of 2.5mg per minute or 50mg per kg body-weight).

Treatment and response. The treatment given was one of the following:

A. *Standard steroid.* Standard steroid treatment was given in a dosage of 2mg per kg body-weight on alternate days up to a maximum dose of 100mg per day for 6 to 8 weeks, and then gradually tapered off and discontinued after one month.

B. *"Steroid pulse".* "Steroid pulse" treatment was given in a dosage of 10mg per kg body-weight intravenously on alternate days for 3 doses.

C. *Symptomatic.* Diuretics and/or indomethacin were used.

The response to treatment is described as improved if the urine was continuously free of protein and the BUN or creatinine was equal to or less than the initial value after 8 weeks of treatment maintained up to the last examination (which in some cases was after a year). The outcome of and a BUN or creatinine greater than or equal to the value before treatment is described as unchanged.

RESULTS

During the study period, 903 males and 827 females (total 1,730) were admitted to the 83-bed medical department of the Black Lion Hospital. Of these, 20 males and 16 females had nephrotic syndrome; there were 24 other cases, making an incidence of 3.5% renal admissions and 2.1% nephrotic syndrome.

Clinical data. The mean age was 34.7 years (range 16 to 62 years). There were 9 cases above the age of 40 years, while the remaining 27 were below 40 years. None of the patients had malaria or skin lesions. There were 2 patients who had a history of sore throat, but there was no history of insect bite, vaccination, drug intake or use of cosmetics. The duration of illness was less than 1 year in 20 cases, 2 to 5 years in 12, and above 5 years in 4 patients. About two-thirds of the cases had no pallor or macroscopic haematuria. Most of the patients had oedema of both the face and legs, and some had ascites in addition. Eighteen patients had hypertension (diastolic blood pressure $\geq$ 95mmHg).

Laboratory data. The haematological, urinary, stool and biochemical results are given in Table 1. The mean 24-hour urine protein was 6.4g per litre (range 2.5g to 14.4g per litre). There was pyuria, haematuria, and hyaline and granular casts in varying degrees in the majority of the cases. The BUN and cholesterol levels were elevated in almost a third of the patients. The serum protein electrophoresis, tested in 15 cases, showed hypoalbuminaemia of less than 2.5g% in all, and elevation of the alpha-2 globulin fraction in 14 patients.

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TABLE 1. Haematological, urinary, stool and biochemical data of 36 nephrotic syndrome cases

Type of test	*Total tests*	*No. of patients*
Haemoglobin	36	
below 13g%		24
above 13g%		12
Erythrocyte sedimentation rate	36	
above 10mm/hr		34
below 10mm/hr		2
24-hour urine protein	36	
2.5 to 5g/l		20
6g/l and above		16
Urine sediment	36	
pyuria		29
haematuria		28
casts		33
Urine culture	28	
positive		2
(1 *Klebsiella*, 1 *Enterobacter*)		
negative		26
Stool examination	34	
positive for ova and parasites		15
negative for ova and parasites		19
Blood urea nitrogen	36	
abnormal (> 25mg%)		13
normal		23
Creatinine	25	
abnormal (> 2.3mg%)		9
normal		16
Cholesterol	36	
abnormal (> 250mg%)		13
normal		23

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The serological reaction for syphilis carried out in 10 cases was negative. Chest X-ray, performed on 33 patients, showed no abnormality in 26, fibrosis in 2, infiltration of the apices compatible with tuberculosis in 3, and pleural effusion in 2 patients. Stool examination was made in 34 patients, and of these 15 were positive for ova or parasites (ascaris in 5; hookworm in 2; giardia in 2; *Taenia saginata* in 2; *Strongyloides* larvae in 3; *Trichuris trichiura* in 1; and *Entamoeba histolytica* cysts in 1).

The histopathological classification as well as the type and outcome of treatment are summarized in Table 2. Twenty-six patients had primary glomerulonephritis (membranoproliferative 12; mesangial 7; post-infective 2; focal 2; idiopathic membranous 2; and rapidly progressive 1). There was no case of minimal lesion nephrotic syndrome. There were 10 cases of secondary glomerular diseases, of which 7 were amyloidosis. Six patients received standard steroid therapy, 11 "steroid pulse" and 14 symptomatic treatment. Five patients were not started on any treatment. Seven of the 11 "steroid pulse", 3 of the 6 standard steroid, and 3 of the 14 symptomatic treatment patients showed improvement. Eleven patients (2 from the standard steroid, 1 from the "steroid pulse" and 8 from symptomatic treatment) were lost to follow-up, and 7 patients (1 from the standard steroid, and 3 each from "steroid pulse" and symptomatic treatment) remained in the same condition.

DISCUSSION

The patients came from various parts of Ethiopia. It is of interest to note that the 2.1% frequency of nephrotic syndrome in this series compares very well with the 2.4% from Ibadan Hospital in Nigeria (11), and the 2.0% from Mulago Hospital in Uganda (12), but is considerably higher than that of North America (quoted in 12). Our finding appears to be in agreement with the generally-held view that nephrotic syndrome is more common in the tropics than in temperate climates (10). The aetiology of nephrotic syndrome was known in 12 (33%) of our cases. Although quartan malaria has been reported to be the cause of African nephrotic syndrome (12), this type of malaria is extremely rare in Ethiopia. Schistosomiasis has also been reported as a cause of nephrotic syndrome (14), but this was not specifically looked for in this study.

The commonest histological finding was proliferative glomerulonephritis, of which membranoproliferative and mesangial proliferation accounted for over 52% of the total, and for 73% of the primary glomerular diseases. Unlike the situation in other reports (11-13, 15, 16), minimal change lesion was not seen in our series. Amyloidosis accounted for slightly over 19% of our cases.

Ten of the 17 patients who were treated with steroid showed improvement (3 from standard treatment, and 7 from "steroid pulse"). However, it is difficult to draw definitive conclusions from these results, since the number of patients is small, and the follow-up period is short. Further studies, using a larger group and a longer follow-up period, should be undertaken.

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TABLE 2. Histological classification, type and outcome of treatment of 36 nephrotic syndrome cases

TYPE OF LESION	No. of patients	% Total	TYPE OF TREATMENT AND OUTCOME									
			Standard steroid				"Steroid pulse"				Symptomatic	
			Total	Improved	Same	Lost to follow-up	Total	Improved	Same	Lost to follow-up	Improved	Same	Lost to follow-up
Primary Glomerular Diseases	26	72.2	6	3	1	2	11	7	3	1	5	2	1	2
Membrano-proliferative glomerulonephritis	12	33.3	3	1	1	1	6	3	2	1	2	-	1	1
Mesangial proliferation	7	19.4	3	2	-	1	2	1	1	-	1	-	-	1
Post-infective glomerulonephritis	2	5.5	-	-	-	-	2	2	-	-	-	-	-	-
Idiopathic membranous	2	5.5	-	-	-	-	-	-	-	-	1	1	-	-
Focal glomerulonephritis	2	5.5	-	-	-	-	1	1	-	-	-	-	-	-
Rapidly progressive glomerulonephritis	1	2.8	-	-	-	-	-	-	-	-	1	1	-	-
Secondary Glomerular Diseases	10	27.8	-	-	-	-	-	-	-	-	9	1	2	6
Amyloidosis	7	19.4	-	-	-	-	-	-	-	-	6	1	2	3
Diabetes	3	8.9	-	-	-	-	-	-	-	-	3	-	-	3

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CHRONIC DISEASE PREVALENCE IN ETHIOPIAN BANK EMPLOYEES

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ABSTRACT. *The prevalence of chronic diseases amongst 2,854 Ethiopian Bank employees was determined at the end of July 1979. Hypertension led the list with a prevalence of 3.8%, followed by bronchial asthma and diabetes mellitus with 3.5% and 1.2% respectively. Other diseases with a prevalence of almost 1% included allergic rhinitis and chronic otitis media. Gout was also not an uncommon disease among the middle-aged and the economically well-off; the same was true of myocardial infarction. Malignancies varied in type, but had a greater predilection for the male.*

In a previous report the number of clinic visits and types of diseases seen at the Bank Employees' Clinic, Addis Ababa, over a period of one year was described (1), but the actual number of patients with specific diseases was not mentioned. The purpose of this communication is to document the number of patients with chronic diseases seen at the clinic from November 1975 until the end of July 1979. These diseases carry serious morbidity and/or mortality.

PATIENTS

From November 1975, all patients who saw the part-time bank physician or were seen in a hospital or specialized clinics were registered daily at the Bank Employees' Clinic. The Registry Book contains the name of the patient, chart number, diagnosis and recommendations, which include medications, sick-leave and referrals. The names of those patients with chronic diseases were obtained from this Registry Book, and the clinical charts were critically reviewed as to the details of work-up and diagnoses.

As in the Framingham study (2), hypertension is diagnosed when a blood pressure of 160mmHg or above systolic, and/or 95mmHg or above diastolic is recorded on at least two occasions.

All the tuberculosis patients were diagnosed either bacteriologically or histologically. All the neoplastic cases were proven histologically except in the hepatomas and gastric cancer, when the diagnosis was made by the typical clinical picture.

All the time of this study, July 1979, there was in all the three banks in Addis Ababa (National, Commercial, and Housing and Savings Banks) a total of 2,850 clinical charts for review, of 2,199 males and 651 females. The healthy employees or patients who left the banks before July 1979 were not included in the study, but 121 males and 14 females employed and present from November 1975 to July 1979 were included.

RESULTS

Table 1 shows the number and types of chronic diseases amongst bank employees. In the male, hypertension leads the list, and asthma, allergic rhinitis and diabetes mellitus had prevalences of over 1%; in the female, however, the diseases with prevalences of

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about 1% and above included asthma, hypertension, chronic otitis media, allergic rhinitis and gallstones, in descending order.

Tables 2 and 3 show the age and sex distribution of hypertension and diabetes mellitus patients respectively. Among the diabetics, 12 (36%) had high blood pressure, and there was 1 with asthma, 1 with cancer of the breast and 1 with psychosis; of these 12 with diabetes and hypertension, all except 1 were males. Of the 33 diabetics, 5 were on insulin, 24 on oral agents, and 4 on diet alone; all had developed the disease after employment. On the other hand, among the 108 hypertensive patients, 12 males and 1 female had high blood pressure at pre-employment physical examination.

Of the 17 patients, all males, with gout, 8 had typical podagra, and 5 of the latter were on hydrochlorthiazide at the time of gouty attack; 9 had hypertension, and 2 of these also had diabetes. Their ages ranged from 39 to 57 (mean 48 years).

Table 4 shows details of malignancies. All patients except 2 were males. The age range was from 35 to 69 (mean 49 years). One woman had breast cancer, and the other had cancer of the body of the uterus.

All 33 patients with chronic otitis media had gross scarring of the eardrums, with perforations in 14, and all had grossly detectable decreased hearing.

The renal and gallstone cases were all proven by X-ray; some patients had undergone surgery. Duodenal ulcer patients were diagnosed either by barium meal or by upper gastrointestinal endoscopy.

All 4 myocardial infarctions had occurred in males since 1977, with 1 death. The age range was 45 to 50 (mean 47 years). The man who died was a diabetic on oral agents, and the other 3 were heavy cigarette-smokers.

DISCUSSION

Since all employees of the banks get free medical service, there is a good chance that those with known chronic diseases come to the Bank Clinic at some time. Of the very few patients who are seen and followed up in hospitals or clinics, their medical certificates, prescriptions and medical bills are brought to the clinic for approval by the bank physician, and the information is registered in their charts. In practice, since the clinic deals only with bank employees, those with chronic diseases are well known to the clinic staff, the nurses and the doctor. It is therefore unlikely that patients with known chronic diseases are missed, which means that the calculated prevalence must be reasonably accurate.

It is, however, possible that some diseases such as duodenal ulcer, liver cirrhosis and hypertension are underdiagnosed because of the nature of the investigations usually undertaken. A duodenal ulcer may pass for simple gastritis unless endoscopies or barium meals – impractical and expensive to perform – are undertaken on all those complaining of peptic symptoms. Cirrhosis is usually cryptic until the full symptoms and/or signs are present. Unless routine blood pressure screening is performed, several hypertensives could be missed.

In all the chronic diseases except gallstones, tuberculosis and chronic otitis media, males outnumber females far in excess of the ratio of the sexes present in the banks. None of the women had myocardial infarction, neoplasms other than in one in the breast and one in the uterus, Bell's palsy, psoriasis, cirrhosis or gout, despite the presence of several postmenopausal women.

The fact that diabetes mellitus is not a rare disease in Ethiopians has been

TABLE 1. Prevalence of chronic diseases among bank employees

Disease	Male	Female	Total	Prevalence (%) Male	Prevalence (%) Female
1. Hypertension	90	18	108	4.1	2.8
2. Asthma	77	23	100	3.5	3.5
3. Allergic rhinitis	35	11	46	1.6	1.7
4. Diabetes mellitus	31	2	33	1.4	0.3
5. Chronic otitis media	17	16	33	0.8	2.5
6. Duodenal ulcer	19	3	22	0.9	0.5
7. Renal stones	18	4	22	0.8	0.6
8. Psychosis	17	2	19	0.8	0.3
9. Gout	17	0	17	0.8	0
10. Neoplasms, malignant	9	2	11	0.3*	0.3
11. Tuberculosis	6	4	10	0.3	0.6
12. Gallstones	2	6	8	0.1	0.9
13. Cirrhosis	7	0	7	0.3	0
14. Psoriasis	6	0	6	0.3	0
15. Bell's palsy	5	0	5	0.2	0
16. Myocardial infarction	4	0	4	0.1*	0

*excluding those who died before July 1979

TABLE 2. Hypertension among Ethiopian bank employees

Age	Male	Female
20-29	6	1
30-39	16	10
40-49	35	7
50-59	21	0
60 and over	2	0

TABLE 3. Diabetes mellitus among Ethiopian bank employees

Age	Male	Female
20-29	1	0
30-39	5	0
40-49	13	2
50-59	12	0
60 and over	1	0

TABLE 4. Malignant neoplasia among Ethiopian bank employees

Type	No.	Age	Sex	Diagnosis Year	Outcome, July 1979
1. Acoustic neuroma	1	37	M	1975	Alive after surgery
2. Carcinoma of the colon	1	35	M	1978	Alive after surgery
3. Renal cell carcinoma	1	46	M	1976	Alive after nephrectomy
4. Breast cancer	1	42	F	1978	Alive after mastectomy
5. Gastric cancer	1	53	M	1979	Died
6. Hepatoma	2	50, 65	M	1978,1979	Died
7. Bronchogenic cancer	1	55	M	1978	Alive
8. Central nervous system tumour	1	53	M	1979	Alive
9. Chronic lymphatic leukaemia	1	52	M	1978	Alive
10. Cancer of uterus	1	50	F	1979	Alive; refused surgery

emphasized previously (3,4), and the current prevalence of about 1% confirms that finding. What is interesting is the paucity of female diabetics in contrast to previous Ethiopian and other African series (3-5), although the age distribution of the current series is similar to that reported by Belcher (3) and Lester *et al.* (4). The prevalence of diabetes mellitus is 2.1% in the USA (6) and over 1% in Britain (7), while it is 1.4% in the male bank community in Addis Ababa. It is important to emphasize, however, that none of the employees was diabetic at employment. In other African countries the prevalences range from 0.1 to 3.2% (8).

High blood pressure was well established in 12 diabetics (36%), in contrast to reports by Belcher (3) and Lester *et al.* (4) from Northern Ethiopia and Central Ethiopia (2% and 11.4% respectively). Although this discrepancy cannot be explained with certainty, "urbanization" of bank employees may contribute to the high incidence of hypertension among our diabetics, in whom hypertension preceded diabetes in 7 patients and was discovered simultaneously in 1 patient.

Among the 3 Ethiopian reports, the management of diabetes differed markedly. Among the patients recorded by Belcher (3), 81% were from rural areas, and 85% of the whole group required insulin, in contrast to only 15% in the current series; the latter finding is close to the 20% of a Western affluent society (7). It is also of interest to note that in the current series, all who are on oral agents except 2 are within the high-income bracket. Lester *et al.* (4) reported that of 383 patients, 137 (36%) required insulin, 236(61%) were on oral agents, and the rest were maintained on diet alone. Lester *et al.* (4) do not, however, indicate where the patients came from. The difference may be due to "urban" and "rural" diabetes, the latter requiring insulin more frequently.

Well-documented high blood pressure was present in 108 patients, with a prevalence of 4.1% in the males and 2.8% in the females. Lester (9) reported high blood pressure in 12% of out-patients, with only one reading. The other casual blood pressure record of Parry (10) reported hypertension in 6.2% of adults above the age of 19 years. These 2 reports have their shortcomings: they have only one initial reading; blood pressures must have been taken by different observers; and there was no attempt to classify the patients into "rural" and "urban" population. In the current series, however, hypertension was well documented with at least 2 high blood pressure records, and, in addition, blood pressures were taken by 2 nurses and a doctor only. As the patients were also very familiar with the clinic staff, the chances of spurious elevations of blood pressures were minimal.

The prevalence of bronchial asthma, 3.5%, in bank employees is even higher than the hospital visits of 1% reported by Lester (11).

All the 4 myocardial infarctions occurred in high-ranking middle-aged officials. That high socio-economic status is the single most important risk factor of myocardial infarction in Ethiopians has been emphasized previously by Teklu *et al.* (12). Three were heavy cigarette-smokers and were overweight. One of the patients who died had diabetes mellitus, and had been on tolbutamide for over 10 years.

The total number of malignancies was small, and they occurred in single cases only of each except for 2 patients with hepatoma. The relative absence of malignant neoplasms in the females, with the exception of one each in breast and uterus, is curious.

The psychotic cases were diagnosed at the Bank Employees' Clinic and by psychiatrists. In all these cases, the manifestations were clear-cut. Three of the patients has such uncontrollable symptoms that they

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were either dismissed or pensioned off. The prevalence of 0.8% and 0.3% in males and females respectively cannot be ignored; the average prevalence is higher than the figure of 0.3% of the general population reported from various African countries (13). Even though only psychosis has been considered here, the prevalence of serious psychiatric diseases such as manic depression, psychoneurosis, hypochondriasm and personality disorders is high. One patient was pensioned off because of depression. Giel and van Luijk (14) reported 19% of patients having psychiatric disorders, as observed in a rural health centre and in an urban general out-patient clinic in Ethiopia.

It can be concluded that hypertension, asthma, allergic rhinitis, chronic otitis media, diabetes, nephrolithiasis and duodenal ulcers are important causes of morbidity in the bank structure. Indeed, the true prevalence of some of these diseases would have been higher than appears in this study if a systematic search had been made amongst all employees. A study of this nature in some of these diseases is currently being undertaken. The prevalences obtained for different chronic diseases amongst bank employees are likely to be applicable to similar other "urban" populations in Ethiopia, with few and slight differences. However, it would be useful to expand this kind of study to include larger "urban" populations, and to compare the results with those in "rural" Ethiopia. This would imply a wider and more community-oriented practice of medicine.

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Alfonzo Guerra, JP, Mulugetta Mengistu, Melamed, MD, and Eyassu Habte-Gabr. 1982. *Ethiop. Med. J. 20, 69*

RENAL AMYLOIDOSIS IN ADULT ETHIOPIANS[1]

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ABSTRACT. *During the 10-month period April 1980 to January 1981, a percutaneous needle biopsy of the kidney was performed on 38 patients with glomerular diseases at the Black Lion Hospital in Addis Ababa. Of these, 6 patients were found to have renal amyloidosis due to tuberculosis (4 cases), and lepromatous leprosy (1 case); the sixth patient had endemic goitre and probably a past chronic lung disease. The pertinent clinical and laboratory data are briefly discussed. Since chronic diseases are very prevalent in Ethiopia, we suggest that patients who suffer from such diseases and have proteinuria should have the necessary investigations for amyloidosis; and further studies should be undertaken in order to determine the extent of the disease.*

Amyloidosis is a group of diseases resulting from systemic or localized deposition of extracellular protein fibril in various tissues and organs. Amyloidosis may be categorized into "immunocyte dyscrasias with amyloidosis" and "reactive systemic amyloidosis" (1); the latter has been reported in connection with various acute recurrent or chronic infections and various forms of inflammatory, parasitic and neoplastic disease(1-5). Chronic infections still remain an important worldwide cause of "reactive amyloidosis".

Seventy-five per cent of 200 cases from India, 54% of 37 cases from a Scottish series and nearly 33% of 22 patients from an American series had "reactive amyloidosis" due to tuberculosis (6). The kidney is the most important site of involvement in all forms of amyloidosis (7,8).

Since Rokitansky's description of the disease in 1842 (quoted in 2), many cases have been reported, but the report from Africa appears to be scanty. Raper (9) reported cases of renal amyloidosis for the first time from Uganda on necropsy material in 1953, and Leather (3) reported 3 cases, diagnosed in life, in 1959. In 1974, Ojwang *et al.* (10) from Kenya and, in 1979, Gold (4) from South Africa reported 4 cases and 7 cases, respectively. Recently, Musa *et al.* (11) found 4 cases of amyloidosis while studying the pattern of nephrotic syndrome in the Sudan.

As far as we know, amyloidosis has never been previously reported from Ethiopia.

[1]This paper was presented at the 17th Annual Conference of the Ethiopian Medical Association in May 1981.

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Thus the objective of this paper is firstly to document 6 cases of "reactive" renal amyloidosis diagnosed in Ethiopian patients at the Black Lion Hospital in Addis Ababa, and secondly to create an awareness of the existence of this disease.

PATIENTS AND METHODS

Between April 1980 and January 1981, percutaneous kidney biopsies were performed on 38 patients with glomerular diseases, using a Menghini needle. Laboratory tests, which included white blood cell count, haemoglobin, erythrocyte sedimentation rate, quantitative and qualitative urine analysis, Bence Jones protein, urine culture, Venereal Diseases Research Laboratory (VDRL), Rose Waaler, blood urea nitrogen, creatinine, total serum protein, serum protein electrophoresis and immunoelectrophoresis, as well as a chest X-ray, were performed on most patients.

RESULTS

Of the 38 patients, 28 had primary and 10 had secondary glomerular diseases. Out of the 10 secondary glomerular disease cases, 6 patients (15.8%) had renal amyloidosis. Of these 6 cases, 4 had proven tuberculosis (3 pulmonary, 1 tuberculosis of the lymph node); 1 had leprosy; and the sixth patient, with endemic goitre, probably had a past chronic lung disease. The pertinent clinical data are shown in Table 1. All patients but one came from the northern part of Ethiopia. The mean age was 29.8 years. Only 1 patient had a transient macroscopic haematuria; 2 patients had chylous ascites.

Laboratory tests (Table 2) showed that 4 patients were anaemic, and 3 were in renal failure of various degree. Only 1 patient had a normal erythrocyte sedimentation rate. The bone marrow tested in 2 patients was normal. The serum protein was low in all 4 cases on whom this was examined, and 1 patient had a high serum alkaline phosphatase level. Urine tests (Table 3) showed all with heavy proteinuria, and, of 5 patients, 4 had a 24-hour urine protein of over 3g%. Only 1 case had urinary infection due to *Klebsiella* species; 1 patient had mild microscopic haematuria, and pyuria was present in 5 patients. The serum and urine protein results in 4 patients (Table 4) indicated that all had hypoalbuminaemia. The $alpha_2$ globulin was elevated in all patients, and the gammaglobulin in two. The I_gG was reduced in 3, I_gA in 2, and I_gM in 1 patient.

DISCUSSION

The deposition of amyloid in various tissues and organs is believed to be a result of a prolonged antigenic stimulation (7,12). In Ethiopia, chronic infections like tuberculosis and leprosy are very prevalent. Besides, the incidence of amyloid-related serum protein (protein ASC) in apparently healthy Ethiopians is high (22%) compared to that in healthy Norwegians (2.9%) (18). It is thus probable that "reactive amyloidosis" is not rare in Ethiopia. The diagnosis of amyloidosis depends on the demonstration of deposits of amyloid material in tissues stained with appropriate stains like Congo red and methyl violet. The green birefringence under polarized light is quite specific for amyloid, but electron microscopy and X-ray diffraction are the most specific histological methods of diagnosing amyloidosis, and can detect even early cases (2,14). The demonstration of amyloid fibrils in the urinary sediment may also be diagnostic (2). In our non-selected group of patients, the prevalence of amyloidosis compares very well with that in selected cases from Iran (15) but sharply contrasts with that in Uganda (9). The 6 patients in this study had normal blood pressure.

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TABLE 1. Clinical data of 6 renal amyloidosis cases

Case	Age (years)	Sex	Address	Duration of illness	Symptoms	Signs	Weight (kg)	Blood pressure (mmHg)	Aetiologic factor
1*	30	F	Assab	3 years	Cough, right side chest pain, fever, sweating, swelling of abdomen and legs. No loin pain or haematuria.	Slight pallor, dullness and reduced air entry at the bases, ascites and leg oedema.	56	100/60	Tuberculosis
2*	40	F	Tigray	1 month	Haematuria, swelling of abdomen and legs, weight loss. No loin pain.	Slight pallor, ascites and leg oedema.	38	120/90	Tuberculosis
3	18	M	Gojjam	3 years	Swelling of body, cough and loin pain. No haematuria.	Slight pallor, goitre and ankle oedema.	49	120/80	?Goitre ?tuberculosis
4	18	F	Tigray	1 year	Swelling of body, loin pain but no haematuria. Was treated for tuberculosis a year before.	No pallor, but slight puffiness of the face, palpable spleen and leg oedema.	50	120/70	Tuberculosis
5	45	M	Assab	1 year	Diarrhoea, cough, fever, sweating, weight loss; also swelling of legs but no loin pain or haematuria.	Pallor, emaciation, lymphadenopathy, enlarged thyroid gland and leg oedema.	39	100/60	Tuberculosis
6	28	M	Shoa	23 years	Swelling of body, but no haematuria or loin pain.	Pallor and leg oedema.	49.5	100/50	Lepromatous leprosy

*had chylous ascites

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TABLE 2. Haematological, biochemical, serological, radiological and stool test data of 6 renal amyloidosis cases

Case	Haemoglobin	Leucocyte count (per mm^3)	Erythrocyte sedimentation rate (mm/hr)	Platelet count (per mm^3)	Blood urea nitrogen (mg%)	Serum protein (g%)	Cholesterol (mg%)	Rose Waaler	VDRL	Stool for ova and parasites	Chest radiograph
1	9.7	8900	120	206,000	9.2	-	-	-	-	*Giardia*	Tuberculosis
2	11.7	5600	95	367,000	37.0	5.5	225	Negative	-	Negative	Tuberculosis
3*	11.4	8800	105	150,000	13.0	4.8	-	Negative	Negative	*Ascaris*	Pleuro-pericardial adhesion
4*	14.3	5100	3	122,000	9.6	4.6	230	Negative	Negative	Negative	Normal
5**	7.0	9000	140	120,000	86.0	4.3	-	Negative	Negative	Negative	Tuberculosis
6	13.0	9800	120	400,000	61.0	-	-	-	-	Negative	-

*had normal bone marrow
**had a high alkaline phosphatase level in serum

TABLE 3. Data on urine tests of 6 renal amyloidosis cases

Case	Protein (qualitative)	24 hrs urine protein (g)	Bence-Jones protein	Red blood cells per high-power field	Leucocytes per high-power field	Urine culture
1	+++	6.7	-	5-6	Plenty	*Klebsiella* sp.
2	++++	-	Negative	3-4	10-15	Negative
3	++++	3.7	Negative	15-16	Plenty	Negative
4	++++	8.8	Negative	5-6	Plenty	Negative
5	+++	1.9	Negative	1-2	30-35	Negative
6	+++	10.0	-	2-3	0-1	Negative

TABLE 4. Serum and urinary proteins in 4 renal amyloidosis cases

Case	Total serum protein (g)	Albumin (%)	α_1-globulin (%)	α_2-globulin (%)	β-globulin (%)	γ-globulin (%)	IgG	IgA	IgM	24 hrs urine protein (g)
2	5.5	36.90	5.0	19.30	15.10	23.50	36.9	155.0	101.9	-
3	4.8	32.50	7.5	15.00	7.50	27.50	280.0	49.4	67.3	3.7
4	4.6	46.00	5.5	18.20	16.60	13.40	280.0	43.4	36.9	8.8
5	4.3	37.38	5.6	15.88	10.28	30.04	-	-	-	1.9

Brandt *et al.* (8) reported that 76% of their cases had normal blood pressure, as did 50% of the cases in the series reported by Triger *et al.* (14).

As stated above, 4 of our patients had tuberculosis, and 1 patient had leprosy. The sixth had endemic goitre and a pleuropericardial adhesion on chest X-ray; we were not quite sure if the amyloidosis in this patient was related to his goitre or to a previous lung pathology. However, because of the X-ray finding and a history of cough, for which he was treated at Yekatit 12 Hospital in Addis Ababa in 1979, it is possible that his amyloidosis was related to a chronic lung disease. A 45-year-old patient had cough, recurrent diarrhoea, anorexia, weight loss, fever, leg oedema and submandibular lymph node enlargement. He was put on antituberculous medication for pulmonary tuberculosis, and a repeat chest X-ray showed a marked improvement. During the course of his hospitalization, his thyroid gland became enlarged, and a biopsy taken from the gland revealed diffuse infiltration by amyloid. He died because of progressive renal failure, and post-mortem liver and kidney biopsies showed amyloid deposit.

We suggest, therefore, that patients with chronic illnesses who have proteinuria should undergo the necessary investigations for amyloidosis. We also suggest that further studies should be conducted on a wider scale in order to determine the magnitude of the problem.

Addendum: Since this paper was written we have encountered 3 further amyloidosis cases out of a total of 25 patients who had renal biopsy for glomerular diseases.

Acknowledgements

We would like to thank Professor J.W. Landells for pathology reports, and Woinero Berhane Yigzaw for secretarial work. We also wish to thank the ward staff who helped in the management of these patients, and the laboratory, X-ray and pathology staff for their technical help.

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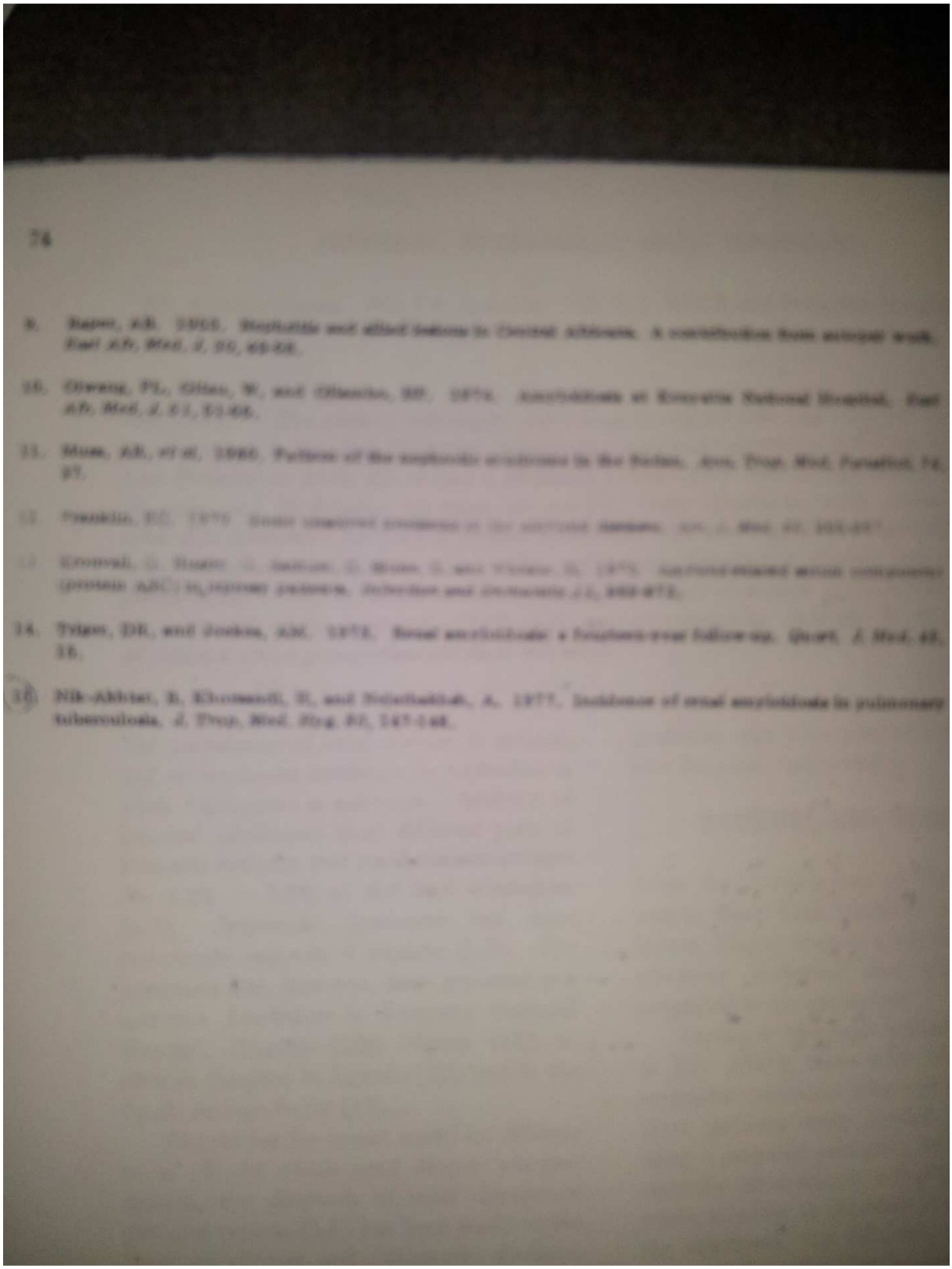
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NEPHROTIC SYNDROME IN ADULT ETHIOPIANS

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ABSTRACT. *The clinical, laboratory and histopathological data and outcome of treatment are described in 36 adult Ethiopian patients with nephrotic syndrome, admitted to the Black Lion Hospital in Addis Ababa over a 14-month period (April 1980 to July 1981). There were 20 males and 16 females; the mean age was 34.7 years. During the study period, nephrotic syndrome accounted for 2.1% of medical admissions. The aetiology of the nephrotic syndrome was known in 12 of the cases. The commonest histological finding was proliferative glomerulonephritis, of which membranoproliferative and mesangial proliferation accounted for over 52% of the total and of 73% of the primary glomerular diseases. There was no case of minimal lesion glomerulonephritis in this study.*

The prevalence of renal diseases in general, and of nephrotic syndrome in particular, in adult Ethiopians is unknown. Analyses of hospital admissions from different parts of Ethiopia indicate that renal diseases account for 1.2% — 2.8% of the total admissions (1-7). Nephrotic syndrome has been mentioned only in 4 reports (6-9). The syndrome has, however, been reported as a common condition in Kenyatta National Hospital, Nairobi (10); Nigeria (11); in Mulago Hospital in Uganda (12); and in the South African Bantu (13).

Except for the recent report by Alfonzo *et al.* (9), in which renal biopsy was performed, the diagnosis of renal diseases in previous reports (1-8) has been made on the basis of clinical and laboratory findings. This paper describes the clinical, laboratory and histopathological reports and outcome of treatment in 36 adults with nephrotic syndrome who were admitted to the Black Lion Hospital, Addis Ababa.

PATIENTS AND METHODS

After the development of the nephrology unit in Black Lion Hospital, in early 1980, kidney biopsy became a routine procedure whenever indicated and when patients consented to the procedure.

During a 14-month period (April 1980 to July 1981), there were 36 adults with nephrotic syndrome who had renal biopsy; these patients were studied prospectively, using a prepared protocol. In addition to a carefully taken history and physical examination, in order to elucidate the aetiology of the syndrome, the following investigations were made: urine for protein and sugar, microscopic examination of urine sediments, 24 hours' urine protein, urine culture;

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complete blood count, serum protein and electrophoresis, cholesterol, creatinine, blood urea nitrogen (BUN); chest X-ray; stool examination for ova and parasites; and serological test for syphilis. The assay of the antistreptolysin 0 titre was not possible. All the patients had a percutaneous kidney biopsy, with the Menghini needle. The kidney tissue was fixed in 10% formalin. Thin paraffin sections of the tissue were then stained with periodic acid Schiff (PAS), Congo Red and haematoxylin-eosin. The slides were then examined only under light microscopy, since fluorescence microscopy was not available.

The criteria for the diagnosis of nephrotic syndrome included the presence of oedema, hypoproteinaemia of less than 6g%, and a significant proteinuria (24-hour protein of more than 2.5g per litre, or proteinuria of 2.5mg per minute or 50mg per kg body-weight).

Treatment and response. The treatment given was one of the following:

A. *Standard steroid.* Standard steroid treatment was given in a dosage of 2mg per kg body-weight on alternate days up to a maximum dose of 100mg per day for 6 to 8 weeks, and then gradually tapered off and discontinued after one month.

B. *"Steroid pulse".* "Steroid pulse" treatment was given in a dosage of 10mg per kg body-weight intravenously on alternate days for 3 doses.

C. *Symptomatic.* Diuretics and/or indomethacin were used.

The response to treatment is described as improved if the urine was continuously free of protein and the BUN or creatinine was equal to or less than the initial value after 8 weeks of treatment maintained up to the last examination (which in some cases was after a year). The outcome of those patients with persistent proteinuria and a BUN or creatinine greater than or equal to the value before treatment is described as unchanged.

RESULTS

During the study period, 903 males and 827 females (total 1,730) were admitted to the 83-bed medical department of the Black Lion Hospital. Of these, 20 males and 16 females had nephrotic syndrome; there were 24 other cases, making an incidence of 3.5% renal admissions and 2.1% nephrotic syndrome.

Clinical data. The mean age was 34.7 years (range 16 to 62 years). There were 9 cases above the age of 40 years, while the remaining 27 were below 40 years. None of the patients had malaria or skin lesions. There were 2 patients who had a history of sore throat, but there was no history of insect bite, vaccination, drug intake or use of cosmetics. The duration of illness was less than 1 year in 20 cases, 2 to 5 years in 12, and above 5 years in 4 patients. About two-thirds of the cases had no pallor or macroscopic haematuria. Most of the patients had oedema of both the face and legs, and some had ascites in addition. Eighteen patients had hypertension (diastolic blood pressure $\geqslant$ 95mmHg).

Laboratory data. The haematological, urinary, stool and biochemical results are given in Table 1. The mean 24-hour urine protein was 6.4g per litre (range 2.5g to 14.4g per litre). There was pyuria, haematuria, and hyaline and granular casts in varying degrees in the majority of the cases. The BUN and cholesterol levels were elevated in almost a third of the patients. The serum protein electrophoresis, tested in 15 cases, showed hypoalbuminaemia of less than 2.5g% in all, and elevation of the alpha-2 globulin fraction in 14 patients.

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TABLE 1. Haematological, urinary, stool and biochemical data of 36 nephrotic syndrome cases

Type of test	*Total tests*	*No. of patients*
Haemoglobin	36	
below 13g%		24
above 13g%		12
Erythrocyte sedimentation rate	36	
above 10mm/hr		34
below 10mm/hr		2
24-hour urine protein	36	
2.5 to 5g/l		20
6g/l and above		16
Urine sediment	36	
pyuria		29
haematuria		28
casts		33
Urine culture	28	
positive		
(1 *Klebsiella*, 1 *Enterobacter*)		2
negative		26
Stool examination	34	
positive for ova and parasites		15
negative for ova and parasites		19
Blood urea nitrogen	36	
abnormal (> 25mg%)		13
normal		23
Creatinine	25	
abnormal (> 2.3mg%)		9
normal		16
Cholesterol	36	
abnormal (> 250mg%)		13
normal		23

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The serological reaction for syphilis carried out in 10 cases was negative. Chest X-ray, performed on 33 patients, showed no abnormality in 26, fibrosis in 2, infiltration of the apices compatible with tuberculosis in 3, and pleural effusion in 2 patients. Stool examination was made in 34 patients, and of these 15 were positive for ova or parasites (ascaris in 5; hookworm in 2; giardia in 2; *Taenia saginata* in 2; *Strongyloides* larvae in 3; *Trichuris trichiura* in 1; and *Entamoeba histolytica* cysts in 1).

The histopathological classification as well as the type and outcome of treatment are summarized in Table 2. Twenty-six patients had primary glomerulonephritis (membranoproliferative 12; mesangial 7; post-infective 2; focal 2; idiopathic membranous 2; and rapidly progressive 1). There was no case of minimal lesion nephrotic syndrome. There were 10 cases of secondary glomerular diseases, of which 7 were amyloidosis. Six patients received standard steroid therapy, 11 "steroid pulse" and 14 symptomatic treatment. Five patients were not started on any treatment. Seven of the 11 "steroid pulse", 3 of the 6 standard steroid, and 3 of the 14 symptomatic treatment patients showed improvement. Eleven patients (2 from the standard steroid, 1 from the "steroid pulse" and 8 from symptomatic treatment) were lost to follow-up, and 7 patients (1 from the standard steroid, and 3 each from "steroid pulse" and symptomatic treatment) remained in the same condition.

DISCUSSION

The patients came from various parts of Ethiopia. It is of interest to note that the 2.1% frequency of nephrotic syndrome in this series compares very well with the 2.4% from Ibadan Hospital in Nigeria (11), and the 2.0% from Mulago Hospital in Uganda (12), but is considerably higher than that of North America (quoted in 12). Our finding appears to be in agreement with the generally-held view that nephrotic syndrome is more common in the tropics than in temperate climates (10). The aetiology of nephrotic syndrome was known in 12 (33%) of our cases. Although quartan malaria has been reported to be the cause of African nephrotic syndrome (12), this type of malaria is extremely rare in Ethiopia. Schistosomiasis has also been reported as a cause of nephrotic syndrome (14), but this was not specifically looked for in this study.

The commonest histological finding was proliferative glomerulonephritis, of which membranoproliferative and mesangial proliferation accounted for over 52% of the total, and for 73% of the primary glomerular diseases. Unlike the situation in other reports (11-13, 15, 16), minimal change lesion was not seen in our series. Amyloidosis accounted for slightly over 19% of our cases.

Ten of the 17 patients who were treated with steroid showed improvement (3 from standard treatment, and 7 from "steroid pulse"). However, it is difficult to draw definitive conclusions from these results, since the number of patients is small, and the follow-up period is short. Further studies, using a larger group and a longer follow-up period, should be undertaken.

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We wish to thank the doctors as well as other health workers who took care of the patients. We would like also to thank the laboratory and X-ray technicians, and the staff in the Histopathology Department, for their assistance. We are grateful to W/o Hana Tamrat for typing the report.

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TABLE 2. Histological classification, type and outcome of treatment of 36 nephrotic syndrome cases

TYPE OF LESION	No. of patients	% Total	TYPE OF TREATMENT AND OUTCOME									
			Standard steroid				"Steroid pulse"				Symptomatic		
			Total	Improved	Same	Lost to follow-up	Total	Improved	Same	Lost to follow-up	Total	Improved	Same	Lost to follow-up
Primary Glomerular Diseases	26	72.2	6	3	1	2	11	7	3	1	5	2	1	2
Membrano-proliferative glomerulonephritis	12	33.3	3	1	1	1	6	3	2	1	2	-	1	1
Mesangial proliferation	7	19.4	3	2	-	1	2	1	1	-	1	-	-	1
Post-infective glomerulonephritis	2	5.5	-	-	-	-	2	2	-	-	-	-	-	-
Idiopathic membranous	2	5.5	-	-	-	-	-	-	-	-	1	1	-	-
Focal glomerulonephritis	2	5.5	-	-	-	-	1	1	-	-	-	-	-	-
Rapidly progressive glomerulonephritis	1	2.8	-	-	-	-	-	-	-	-	1	1	-	-
Secondary Glomerular Diseases	10	27.8	-	-	-	-	-	-	-	-	9	1	2	6
Amyloidosis	7	19.4	-	-	-	-	-	-	-	-	6	1	2	3
Diabetes	3	8.9	-	-	-	-	-	-	-	-	3	-	-	3

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RENAL AMYLOIDOSIS IN ADULT ETHIOPIANS[1]

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ABSTRACT. *During the 10-month period April 1980 to January 1981, a percutaneous needle biopsy of the kidney was performed on 38 patients with glomerular diseases at the Black Lion Hospital in Addis Ababa. Of these, 6 patients were found to have renal amyloidosis due to tuberculosis (4 cases), and lepromatous leprosy (1 case); the sixth patient had endemic goitre and probably a past chronic lung disease. The pertinent clinical and laboratory data are briefly discussed. Since chronic diseases are very prevalent in Ethiopia, we suggest that patients who suffer from such diseases and have proteinuria should have the necessary investigations for amyloidosis; and further studies should be undertaken in order to determine the extent of the disease.*

Amyloidosis is a group of diseases resulting from systemic or localized deposition of extracellular protein fibril in various tissues and organs. Amyloidosis may be categorized into "immunocyte dyscrasias with amyloidosis" and "reactive systemic amyloidosis" (1); the latter has been reported in connection with various acute recurrent or chronic infections and various forms of inflammatory, parasitic and neoplastic disease(1-5). Chronic infections still remain an important worldwide cause of "reactive amyloidosis".

Seventy-five per cent of 200 cases from India, 54% of 37 cases from a Scottish series and nearly 33% of 22 patients from an American series had "reactive amyloidosis" due to tuberculosis (6). The kidney is the most important site of involvement in all forms of amyloidosis (7,8).

Since Rokitansky's description of the disease in 1842 (quoted in 2), many cases have been reported, but the report from Africa appears to be scanty. Raper (9) reported cases of renal amyloidosis for the first time from Uganda on necropsy material in 1953, and Leather (3) reported 3 cases, diagnosed in life, in 1959. In 1974, Ojwang *et al.* (10) from Kenya and, in 1979, Gold (4) from South Africa reported 4 cases and 7 cases, respectively. Recently, Musa *et al.* (11) found 4 cases of amyloidosis while studying the pattern of nephrotic syndrome in the Sudan.

As far as we know, amyloidosis has never been previously reported from Ethiopia.

[1]This paper was presented at the 17th Annual Conference of the Ethiopian Medical Association in May 1981.

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Thus the objective of this paper is firstly to document 6 cases of "reactive" renal amyloidosis diagnosed in Ethiopian patients at the Black Lion Hospital in Addis Ababa, and secondly to create an awareness of the existence of this disease.

PATIENTS AND METHODS

Between April 1980 and January 1981, percutaneous kidney biopsies were performed on 38 patients with glomerular diseases, using a Menghini needle. Laboratory tests, which included white blood cell count, haemoglobin, erythrocyte sedimentation rate, quantitative and qualitative urine analysis, Bence Jones protein, urine culture, Venereal Diseases Research Laboratory (VDRL), Rose Waaler, blood urea nitrogen, creatinine, total serum protein, serum protein electrophoresis and immunoelectrophoresis, as well as a chest X-ray, were performed on most patients.

RESULTS

Of the 38 patients, 28 had primary and 10 had secondary glomerular diseases. Out of the 10 secondary glomerular disease cases, 6 patients (15.8%) had renal amyloidosis. Of these 6 cases, 4 had proven tuberculosis (3 pulmonary, 1 tuberculosis of the lymph node); 1 had leprosy; and the sixth patient, with endemic goitre, probably had a past chronic lung disease. The pertinent clinical data are shown in Table 1. All patients but one came from the northern part of Ethiopia. The mean age was 29.8 years. Only 1 patient had a transient macroscopic haematuria; 2 patients had chylous ascites.

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The deposition of amyloid in various tissues and organs is believed to be a result of a prolonged antigenic stimulation (7,12). In Ethiopia, chronic infections like tuberculosis and leprosy are very prevalent. Besides, the incidence of amyloid-related serum protein (protein ASC) in apparently healthy Ethiopians is high (22%) compared to that in healthy Norwegians (2.9%) (18). It is thus probable that "reactive amyloidosis" is not rare in Ethiopia. The diagnosis of amyloidosis depends on the demonstration of deposits of amyloid material in tissues stained with appropriate stains like Congo red and methyl violet. The green birefringence under polarized light is quite specific for amyloid, but electron microscopy and X-ray diffraction are the most specific histological methods of diagnosing amyloidosis, and can detect even early cases (2,14). The demonstration of amyloid fibrils in the urinary sediment may also be diagnostic (2). In our non-selected group of patients, the prevalence of amyloidosis compares very well with that in selected cases from Iran (15) but sharply contrasts with that in Uganda (9). The 6 patients in this study had normal blood pressure.

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TABLE 1. Clinical data of 6 renal amyloidosis cases

Case	Age (years)	Sex	Address	Duration of illness	Symptoms	Signs	Weight (kg)	Blood pressure (mmHg)	Aetiologic factor
1*	30	F	Assab	3 years	Cough, right side chest pain, fever, sweating, swelling of abdomen and legs. No loin pain or haematuria.	Slight pallor, dullness and reduced air entry at the bases, ascites and leg oedema.	56	100/60	Tuberculosis
2*	40	F	Tigray	1 month	Haematuria, swelling of abdomen and legs, weight loss. No loin pain.	Slight pallor, ascites and leg oedema.	38	120/90	Tuberculosis
3	18	M	Gojjam	3 years	Swelling of body, cough and loin pain. No haematuria.	Slight pallor, goitre and ankle oedema.	49	120/80	?Goitre ?Tuberculosis
4	18	F	Tigray	1 year	Swelling of body, loin pain but no haematuria. Was treated for tuberculosis a year before.	No pallor, but slight puffiness of the face, palpable spleen and leg oedema.	50	120/70	Tuberculosis
5	45	M	Assab	1 year	Diarrhoea, cough, fever, sweating, weight loss; also swelling of legs, but no loin pain or haematuria.	Pallor, emaciation, lymphadenopathy, enlarged thyroid gland and leg oedema.	39	100/60	Tuberculosis
6	28	M	Shoa	23 years	Swelling of body, but no haematuria or loin pain.	Pallor and leg oedema.	49.5	100/50	Lepromatous leprosy

*had chylous ascites

Brandt *et al.* (8) reported that 76% of their cases had normal blood pressure, as did 50% of the cases in the series reported by Triger *et al.* (14).

As stated above, 4 of our patients had tuberculosis, and 1 patient had leprosy. The sixth had endemic goitre and a pleuropericardial adhesion on chest X-ray; we were not quite sure if the amyloidosis in this patient was related to his goitre or to a previous lung pathology. However, because of the X-ray finding and a history of cough, for which he was treated at Yekatit 12 Hospital in Addis Ababa in 1979, it is possible that his amyloidosis was related to a chronic lung disease. A 45-year-old patient had cough, recurrent diarrhoea, anorexia, weight loss, fever, leg oedema and submandibular lymph node enlargement. He was put on antituberculous medication for pulmonary tuberculosis, and a repeat chest X-ray showed a marked improvement. During the course of his hospitalization, his thyroid gland became enlarged, and a biopsy taken from the gland revealed diffuse infiltration by amyloid. He died because of progressive renal failure, and post-mortem liver and kidney biopsies showed amyloid deposit.

We suggest, therefore, that patients with chronic illnesses who have proteinuria should undergo the necessary investigations for amyloidosis. We also suggest that further studies should be conducted on a wider scale in order to determine the magnitude of the problem.

Addendum: Since this paper was written we have encountered 3 further amyloidosis cases out of a total of 25 patients who had renal biopsy for glomerular diseases.

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ANALYSIS OF ADULT TUBERCULOSIS ADMISSION TO ST PETER'S SANATORIUM, ADDIS ABABA

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ABSTRACT. *An analysis was made of 861 pulmonary tuberculosis patients admitted to St Peter's Tuberculosis Sanatorium over a period of one year. The majority were young males with far advanced disease who came from Addis Ababa. Hospitalizations were 3 months or less in 90% of cases, and mortality was 9.2%. Patients were not kept in hospital until negative acid-fast bacilli conversion in sputum. There was no direct correlation between the degree of Mantoux positivity and sputum positivity. During the course of tuberculosis chemotherapy most patients gained weight, while a significant number either remained the same or even lost weight, showing that gain in weight cannot be taken as a clinical criterion of response to anti-tuberculosis therapy.*

The number of patients treated in the Sanatorium compared to the vast pool of infectious tuberculosis cases is so small that the role it plays in the control of tuberculosis in Ethiopia is doubtful.

St Peter's Tuberculosis Sanatorium is the largest and oldest of the three sanatoria in Ethiopia. The Sanatorium was opened in 1963, and now has a total of 190 beds (160 adult and 30 paediatric beds).

It is the purpose of this paper to describe the clinical characteristics of adult tuberculosis admissions, and assess results of therapy for the period from September 1978 to August 1979.

PATIENTS AND METHODS

The total number of adult tuberculosis admissions for the year under consideration was obtained from the standard discharge summary sheets and clinical charts.

With only very rare exceptions, patients were admitted to St Peter's Sanatorium from the Tuberculosis Training and Demonstration Centre, Addis Ababa. Again with very few exceptions, the patients on admission had a 70mm chest film, sputum acid-fast bacilli (AFB) smears, and Mantoux test. The diagnosis of pulmonary tuberculosis was established mainly on the finding of AFB in sputum, but occasionally also on clinical grounds such as radiology and symptoms.

The patients were analysed with regard to age, sex, domicile, chest X-ray, sputum AFB smears and results of the Mantoux test. The hospital course was scrutinized especially for clinical improvement: general

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well-being, weight changes and sputum conversions.

RESULTS

Table 1 shows the age and sex distribution of hospitalized patients. A total of 861 patients was admitted; 164 (19%) were retreatment cases. About 70% were aged 30 years or younger, and over 92% were aged 45 years and younger. The age distribution was similar in both sexes. Males comprised 63% of the admissions.

More than one-third of the patients came from Addis Ababa, and more than three-quarters came from Addis Ababa and the surrounding Administrative Region of Shoa (Table 2).

Of the 362 patients with Mantoux records, 80% were positive. In 16%, induration of 21mm or greater was noted (Table 3). Chest X-ray on admission revealed cavitary disease in 80%; only 2 of 400 patients had miliary tuberculosis (Table 4).

The duration of hospital stay is shown in Table 5. Over 90% of patients were hospitalized for 3 months or less; only 2 patients were in hospital for more than 6 months. Seventy-nine (9.2%) of the patients died, of whom 44 (56%) died within the first 15 days of hospitalization. Eighty per cent of the deaths occurred within one month of admission. More than 89% of patients had positive AFB on admission, and slightly fewer than half of these were still positive at the time of discharge (Table 6). Analysis of weight changes during hospitalization showed that 24 patients (7%) of 335 patients with adequate weight records had no weight changes; 9% lost weight; 20% gained 1 or 2 kilograms, and 64% gained 3kg or more. Clinical improvement appeared in 62%, i.e., weight gain, sputum conversions and a generalized sense of well-being; 26% showed little or no improvement, and, as stated above, 9% died. Concerning the remaining 3%, information was not available.

DISCUSSION

It was estimated more than a decade ago that there were half a million cases of active tuberculosis in Ethiopia (1). However, recent estimates put the figure at more than 800,000 (2). Pulmonary tuberculosis accounts for 5% – 18% of all medical admissions to general hospitals in Ethiopia (3-7).

Our study showed that the majority of tuberculosis patients were in the young and most potentially productive age-group. This is similar to previous reports from Gondar and Massawa (4,8). About 80% of our patients were treated for tuberculosis for the first time.

The vast majority of the patients came from Addis Ababa and Shoa. Although Addis Ababa contains only 3% of the population of Ethiopia, more than 33% of the patients were from the capital. An important reason for this high figure is easy access of the hospital to local patients, but a contributory factor may be the high prevalence of tuberculosis in Addis Ababa (9).

The hospital stay varied from a few days to several months, with the majority staying up to 3 months. On the other hand, most of Belcher's patients in northern Ethiopia stayed in hospital for 4 to 6 weeks only (8), while the Tuberculosis Sanatorium in Harar kept almost all patients in hospital for several months and even years (10). The 9% mortality rate in our patients is the same as that in a recent report from a general hospital in Addis Ababa (7).

The advanced nature of tuberculosis in our patients is also reflected by the high rate of mortality in the first 2 weeks of admission. We have observed that the degree of Mantoux positivity has no direct

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TABLE 1. Age and sex distribution of tuberculous patients

Age in years	Male		Female		Total		Retreatment cases	
	No.	%	No.	%	No.	%	No.	%
16-30	374	69.0	219	69.0	593	69.0	94	57.3
31-45	129	23.8	71	22.3	200	23.1	57	34.8
46-60	31	5.5	23	7.2	54	6.3	9	5.5
Over 60	7	1.3	4	1.2	11	1.3	3	1.8
No record	2	0.4	1	0.3	3	0.3	1	0.6
Total	543	100.0	318	100.0	861	100.0	164	100.0

TABLE 2. Distribution of patients according to domicile

Domicile	Male	%	Female	%	Total	%
Addis Ababa	178	33.0	124	38.4	302	35.1
Shoa	229	42.6	138	42.7	367	42.6
Other regions	129	24.0	59	18.3	188	21.8
No record	2	0.4	2	0.6	4	0.5
Total	538	100.0	323	100.0	861	100.0

TABLE 3. Mantoux test induration
in patients with positive acid-fast bacilli smears

Induration (mm)	No.	%
0-4	52	14.4
5-9	17	4.7
10-15	142	39.0
16-20	93	25.7
Over 21	58	16.2
Total	362	100.0

TABLE 4. Admission chest X-ray findings in tuberculous patients

Chest X-ray	*No.*	*%*
Bilateral multicavitary TB	243	61.1
Bilateral disease with unilateral cavities	38	9.5
Unilateral cavitary TB	33	8.3
Bilateral non-cavitary TB	64	16.0
Unilateral non-cavitary TB	5	1.3
Others (miliary, effusion, pneumothorax, etc.)	15	3.8
Total	398	100.0

TABLE 5. Duration of hospital stay and relation to death

Hospital stay (days)	*No.*	*%*	*Died*
0-15	51	6.0	44
16-30	44	5.0	19
31-60	321	37.3	8
61-90	365	42.4	4
91-120	65	7.5	2
121-180	13	1.5	1
181 and over	2	0.3	1
Total	861	100.0	79

Note. Most of the discharges in the first month were against medical adv
the death rate listed here would have increased but for this facto

TABLE 6. Sputum acid-fast smear conversion

Sputum smear	*Admission*		*Discharge*	
	No.	*%*	*No.*	*%*
Positive acid-fast bacilli	768	89.2	351	40.8
Negative acid-fast bacilli	41	4.8	368	42.7
No record on AFB status	52	6.0	142	16.5
Total	861	100.0	861	100.0

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correlation with AFB smears. Of the total number of patients with positive AFB on admission, about half were negative at the time of discharge. The fact that a large proportion of patients were discharged with positive AFB should not be regarded as disturbing, since initiation of chemotherapy alone reduces infectiousness very significantly (11). Moreover, ambulatory and sanatorium-treated patients have the same rate of infectiousness (12).

Clinical improvement was shown in 62% of patients, which brings the total number of effectively treated patients in hospital to about 400 per year. In terms of figures of cure or decrease in the infectious tuberculosis pool, the Sanatorium has indeed played a very minor role.

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CASE REPORT

A *FORME FRUSTE* OF MARFAN'S SYNDROME PRESENTING WITH ECTOPIA LENTIS AND LATE SYSTOLIC CLICK

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Marfan's syndrome is a heritable disease transmitted as an autosomal dominant trait with incomplete penetrance of the gene resulting in variable phenotype (1). In recent years a wide spectrum of clinical expressions of this syndrome have been recognized and termed *formes frustes* (2, 3). These are incomplete variants which have findings in only one or two systems and lack the classical features. Such a case is presented here.

CASE REPORT

H.F., a 16-year-old Ethiopian girl, was admitted to Black Lion Hospital in September 1979 with complaints of headache and failing vision of 10 years' duration. She had been wearing eye-glasses for the previous 3 years, and her headache had subsequently improved. She denied dyspnoea, orthopnoea and cough. There was no family history of similar illness, and both parents and siblings were healthy. The patient was an eighth-grade student. Her class performance had been satisfactory.

Physical examination on admission showed a young girl of medium height and thin stature, who looked well except for the heavy eyeglasses she wore. Ophthalmological examination showed myopia and bilateral upward displacement of the lenses. There was no chest deformity, and the lungs were clear to auscultation. Cardiovascular examination was normal except for a late systolic click heard over the apex. The abdomen was flat and soft, and there was no hepatosplenomegaly. Locomotor examination was normal. There was no clubbing of fingers or toes. Her fingers appeared long and spidery. Her height was 155cm with the upper segment (US) measuring 76cm and lower segment (LS) 79cm. The ratio of US:LS was 0.96. The total arm span was 169cms. Neurological examination was normal.

The results of urinalysis, complete blood count, haemoglobin and fasting blood sugar were normal, as was the electrocardiogram. The urine nitroprusside test was negative. Roentogenogram of the chest, skull, hands and barium swallow were also normal. Phonocardiography and echocardiography were not done.

The patient was followed for 3 years, during which her clinical findings remained stable.

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DISCUSSION

Marfan's syndrome is a generalized disorder of connective tissue, but the clinical manifestations consist mainly of ocular, cardiac and skeletal abnormalities. The clinical features of Marfan's syndrome have been described by McKusick (4, 5).

Accurate diagnosis is extremely difficult when the full spectrum of the clinical abnormality is not manifest and if the family history is negative. The term *forme fruste* implies that not all the classical features are present and that the diagnosis is not quite secure. To overcome such diagnostic problems, Bowers (6) suggests that one major and one minor criterion should be present: either an ectopia lentis or a positive family history is considered a major diagnostic criterion and any one of the skeletal stigmata, cardiovascular lesions or increased excretion of urinary hydroxyproline as minor. Our patient lacked a positive family history. However, in some cases, genetic mutation takes place, and such isolated cases occur in 15% of Marfan's syndrome (5, 7). Our patient had one major criterion, ectopia lentis, and one minor criterion – a systolic click over the apex. Mid-late systolic clicks are believed to be due to mild mitral incompetence, which may be a consequence of snapping of elongated or fibrous chordae tendinae or prolapse of a mitral leaflet (7-9). In Marfan's syndrome, deformities of the mitral valve are well known.

The finding of the total arm span as longer than the height, with the ratio of upper segment to lower segment of 0.96, is consistent with the disorder.

Two conditions have to be considered in the differential diagnosis of our patient. Homocystinuria, with its effect on connective tissue, is the most important clinico-pathological entity to be distinguished from Marfan's syndrome. In this disorder, a dislocated lens is found in 95% of cases (5, 7) and the skeletal disorders are also similar to those of Marfan's syndrome. However, the specific laboratory test for homocystinuria, the cyanide-nitroprusside test, was negative. The second clinical entity, with dislocation of the lens as its prominent feature, is Weill-Marchesani syndrome (4, 5, 7). In this, the stature is short, and the hands and feet are particularly short, with stiff joints in the majority of cases. Our patient did not have these characteristics.

Early diagnosis of a *forme fruste* of Marfan's syndrome is important, as the consequences of some of the cardiac and skeletal abnormalities can be prevented with the administration of drugs: oestrogen-progestogen in an affected girl is said to prevent scoliosis before puberty, and propranolol and reserpine to prevent aortic dilatation (2), but the later effect of these is not well established (7).

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CASE REPORT

HAEMOPHILIA A IN AN ETHIOPIAN FAMILY, AND A BRIEF REVIEW OF THE DISEASE

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ABSTRACT. *A 19-year-old male Ethiopian suffering from haemophilia A is presented. One of his male siblings bled to death following circumcision, and another shows mild symptoms of the disease; all were initially suspected to have a hereditary bleeding disorder because of excessively prolonged bleeding after circumcision. Reports from various parts of Africa seem to indicate that the disease is not as rare in Blacks as was previously thought.*

The hereditary bleeding disorders include a number of different diseases. The most common are haemophilia A (classical haemophilia, factor VIII deficiency) and haemophilia B (Christmas disease, factor IX deficiency), both inherited as X-chromosome-linked recessive disorders; and von Willebrand's disease, inherited as an autosomal dominant. Haemophilia A is the commonest of all hereditary bleeding disorders, accounting for about 80% (1).

The literature on haemophilia in the tropics seems to be very scanty. In Africa, it was generally thought that haemophilia was rare among the Blacks. However, since the description of haemophilia in an African child in 1950 (2), an increasing number of cases has been reported from different parts of Africa: from Uganda, Kenya, Tanzania, Nigeria and Senegal (3-10).

In Ethiopia, no case of haemophilia has been previously reported. In this paper, we present the case of a patient with haemophilia A, two of whose siblings are also affected with the same disease.

CASE REPORT

Case No. 36026 is a 19-year-old Ethiopian male readmitted to the Black Lion Hospital in Addis Ababa on 11 August 1981 because of swelling of the left knee and epistaxis.

The patient was quite well until the age of 8 years, when he had profuse bleeding soon after circumcision. He was admitted to a provincial hospital in Yirga Alem, southern Ethiopia, where he received blood transfusion, and the bleeding stopped. But later he was referred to Addis Ababa for further investigation of his bleeding disorder, and was admitted several times to different hospitals, but mainly to the Black Lion Hospital, because of recurrent haemarthrosis of the big and small joints, painless

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haematuria, epistaxis, and melaena which he had only once. In all these admissions he was given fresh blood, and the bleeding was controlled. The haemarthrosis was mostly spontaneous, but sometimes following trivial trauma. He had been getting factor VIII concentrate since 1979, and his symptoms were fairly controlled.

Four days before the present admission the patient again developed spontaneous haemarthrosis of the left knee-joint, which was painful and hot; he was unable to carry out any active movement on that joint. Two days later he developed epistaxis and a painless haematuria, but no rectal bleeding.

The patient's father is alive and healthy. His mother and maternal grandmother had excessive periods and post-partum haemorrhage following each delivery. He had 9 siblings, 5 males and 4 females. One of his brothers died soon after delivery, from an unknown cause; he did not bleed excessively from the umbilical stump. Another brother died at the age of 6 years from bleeding following circumcision; he had profuse bleeding from the umbilical stump after birth. Of the remaining 3 brothers, one of them, 14 years old, has a mild form of recurrent haemarthrosis and epistaxis, for which he was admitted twice to hospital, and the other two, 16 and 27 years old respectively, are healthy. His 4 sisters are healthy and one of them has recently given birth to a healthy girl.

On examination, the patient was well built. He had epistaxis. His blood pressure was 100/70mmHg, temperature 37.5°C (axillary) and pulse 100/min. There was no conjunctival pallor, jaundice or bleeding from the oral cavity. The left knee-joint was swollen, tender and warm, and there was evidence of fluid in the joint space. The rest of the physical examination was unremarkable.

The bleeding time and prothrombin time were normal. The clotting time was over 16 hours, the partial thromboplastin time was prolonged, and the thromboplastin generation test showed a defect in adsorbed plasma but was normal in serum. The assay of factor VII was not made, because of lack of facilities. The urine showed microscopic haematuria. The platelet count was 285,000 per mm^3, haemoglobin 12.8g%, erythrocyte sedimentation rate 70mm in the first hour, white blood cell count 5,000 per mm^3, with a normal differential. A left knee-joint X-ray showed erosion of the intercondylar space and articular surface of the tibia.

The patient was given fresh blood, and his nose was packed with gauze soaked in adrenalin. A cold compress was applied to the left knee. The bleeding was controlled and the haemarthrosis subsided. Then physiotherapy was gradually started, and the patient left the hospital in good condition.

DISCUSSION

Haemophilia A is a world-wide disease, although the prevalence may vary from place to place and from one race to another; this variability may depend on the means available for the detection of the case. The prevalence may increase as methods of detection also improve, and, with modern treatment, which allows haemophiliacs to live longer and to reproduce, there will be a further increase in their number.

In Africa, the incidence of haemophilia in Blacks is unknown, and, in the absence of this knowledge, it is not justifiable to comment that haemophilia is less common there than in Western countries. In fact, since 1950, when Lambotte-Legrand and his colleague (2) described a case of haemophilia in an African, many cases have been reported. It is possible that many cases have been missed and are still being missed because of lack of awareness of the disease and the limitations of laboratory facilities

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FIGURE. Pedigree of cases of haemophilia A

+ : dead

○ : healthy and/or female carriers

□ : unaffected males

◔ : female carriers; symbol 1 shows the proposita

■ : affected males

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The clinical picture and mode of inheritance in both haemophilia A and B are the same; hence laboratory tests, and in particular the assay of the specific factor, are crucial. The degree of severity of the disease depends on the level of the factor implicated and varies from the severe to the subhaemophilic form. Males are the usual victims, but females who are heterozygotes or homozygotes for the defective gene can also suffer from the disease. Some females can develop spontaneous haemophilia, probably as a result of a newly emerging mutant gene.

Our patient has a normal bleeding and prothrombin time. The coagulation time is prolonged, and the partial thromboplastin time is abnormal. The thromboplastin generation test was defective in adsorbed plasma but normal in the serum. These findings, together with the clinical picture, strongly suggest that the patient is suffering from haemophilia A.

The pedigree (Figure) shows that 50% of the males are affected, which clearly indicates an X-linked inheritance of the disease; the mother being [illegible] patient's mother and maternal grandmother had excessive periods and post-partum haemorrhages, which may indicate the carrier state. The best method of detecting carriers is to determine the ratio between factor VIII coagulation activity and the amount of a factor VIII-related protein, by means of electroimmunoassay. A reduction of the ratio in the assay indicates a carrier state. This test was not available in our setting; hence we do not know which of the female siblings are carriers. We suggest that the hereditary bleeding disorders should be considered in those patients with excessively prolonged bleeding after circumcision or other types of trauma, and with a spontaneous haemarthrosis.

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CASE REPORTS

ADULT POLYCYSTIC KIDNEY DISEASE IN ETHIOPIANS

Berhanu Habte, MD, and Arefaine Abraha, MD

Polycystic disease of the kidneys is a hereditary disease with worldwide prevalence. There are two basic types: an autosomal dominant adult form which manifests with reneal insufficiency in middle age, and an autosomal recessive infantile form which leads to renal failure in childhood. Various other less common congenital and acquired cysts occur in the kidneys and should not be confused with polycystic kidney disease (1).

In the western world, adult polycystic kidney disease (APKD) is a significant health problem, accounting for 8.3% of cases going on to regular dialysis in Europe (2). In African literature (3-6), there is hardly any mention of polycystic kidney disease in analyses of hospital admissions. In an extensive analysis of medical admissions to 3 different hospitals in Addis Ababa, Ethiopia (7), there is mention of one case of "congenital cystic kidney".

Over the past 3 years we have come across 2 clear-cut cases of APKD, and 2 other patients who probably have the disease. This paper documents clinical findings in these patients with a view to alerting physicians practising in this country to the existence of the condition, so that appropriate management is undertaken in good time.

CASE REPORTS

Case 1. A 43-year-old female patient was noted as having bilaterally enlarged kidneys 2 years previously, while she was undergoing physical examination for an attack of headache. On subsequent questioning she revealed that she had had recurrent aching pain in the right flank for 17 years, and a similar type of pain in the left flank for 3 years. There was no history of haematuria, dysuria or frequency. Her father and a paternal uncle died of kidney disease at the ages of 55 and 65 respectively. A 25-year-old daughter had recently been diagnosed as having polycystic kidney disease and renal calculus. A 20-year-old son had hypertension.

On examination the blood pressure was 160/90mmHg. The kidneys were grossly enlarged and slightly tender, the right being larger than the left. There was no hepatomegaly.

Investigations in Sweden a year before revealed blood urea nitrogen (BUN) of 26mg/dl, serum creatinine of 2.4mg/dl and normal serum electrolytes. The urine showed pyuria; there was no proteinuria, and the culture was negative. Ultrasonography showed bilaterally enlarged kidneys with multiple cysts. Cysts were not

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detected in the liver. Recent laboratory data showed BUN of 25mg/dl and serum creatinine of 2.8mg/dl.

Case 2. A 30-year-old female first presented at another hospital in Addis Ababa about 10 years previously with frank haematuria. Six years later, the patient came to Black Lion Hospital with recurrence of haematuria. Both kidneys were palpable and non-tender. Plain film of the abdomen showed a calculus in the right kidney area. An intravenous pyelogram (IVP) showed gross enlargement of both kidneys with marked attenuation of the pelvic calyceal system. The BUN was normal. No further measures were taken, as the patient became asymptomatic.

About 2½ years previously, the patient was noted to be hypertensive, and therapy was initiated. At about the same time, mild renal impairment was noted. Episodes of frank haematuria continued to occur, though infrequently, accompanied by left flank pain and sometimes right flank pain. The most recent renal function studies showed BUN of 49mg/dl and serum creatinine of 2.8mg/dl.

There was a prominent family history of kidney disease: the father died of renal failure due to polycystic kidney disease at the age of 65 years; an uncle died of renal failure at the age of 57; one cousin was known to have kidney disease, while two others were suffering from renal stones. A younger brother died at 16 years of age from a seizure disorder. A younger sister, who also had a seizure disorder, died from an obstetric accident.

Case 3. A 50-year-old female, a known psychotic, was first admitted to Black Lion Hospital 5 months previously with a 4-year history of heaviness and pain in the epigastrium. The liver was found to be enlarged and there were masses in the flanks. An exploratory laparotomy was performed and revealed bilateral polycystic kidneys and a polycystic liver. The cysts contained clear fluid. Several of the cysts in the left kidney were drained.

Recently the patient was admitted for control of hypertension. A satisfactory family history could not be obtained, as the patient was in a state of withdrawal, but her daughter indicated that the patient's mother died of a hypertensive stroke, and that several cousins had hypertension. On examination, the blood pressure was 160/110mmHg. The liver was enlarged, firm and coarsely nodular. The right kidney was grossly enlarged, but the left one was not palpable. BUN and creatinine were normal.

Case 4. A 46-year-old man was referred from a general hospital in Addis Ababa because of anuria of 5 days' duration. The evening before the onset of anuria, the patient had gross haematuria with passage of clots. Ten years previously, a left nephrectomy was performed in a police hospital, for renal calculi; the kidney was reported to be grossly enlarged and contained multiple cysts of varying size. Five years later, hypertension was documented and treatment started. There was no family history of renal disease or hypertension.

Physical examination revealed a well-built man with a blood pressure of 170/90mmHg. The right kidney was grossly enlarged and tender. Blood urea was 152mg/dl and serum creatinine was 9.7mg/dl. Plain film of the abdomen did not reveal radio-opaque calculi.

A large volume of urine drained from the right kidney when a retrograde catheter was inserted. The BUN and creatinine returned to normal over the following 6 days. Since no obstructing lesion was demonstrated on pyelography, the anuria was ascribed to clot obstruction of the ureter. A recent IVP was not taken, but an

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IVP performed prior to the left nephrectomy 10 years previously showed clear signs of polycystic disease.

DISCUSSION

A firm diagnosis of APKD requires bilateral involvement of the kidneys with multiple cysts, and a family history compatible with autosomal dominant inheritance (8). Case 1 had clinical and ultrasonographic evidence of bilateral cystic kidneys, while Case 2 had grossly enlarged kidneys, which, on urography, showed signs of polycystic disease. Both patients had at least one other family member affected by the disease and several others with a history of renal disease or hypertension, thus satisfying the criteria for diagnosis of APKD. Case 3 lacked a definite family history of polycystic kidney disease, but the fact that she had a polycystic liver identifies her as a very probable case of APKD, since 50% of cases of multiple liver cysts occur in association with polycystic kidney disease (9). Case 4 can only be taken as a probable case, as there was no suggestive family history. It should be noted, however, that the family history may be negative in up to 30% of cases, and this may be due to gene carriers that go through life without clinical manifestations of the disease (10).

Initial symptoms consisting of loin pain and/or haematuria generally occur between 30 and 40 years of age (11). Of patients in this age group, 15% are diagnosed accidentally when undergoing physical examination for some other reason. Renal impairment is gradual, leading to terminal renal failure in the 5th and 6th decades. Both Cases 1 and 2 had a mild elevation of the serum creatinine, which had not shown a marked change over the past 1–2 years. Hypertension is a common accompanying finding. Patients with APKD are predisposed to calculus formation, as seen in Case 2 and 4, and in the daughter of Case 1. Urinary tract infection is also a troublesome complication, as it may occur in cysts that are not draining.

Hepatic cysts occur in 30% of cases of APKD, but they rarely lead to significant functional impairment. Cysts may also occur in the pancreas, spleen, thyroid and ovaries. A more significant association is that of cerebral aneurysms, which were discovered in 22% of autopsied cases in one series (12), and cause fatal subarachnoid haemorrhage in 9% of cases of APKD (13). The history of seizure disorder in the 2 siblings of Case 2 may be a manifestation of cerebral aneurysm.

It is important to make an early diagnosis of APKD in order to detect and treat hypertension and urinary tract infections. Since renal failure is very gradual, the life of the patient can be prolonged by many years if these measures are taken in good time. When end-stage renal failure supervenes, dialysis and transplantation might be performed successfully.

In the past, accurate genetic counselling was difficult, due to difficulty in making a diagnosis early enough in asymptomatic individuals at risk of developing the disease. Currently, the use of high-dose urography with nephrotomography, radionuclide scanning and ultrasonography enable a diagnosis to be made in over 95% of individuals at risk who are aged over 19 years (14).

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CLINICAL PROFILE OF ACUTE RENAL FAILURE IN AN ADDIS ABABA REFERRAL HOSPITAL

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ABSTRACT. *Case records of 38 patients with a diagnosis of acute renal failure (ARF) admitted to the chief referral hospital in Addis Ababa between March 1980 and March 1983 were analysed. There were 9 males (average age 44 years) and 29 females (average age 30 years). Four patients had obstructive uropathy, and 34 had renal parenchymal causes of ARF, among which acute tubular necrosis (ATN) was the commonest cause of ARF (25 patients), followed by severe glomerulonephritis (6 patients). Septic abortion was the most important pathogenetic factor leading to ATN (13 patients). Hypotension and septicaemia together accounted for 8 cases. Oliguria occurred in 21 patients with ATN, the initial phase with an average duration of 5.4 days, and the oliguric phase for 18 days. Four patients had non-oliguric ARF. Thirty-one patients were treated by dialysis. There was a total of 11 deaths, the causes being renal failure in 4; septic complications in 3; haemorrhagic complications in 3; and unknown in 1 patient. Septic abortion was evidently a very common cause of ATN; such patients should have prompt resuscitation and close monitoring of renal function from the time of admission.*

The pattern of aetiologic factors in acute renal failure (ARF) in the "developed" world has changed over the years as a result of advances in medical care. Whereas obstetric and medical disorders dominated as aetiologic factors in earlier years (1, 2), current literature indicates that post-surgical cases are more prevalent (3, 4). In developing countries, ARF mainly follows obstetric accidents and various medical diseases (5).

The pattern of ARF in Ethiopians has not been previously documented. The present study summarises our experience in ARF in the main referral hospital of the country over a period of 3 years.

PATIENTS AND METHODS

Data were collected from case records of patients with ARF admitted to the Black Lion Hospital in Addis Ababa from March 1980 to March 1983. About 40% of the patients were referred from other hospitals in the city, and 10% were referred from the countryside.

Patients were said to be in ARF if they presented with an acute deterioration in renal function, as evidenced by a rapid rise of the serum creatinine to above 2mg/dl or the blood urea nitrogen (BUN) to above 40mg/dl, in spite of correction of of haemodynamic disturbances. Oliguria

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was defined as a twenty-four-hour urinary volume of above 400ml. Non-oliguric ARF was diagnosed when patients had 24-hour urinary volumes consistently greater than 600ml throughout the azotaemic phase of their illness.

In cases with acute tubular necrosis (ATN), the initial phase was taken to be the period from the onset of the likely precipitating event to the onset of oliguria. Patients were considered to be in the diuretic phase when urine volume spontaneously rose above 1000ml/24 hours.

Dialysis was undertaken in patients with severe azotaemia (BUN > 100mg%) when they developed persistent uraemic symptoms or showed evidence of severe hyperkalaemia or fluid overload. Peritoneal dialysis was the preferred dialysis technique because of its simplicity. Haemodialysis was undertaken in patients where peritoneal dialysis was contra-indicated because of recent abdominal surgery, and in cases with prolonged peritoneal dialysis complicated by repeated peritonitis.

More emphasis is placed on cases of ATN in the analysis of results and the discussion.

RESULTS

A total of 38 patients was found to fulfil the criteria for the diagnosis of ARF. Nine patients were male (mean age 44 years, range 1-63 years), and 29 were female (mean age 30 years, range 18-70 years). Twenty-three of the patients went into ARF following obstetric complications, while medical and surgical complications accounted for 9 and 6 respectively.

Four patients had obstructive uropathy; the remaining 34 had renal parenchymal diseases leading to ARF, listed specifically in Table 1. The single case of acute interstitial nephritis, diagnosed histologically, was considered to be due to hypersensitivity to ampicillin. The haemolytic uraemic syndrome occurred in a 1-year-old child who presented with severe gastroenteritis.

The main pathogenetic factors leading to ATN in 25 patients are shown in Table 2. Septic abortion was the most important pathogenetic factor, affecting 13 patients. It was common to find a multiplicity of predisposing events in the individual patient; in fact, 21 of the 25 patients had 3 or more predisposing conditions. Pregnancy and sepsis were the most frequent, occurring in 23 and 21 of the cases respectively. Hypotension occurred in 14 patients.

The dominant clinical features at presentation were those of the underlying disease. Table 3 depicts the main clinical derangements resulting from renal functional impairment in patients with ATN. Oliguria was very common, occurring in 21 patients; non-oliguric ARF occurred in 4 patients. Variable degrees of peripheral oedema occurred in 10 patients, but congestive heart failure as a result of fluid overload was not seen.

In patients with oliguric ARF due to ATN, the initial phase lasted for a mean of 5.4 days (range 0-12 days). The oliguric phase, with an average urine volume of 162ml per 24 hours, lasted for an average of 18 days (range 0-28 days). Of the 10 patients who had adequate urine volume measurements during the recovery phase, only 3 had urine volumes greater than 1500ml per 24 hours.

Table 4 shows the type and duration of dialysis therapy employed, and the number of fatal cases. Of the 7 patients who did not undergo dialysis, 6 did not require it, and the seventh expired before it could be instituted. Two of the 6 patients who did not require dialysis had non-oliguric ARF. Six of the 21 who were

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TABLE 1. Renal parenchymal causes of acute renal failure in 34 patients

Disease	Males	Females	Total	(%)
Acute tubular necrosis	2	23	25	(73.5)
Glomerulonephritis	2	4	6	(18.0)
Interstitial nephritis	1	-	1	
Haemolytic uraemic syndrome	1	-	1	
Postpartum acute renal failure	-	1	1	

TABLE 2. Main pathogenetic factors leading to acute tubular necrosis in 25 patients

Pathogenetic features	No.	(%)
Septic abortion	13	(52.0)
Hypotension	5	(20.0)
Septicaemia	3	
Aminoglycoside toxicity	2	
Eclampsia	1	
Incompatible blood transfusion	1	

TABLE 3. Clinical features of acute tubular necrosis

Clinical features	No. of cases	(%)
Oliguria	21	(84.0)
Oedema	10	(40.0
Mental changes	8	(32.0)
Acidosis	6	
Bleeding tendency	6	
Diarrhoea and vomiting	4	
Uraemic frost	2	
Uraemic pericarditis	2	

TABLE 4. Type and duration of dialysis therapy

Dialysis therapy	Duration (days) median	Duration (range)	No. of patients	No. of fatalities
No dialysis	-	-	7	1
Haemodialysis only	5.0	(2-14)	8	3
Peritoneal dialysis only	4.5	(1-14)	21	6
Haemodialysis and peritoneal dialysis	29.0	-	2	1

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treated only by peritoneal dialysis developed peritonitis, satisfactorily controlled by administering antibiotics intraperitoneally, and continuing peritoneal lavage. No significant complications occurred as a result of haemodialysis.

A total of 11 patients died (3 male and 8 female), of whom 8 had ATN. Four patients were considered to have died of the direct effects of uraemia. Septic complications and haemorrhagic complications each accounted for the death of 3 patients. One patient died of unknown causes.

DISCUSSION

In our series, as well as in series from other "developing" countries (5), obstetric accidents and medical diseases were the main aetiologic factors. Among obstetric complications, septic abortion was the most important predisposing event leading to ARF.

Septic abortion provides a perfect setting for the development of ATN. Firstly, there may be significant haemorrhage leading to hypovolaemia. Secondly, there is an infectious process which may be complicated by endotoxaemia and septicaemia. With endotoxaemia, a Schwartzman type of reaction may occur, leading to acute renal tubular necrosis or cortical necrosis (6, 7). Thirdly, the hypercoagulable state noted during parturition (8) may also occur with abortion, thereby facilitating thrombus formation in the microcirculation. The high incidence of a haemolytic picture in our patients may indeed be evidence for some degree of disseminated intravascular coagulation.

Recently it has been emphasised that ARF occurs quite commonly without the presence of oliguria. In one series (9), the incidence of non-oliguric ARF was 37 among 92 patients (40%). The incidence of non-oliguric ARF in our much smaller group of patients was 16% only. Unless renal function is determined routinely in high-risk patients, and since non-oliguric patients may not be seriously ill, it is possible that some cases are missed, and this may be the explanation for the low incidence in our series. An additional explanation could be the rarity, among our patients, of nephrotoxic cases of ARF, which have been noted to lead to non-oliguric ARF more frequently than ischaemic causes. It is noteworthy that one of our patients with non-oliguric ARF had gentamicin nephrotoxicity.

In our oliguric patients the average duration of the oliguric phase was considerably longer than the usual quoted figure of 10–14 days. Although the average urine volume amounted to 162ml in 24 hours, most patients had anuria during the first week of illness. This may be a reflection of inadequate fluid and electrolyte replacement at the onset of illness.

The comparatively low mortality rate of 8 (32%) in our 25 patients with ATN is in agreement with other reports on ATN associated with obstetric accidents and medical conditions (10, 11). In modern series in developed countries, with a higher proportion of surgical and traumatic causes of ATN, mortality rates are much higher, at about 70% (4, 12). The availability of mechanical respirators and other intensive care facilities in recent years permits the survival of critically ill patients with multiple organ failure to the time that they require dialysis. The majority of such patients, however, succumb to other fatal complications and contribute to the high mortality figures for ARF.

We conclude that septic abortion is a very important predisposing event leading

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to ATN, and such patients should be regarded as a high-risk group. Vigorous resuscitation of these patients, with prompt and adequate antibiotic therapy, may decrease the subsequent development of renal failure; renal function should be monitored closely for early detection of ARF. Avoidance of harmful practices to procure abortion, is, of course, the best solution to the problem.

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CORRESPONDENCE

The Editor, *Ethiopian Medical Journal*,
P.O. Box 3472, Addis Ababa.

Dear Sir,

Re beta-lactamase-producing *Neisseria gonorrhoeae* in Addis Ababa

Dr Elizabeth Archer raised a question in her letter in the January 1984 issue of the *Ethiopian Medical Journal* (Volume 22, p. 67) regarding the selection of 147 male patients with acute gonococcal urethritis; we reported that 31% of these were infected with penicillinase-producing *Neisseria gonorrhoeae* (PPNG) strains (1).

The detection of PPNG formed part of our study of a multi-drug single-dose trial in the treatment of acute male gonococcal urethritis. The selection of the 147 male patients was carefully made. Two of the criteria used were (a) no treatment given for the presenting disease of acute gonococcal urethritis, and (b) no antimicrobial drug taken for any reason during a period of one week prior to the day the patients were seen at the Venereal Disease Clinic, Addis Ababa. There was no specific intention of selecting patients who had failed to respond to penicillin treatment for the acute urethritis they presented with.

We hope this will be sufficient to answer Dr Archer's question on rates of PPNG – a serious problem that is increasingly being reported in this part of the world.

Yours, etc.,

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A FOUR-YEAR REVIEW OF SYSTEMIC LUPUS ERYTHEMATOSUS

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ABSTRACT. *Systemic lupus erythematosus (SLE) was diagnosed in 16 Ethiopian patients admitted to Black Lion Hospital and the hospital of the All Africa Leprosy and Rehabilitation Training Centre (ALERT), Addis Ababa. The initial presenting symptoms of the patients are analysed in relation to the time lapse between onset of the symptoms and the definite diagnosis of SLE. No serious delay in diagnosis of patients with multi-system involvement occurred. However, in 6 patients who presented with single-organ involvement, there was a delay in diagnosis of more than 10 months. The clinical manifestations of SLE were the same as those seen elsewhere.*

Systemic lupus erythematosus (SLE) is an auto-immune disease characterized by tissue injury due to immunological reactions against the host's own tissue. SLE is considered a rare condition in tropical Africa (1,2). It is encountered frequently in American blacks, and there appears to be a genuine difference in the incidence of SLE between black Americans and Africans (2-5). The purpose of this paper is to review the clinical picture of SLE in Ethiopians seen over a period of 4 years at Black Lion Hospital and in the hospital of the All Africa Leprosy Rehabilitation and Training Centre (ALERT), Addis Ababa.

PATIENTS AND METHODS

A retrospective analysis of 6 patients was made, while 10 patients were studied prospectively; 13 were females and 3 were males. The patients were seen at the 2 hospitals from September 1978 to April 1982. All patients had thorough clinical and laboratory assessments, and those who fulfilled more than 4 of the American Rheumatism Associationcriteria for SLE (6) were included in our study.

RESULTS

Sixteen patients were finally diagnosed as having SLE.

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The age range was between 14 and 60 years (mean 22 years); 14 of the 16 were 30 years old or younger.

The clinical manifestations are presented in Table 1. All patients had arthritis and/or arthralgia and skin lesions. In more than 50% constitutional symptoms such as malaise, weight loss and poor appetite were present.

Table 2 shows the laboratory findings. All the patients had an erythrocyte sedimentation rate (ESR) of greater than

TABLE 1. Clinical features in 16 systemic lupus erythematosus patients

	Symptoms/signs	*No.*
1.	Arthritis/arthralgia	16
2.	Malaise	14
3.	Skin lesions	
	Butterfly rash	13
	Alopecia	12
	Ulcerations	5
4.	Anorexia	12
5.	Fever (temperature > 37.5°C oral)	10
6.	Sweating	9
7.	Weight loss	8
8.	Oedema	8
9.	Neuropsychiatric features	7
10.	Pleurisy	5
11.	Reynaud's phenomena	4

TABLE 2. Laboratory findings in SLE patients

Findings	*No.*
Erythrocyte sedimentation rate (> 50mm/hr)	16/16
Positive lupus erythematosus cells	14/16
Positive antinuclear antibodies	14/15
Anaemia (Hb < 11gm/dl)	11/16
Leucopenia (white blood cell count < 3000/cm^3)	8/16

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50mm in the first hour. Antinuclear antibodies (ANA) and lupus erythematosus cells (LE cells) were each positive in 87%. However, positive VDRL and rheumatoid factor were each seen only in 1/16 patients. Proteinuria of 3gm/24 hours or more was seen in 5/16 patients; 8/16 had urinary casts; and 2 had persistent haematuria. Percutaneous renal biopsy was done in 3: one showed minimal lesion, and lupus nephritis was seen in the other two.

Although the diagnosis of SLE was made fairly quickly in the majority, there was a delay of over 10 months in 6 of the patients. Two of these 6 were diagnosed as having rheumatoid arthritis, one as polyarthritis of unknown actiology, one as discoid lupus, and the remaining 2 as nephrotic syndrome and glomerulonephritis. The patient with polyarthritis died 10 months later of renal failure with central nervous system (CNS) involvement. The discoid lupus patient later developed seizures, went into coma and died; the diagnosis of SLE was made at necropsy.

Six of the 16 patients died during follow-up; all of these had CNS involvement, terminally manifested by psychosis, convulsions and coma. Three of these also had renal failure, contributing significantly to their deaths.

DISCUSSION

Our cases illustrate the usual protean manifestations of SLE. These manifestations were similar to those seen elsewhere (1-3). It is important to realize that SLE often fails to present with a classical picture, and because of this it can be difficult to detect the disease early. On the other hand, if we keep in mind the criteria of the American Rheumatism Association to diagnose SLE (6), initial clinical presentation may create a high degree of suspicion. Some patients continue to have signs and symptoms related to one organ only for a long time, and only eventually manifest the full picture of SLE. For example, 2 of our patients had only nephrotic syndrome and nephritis, one of whom had persistent haematuria with red blood cell casts for a long time before she was diagnosed as having SLE. The same held true for the 2 female patients who presented with rheumatoid arthritis, and for the patient with polyarthritis who died of renal failure with CNS involvement. Three patients had signs and symptoms of hepatic failure with abnormal liver function tests; in one of these, liver biopsy confirmed SLE. It is interesting to note that one of our patients, with localized discoid lupus, progressed to systemic lupus erythematosus, as recorded elsewhere (6,7).

All patients who were acutely ill or had renal and/or CNS involvement were treated with high-dose corticosteroids. None of the patients received immunosuppressive drugs. Of our cases, 1 of 3 males and 5 of 13 females died during the follow-up. Most of these patients died of CNS and/or renal involvement. The mortality rate and end organ involvement causing death is in keeping with other reports from Africa and North America (1, 8).

In the past decade an advance in SLE detection has been the recognition that mild forms of the disease far outnumber the serious and "classical" forms. Therefore, patients presenting with recurrent arthritis, nephrotic syndrome and nephritis, with other constitutional symptoms, should have lupus erythematosus cell preparation and ANA determination for early diagnosis of SLE.

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Sural Nerve Biopsy in Leprosy Patients After Varying Periods of Treatment: Histopathological and Bacteriological Findings on Light Microscopy[1]

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Publications in recent years ([1, 2, 4, 9–12, 18, 19]) have dealt with various aspects of neural involvement in leprosy, and the histopathological features have been particularly well reviewed by Weddell and Pearson ([21]). Many authorities consider that neural invasion occurs early; that it is invariable in all cases of leprosy, whatever the stage or classification; that bacilli may persist in nerves even after many years of apparently regular treatment at satisfactory dosage; and that in some cases, admittedly rare, the peripheral nervous system only is affected, giving rise to "pure neural leprosy". To the histopathologist, the neural element in the pathogenesis of this disease is not in doubt, but no convincing explanation has ever been forthcoming for what appears to be an exceptional predilection of *Mycobacterium leprae* for nerve tissues ([19]), including the Schwann cell. The numerous factors governing the granulomatous response have been described by Spector, *et al.* ([17]) and Ridley has reviewed the subject of macrophage stimulation and activity in lepromatous leprosy ([14]). Rea and Taylor ([13]) studied the mean serum lysozyme (muramidase) levels and the tissue distribution of this enzyme in the skin of patients affected by different types of leprosy and Cologlu, in a publication in Turkish ([3]), reported findings in skin biopsies, drawing attention to the presence of leprosy bacilli in structures such as endothelial lining cells of vessels, Schwann cells, and smooth muscle cells in arrector pili muscle—all of which failed to show any lysosomal activity on special stains. These observations, together with some uncertainty about the origin of mononuclear infiltrating cells within nerves affected by leprosy, led us to the present investigation in which biopsies were taken from the sural nerve (and the skin) of patients with various types of leprosy, including some with adverse reactions based on cell-mediated immune processes. The muramidase findings, using immunohistological techniques, are reported separately ([8]).

The routine findings on examination of these sural nerve biopsies with a hematoxylin and eosin (H&E) stain (for the infiltrative changes) and a modified Ziehl-Neelsen stain (for acid-fast bacilli) were, however, of considerable interest. Especially in view of the limited number of publications in the literature on sural nerve biopsy in leprosy, we report here the findings in a group of 18 patients from Ethiopia, after varying periods of treatment with antileprosy drugs.

PATIENTS AND METHODS

Eighteen Ethiopian leprosy patients attending the All-Africa Leprosy Rehabilitation and Training Centre in Addis Ababa were included in this study. The initial clinical examination included a classification of their type of leprosy, using the Ridley-Jopling scale ([16]). There was no evidence that any patient suffered from diabetes mellitus, amyloidosis, severe malnutrition, or alcoholism. A careful examination for anesthesia or hypesthesia, especially in the region of sensory supply of the sural nerves, was carried out in all patients prior to biopsy.

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TABLE 1. *Eight patients with lepromatous (LL) leprosy and borderline lepromatous (BL) leprosy.*

Case no.	Sex/age	Clinical classification	Therapy		Bacilli		Histopathological findings	
			Drug(s)	Duration (yr)	Skin	Nerve	Skin	Nerve
1	M/31	BL	DDS[a]	10	few	0	LL, regressing	LL, regressing
2	M/12	LL (ENL)[b]	DDS/RMP[c]	2	0	0	LL, regressing	LL, regressing
3	M/31	LL	DDS	1	many	many	LL, active, relapsing	LL, active, relapsing
4	M/57	LL	DDS	7	few	0	LL, widespread pathology	LL
5	M/63	BL	DDS	12	many	many	LL, extensive pathology	LL
6	F/10	LL (histoid)	DDS/RMP	12	many	many	LL, active with histoid features	LL, active
7	M/38	LL	DDS/RMP	1	many	many	LL	LL, active
8	M/23	LL	DDS/RMP	1	many	many	BL, extensive pathology	BL/LL, grossly abnormal

[a] DDS = dapsone.
[b] ENL = erythema nodosum leprosum.
[c] RMP = rifampin.

At the time of intake, all patients had received treatment with either dapsone (DDS) alone or with dapsone plus rifampin (RMP), as shown in Tables 1 and 2, from which it can be seen that the period of treatment at the time of the biopsy varied widely, between extremes of one month and 12 years. The relevance of these periods in relation to the microscopic findings are discussed below.

Skin biopsies were taken from active lesions by standard techniques under local anesthesia. Where no active lesion could be detected, a biopsy was taken from the site considered, from examination of the records, to have previously shown a lesion. In no instance was a biopsy taken from an active lesion or from a site in close proximity to either sural nerve. Sural nerve biopsies were taken according to standard techniques ([3]) (but removing fascicles only about 10 mm in length) from either the right or the left leg, whether or not the sural nerve was enlarged and palpable. In fact, the nerves were palpable in all cases except numbers 16 and 17 (Table 2). In no instance was the nerve biopsy incision made either through or near a skin lesion. Specimens of skin and nerve were fixed in formaldehyde-mercuric chloride-acetic acid (FMA) solution for 2 hr, then transferred to 70% alcohol for 24 hr before embedding in paraffin. Sections were cut at 5 μm and stained with H&E and a modified Fite stain ([7]) for acid-fast bacilli. Sections were also stained for muramidase; technical details are to be described in a separate publication ([8]).

RESULTS

Our results are summarized in Tables 1 and 2. Although it is acknowledged that there is some clinical and immunological overlap in patients within the "borderline" or "dimorphous" group, we have combined in one table borderline-lepromatous (BL) and lepromatous (LL) patients, since in practice the treatment and management of these two groups is somewhat similar. Furthermore, they are both types of leprosy in which large, or very large, numbers of leprosy bacilli are widespread in the tissues. By contrast, Table 2 contains essentially mid-borderline (BB), and borderline-tuberculoid (BT) cases, including four cases of the latter classification who were at the time of biopsy in reversal (upgrading) reaction ([13]), albeit modified by treatment with steroids. The latter cases were methodically included in view of a previous

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TABLE 2. *Ten patients with mid-borderline (BB) or borderline tuberculoid (BT) leprosy.*

Case no.	Sex/ age	Clinical classi-fication	Therapy		Bacilli		Histopathological findings	
			Drug(s)	Du-ration (mo)	Skin	Nerve	Skin	Nerve
9	F/33	BB	DDS[a]	1	0	few	BB upgrading to BT	BB upgrading to BT
10	M/22	BB	DDS/RMP[b]	24	0	many	Nonspecific; not diagnostic of leprosy	BL, grossly abnormal
11	F/27	BB/BL	DDS/Pred[c]	2	few	few	BB upgrading to BT	BB upgrading to BT
12	M/16	BT in reaction	DDS/Pred	9	0	0	BT upgrading to TT[d]	BT upgrading to TT
13	M/17	BT in reaction	DDS/Pred	4	0	0	BT upgrading to TT	BT upgrading to TT
14	F/23	BT in reaction	DDS/Pred	24	0	0	Nonspecific; not diagnostic of leprosy	BT
15	M/28	BT in reaction	DDS/Pred	60	0	0	Nonspecific; not diagnostic of leprosy	BT
16	M/50	BT	DDS	36	0	0	Nonspecific; not diagnostic of leprosy	Normal
17	M/16	BT	DDS	24	0	0	BT/TT	Normal
18	F/40	BT	DDS/Pred	3	0	0	Borderline changes but further classi-fication not possible on material submitted	BT

[a] DDS = dapsone.
[b] RMP = rifampin.
[c] Pred = prednisolone.
[d] TT = tuberculoid leprosy.

observation ([13]) particularly of high serum levels of muramidase and intense granular reaction patterns in the tissues during such reactions.

In the case of the eight BL and LL patients in Table 1, infiltrative changes were often marked and widespread from one end of the biopsy to the other. The perineurium was frequently obliterated or heavily infiltrated and the normal structure of the endoneurial area destroyed; bacilli were widespread, including globi (Fig. 1). These changes, together with large numbers of bacilli, were also observed in Cases 5 and 6, in whom the period of treatment was more than 12 years. Cases 5 and 6 had many bacilli in all areas and Case 6 showed clinical and histopathological evidence of histoid leprosy, as described by Wade in 1963 ([20])—the nerve did not show histoid features. In Case 2, the patient clinically had erythema nodosum leprosum (ENL) on the skin, but no evidence of ENL was found on histopathological examination of the nerve.

In the ten patients with borderline-tuberculoid (BT) or mid-borderline (BB) leprosy in Table 2, the histopathology in skin was nonspecific and not diagnostic of leprosy in Cases 10, 14, 15 and 16. In Case 18, the changes were suggestive of borderline (dimorphous) leprosy, but a more precise classification could not be made on the material submitted. Nevertheless, in Case 10 the changes were gross, and in Cases 14, 15 and 18, there was very definite evidence of borderline-tuberculoid (BT) leprosy in the nerve. Possible reasons for the negative findings in skin in the above cases and the

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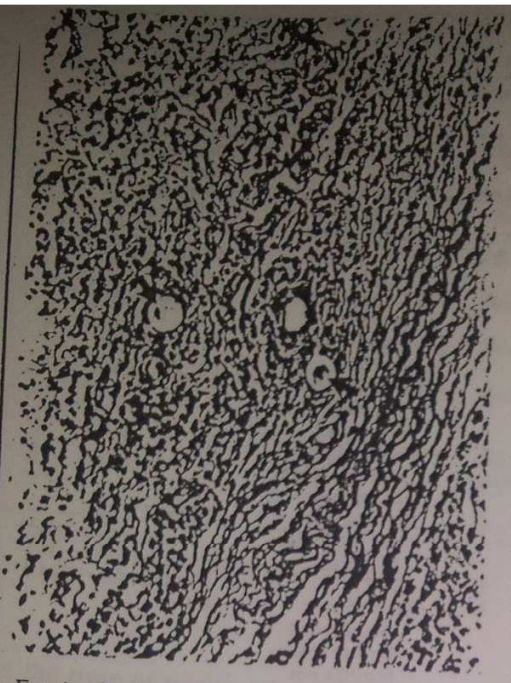


FIG. 1. Sural nerve biopsy; lepromatous (LL) leprosy, treated with daily dapsone for one year. Endoneurial area shows extensive fibrosis, together with infiltration by histiocytes and some lymphocytes. Bacilli are widespread and some lie in large globi in vacuoles within multi-nucleate cells (arrows). Bacillary material in these vacuoles was shown, on Fite staining, to be acid-fast and bacillary (H&E ×250).

normal findings in the nerve in Cases 16 and 17 are discussed below. In several cases it was remarkable that the entire area of the section was pathological (Fig. 2), all fascicles showing endoneurial and perineurial infiltration. Cellular infiltration by histiocytes, epithelioid cells, and lymphocytes (Fig. 3) was often intense and widespread, with virtually complete replacement of normal structure. Case 12 was of exceptional interest in that there was not only a massive replacement of nerve tissue by lymphocytes, but also extensive caseation necrosis of the endoneurial zone (Fig. 4).

DISCUSSION

The clinical records and history of drug intake were incomplete in some of these patients and in view of the fact that most of them were taking drugs as outpatients, it is possible that regularity of intake, especially in the long-treated LL and BL cases, was far from satisfactory. Those in Table 1 with extensive disease and many bacilli in their biopsies were referred for further investigations of drug resistance, notably to dapsone, an increasingly common phenomenon in Ethiopia and many other countries. The striking features on microscopic examination of the nerve tissues in this group of eight cases were the extent and severity of typically lepromatous changes; foamy macrophages were seen in all cases, and they often extended throughout the entire biopsy. The correlation between clinical and histopathological findings was close in this group, except that in Cases 1 and 5 the classification in nerve was lepromatous rather than borderline-lepromatous. The histoid findings in Case 6 were not present in the nerve and indeed this form of leprosy has to our knowledge so far been described in only one case, occurring in India (K. Ramanujam, personal communication, 1980).

The nonlepromatous cases in Table 2 are less straightforward in the matter of interpretation. The apparent lack of correspondence in some cases between the clinical findings and those in skin and nerve may, however, be inherent in the types of leprosy from which these patients suffered, since it has long been known that the borderline forms exhibit skin and nerve lesions which are asymmetric and "patchy" in distribution. The negative findings in nerve in Cases 16 and 17 may therefore be due to the fact that the sural nerve biopsied was not affected by the disease. In the case of the skin biopsies which showed only nonspecific, nondiagnostic changes, it is more than likely that long periods of drug treatment had resulted in the virtual disappearance of lesions, so that any selection of a skin site for biopsy was impossible. In the eight cases showing abnormal changes in nerve, the striking overall finding was again the extent and intensity of the pathology in the material submitted (Figs. 2–4), including caseation necrosis (Fig. 4).

There were no difficulties in locating sural nerves or in obtaining adequate tissue. All biopsy wounds healed by first intention and there was no evidence of an increase of neural deficit in the area supplied as a result of the procedure.

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FIG. 2. Sural nerve biopsy; borderline tuberculoid (BT) leprosy. All four fascicles show marked infiltration of virtually the entire endoneurial area (E) with multi-layering and infiltration of the perineurium (P). EP = epineurium. (H&E ×20).

We conclude that sural nerve biopsy in experienced hands is safe and that it has revealed pathological changes of significance in this group of patients. Enna, *et al.* ([6]), in an evaluation of biopsy of this nerve in leprosy, commented that it had ". . . been found to show evidence of activity in some cases of borderline and lepromatous leprosy which have been inactive by the usual criteria for several years." This observation and the findings in the present study suggest that the procedure may be indicated in the further investigation of both treated and untreated patients with different types of leprosy. This, in our view, should be attempted only by experienced observers, including an operator who is trained in nerve biopsy. Furthermore, the procedure should certainly not replace the examination of well-selected and processed skin biopsies, together with the use of routine slit-skin smears in the diagnosis and classification of this disease. For special investigations, however, it is a potentially valuable procedure which may throw light on the pathogenesis of leprosy in untreated, treated, and relapsed patients.

SUMMARY

As part of a larger study of nerve biopsies from leprosy patients in Ethiopia for the presence of muramidase (lysozyme), sections were also examined by light microscopy after staining with hematoxylin and eosin for cellular infiltrate and a modification of the Ziehl-Neelsen stain for leprosy bacilli. The muramidase findings will be reported separately. This paper describes the infiltrative and bacterial findings in a group of 18 patients, including four with nonlepromatous forms of leprosy who were suffering from delayed hypersensitivity reaction at the time of biopsy. The findings were unexpectedly interesting and revealing. Lepromatous and borderline-lepromatous patients all showed endoneurial and perineurial infiltration of considerable extent and, in several instances, bacilli were wide-

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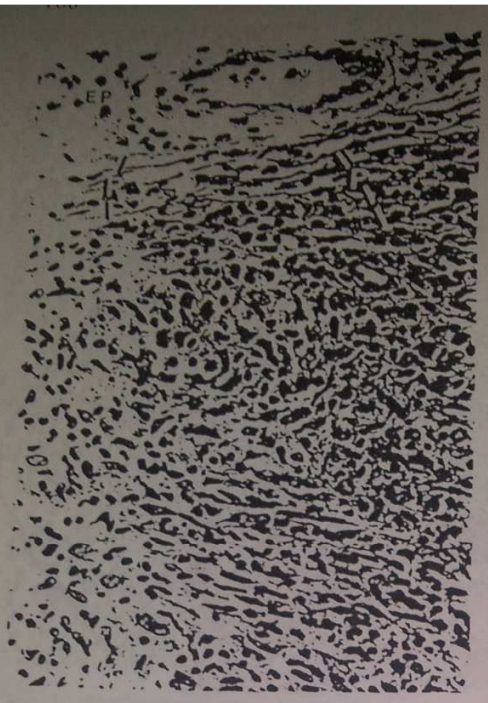


FIG. 3. Sural nerve biopsy: borderline tuberculoid (BT) leprosy. Endoneurial area is heavily infiltrated by histiocytes (many showing epithelioid change) and lymphocytes. Perineurium (P) is multi-layered and infiltrated, mainly by lymphocytes. EP = epineurium. (H&E ×400).

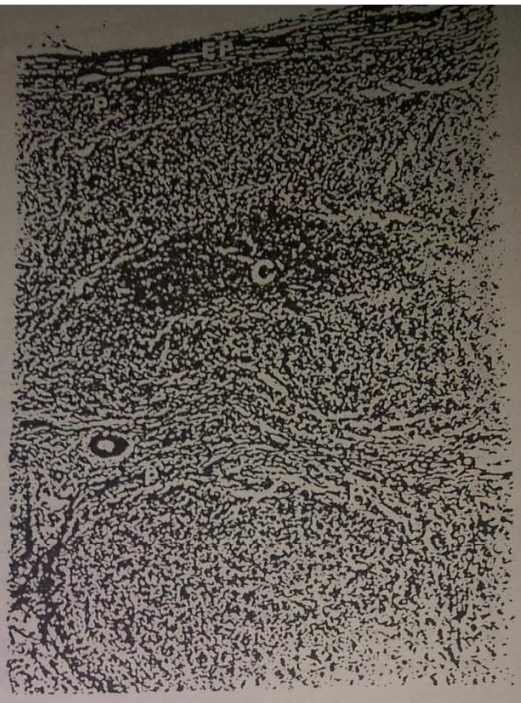


FIG. 4. Sural nerve biopsy: borderline tuberculoid (BT) leprosy. All fascicles are extensively infiltrated and there are large areas of caseation necrosis (C). P = perineurium; EP = epineurium. (H&E ×20).

spread from one end of the biopsy to the other; in two patients, solid-staining bacilli and globi were found, indicating relapse. In all except two of the nonlepromatous patients (mainly borderline-tuberculoid) there was an extensive and severe granulomatous infiltration, and in one case there was marked caseation in the endoneurial zone.

Within the limits of the present study, the findings indicate that biopsy of a peripheral nerve, even when it is not obviously associated with a skin lesion, may reveal pathological changes which are greater in degree than those suggested by skin biopsy or clinical examination. These observations in a somewhat heterogeneous group of patients treated for varying periods of time, and in a study which was not prospectively planned, suggest that similar observations in a larger group of untreated and treated patients, including those who have relapsed, may be of value.

Sural nerve biopsy should be performed only by a medically qualified and experienced operator, but it is not technically difficult, did not give rise to sensory deficit in this series, and is potentially highly revealing of pathological change.

RESUMEN

Como parte del estudio realizado en Etiopía para la búsqueda de muramidasa (lisozima) en biopsias de nervios de pacientes con lepra, los cortes histológicos de estos pacientes se tiñeron con hematoxilina-eosina y con el colorante de Ziehl-Neelsen, y se examinaron por microscopía de luz para localizar infiltrados celulares y bacilos de la lepra. Los hallazgos sobre la muramidasa se publicarán en forma separada. En este trabajo se describen los hallazgos sobre los infiltrados y los bacilos de la lepra en un grupo de 18 pacientes (4 con lepra no lepromatosa) que mostraban una reacción de hipersensibilidad retardada al momento de la biopsia. Los hallazgos fueron muy interesantes y reveladores. Todos los pacientes con lepra lepromatosa e intermedia mostraron infiltración endoneurial y perineurial de considerable extensión. En varios casos se encontraron bacilos dispersos de un extremo al otro de la

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biopsia; en dos pacientes se encontraron bacilos sólidamente teñidos y globi sugerentes de recaídas. A excepción de 2 pacientes no lepromatosos (intermedios-tuberculoides), todos los demás mostraron una infiltración granulomatosa extensa y severa, en un caso hubo marcada caseificación en la zona endoneurial.

Dentro de las limitaciones del estudio, los hallazgos indican que la biopsia de un nervio periférico, aún cuando no esté asociado en forma obvia con una lesión de la piel, puede revelar cambios patológicos de mayor magnitud que los sugeridos por la biopsia de la piel o por el exámen clínico. Las observaciones hechas en este estudio que no se planeó en forma prospectiva, con pacientes más bien heterogéneos desde el punto de vista clínico y de tratamiento, sugieren la importancia de realizar un estudio similar en un grupo de pacientes más grande y mejor controlado desde diversos puntos de vista.

La biopsia del nervio sural, aunque técnicamente no es difícil, debe hacerse solo por un cirujano calificado y experto a fin de no ocasionar un déficit sensorial; el estudio de la biopsia neural puede, potencialmente, revelar los cambios patológicos.

RÉSUMÉ

Dans le cadre d'une étude plus large portant sur les biopsies nerveuses chez des malades de la lèpre en Ethiopie, concernant la présence de muramidase (lysosome), on a examiné des coupes par microscope optique après coloration par l'hématoxyline et l'éosine, en vue de déceler les infiltrations cellulaires, ainsi qu'une modification de la coloration de Ziehl-Neelsen pour les bacilles de la lèpre. Les observations se rapportant à la muramidase seront relatées séparément. Cet article décrit les observations se rapportant à l'infiltration et aux manifestations bactériologiques, dans un groupe de 18 malades, dont quatre atteints d'une forme de lèpre non lépromateuse, souffrant d'une réaction d'hypersensibilité retardée au moment de la biopsie. Les observations ont été particulièrement intéressantes et révélatrices. Tous les malades lépromateux et lépromateux-borderline présentaient une infiltration très étendue endoneurale et périneurale; dans plusieurs cas, les bacilles étaient largement répandus d'une extrémité de la biopsie à l'autre; chez deux malades, on a trouvé des bacilles solides à coloration uniforme et des globi, ce qui témoigne d'une récidive. Dans tous les cas de malades non lépromateux, et particulièrement chez les malades borderline-tuberculoides, sauf deux, on a constaté une infiltration granuloma teuse étendue et prononcée; dans un cas, on a noté une caséification notable de la zone endoneurale.

Dans les limites de cette étude, ces observations indiquent que la biopsie d'un nerf périphérique, même lorsqu'il n'est pas associé de façon manifeste avec une lésion cutanée, peut révéler des modifications pathologiques d'un degré plus prononcé que ne le suggère la simple examination clinique ou une biopsie. Ces observations, menées dans un groupe quelque peu hétérogène de malades, traités pour des durées variées, recueillies au cours d'une étude qui n'était pas planifiée pour être prospective, suggèrent que des observations semblables pourraient fournir des informations valables, si elles étaient recueillies chez un nombre plus élevé de malades, tant traités que non traités, y compris ceux qui ont présenté des récidives.

La biopsie du nerf sural ne devrait être pratiquée que par du personnel qualifié et expérimenté; cette biopsie n'est cependant pas difficile du point de vue technique; elle n'a pas entraîné de pertes sensorielles dans cette série de malades; elle peut fournir des renseignements fort intéressants quant aux modifications pathologiques.

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THE PATTERN OF EPILEPSY IN ETHIOPIA: ANALYSIS OF 468 CASES

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ABSTRACT. *An analysis of 468 consecutive Ethiopian epileptics seen in neurology clinics in Addis Ababa over a 3-year period is presented. The highest incidence of epilepsy was seen in males aged 11-20 years, and there was a preponderance of males (60.3%). Of the clinically classifiable epilepsies (83%) analysed, the majority (60.1%) had grand mal; 19.3% had partial complex (temporal lobe); and 11.6% had secondary generalized seizures. Petit mal was noted in only 2.1%. Positive histories of seizures in family members and febrile convulsions were obtained in only 6.4% and 7.7% respectively. The investigations, including electroencephalography and treatment of the patients, are briefly discussed, and the results also compared to experiences in other African countries.*

Although accurate prevalence figures are not easily available, epilepsy is believed to be a common neurological disorder in Africa. Previous studies (1-3) have reported incidence rates varying from 3 to 20 per thousand. The very high incidence of 2% comes from the study of Jilek-Aall *et al.* (2) among the Wapogora tribe of Tanzania, where genetic factors have been implicated. Very little is known about epilepsy in Ethiopia. Giel (4) in 1970, from morbidity surveys in Ethiopia, reported prevalence rates of 5 per thousand in an urban area and 8 per thousand in a rural community. We have recently confirmed this prevalence rate in a pilot epidemiological study in the rural community of Koshe, 200km from Addis Ababa (unpublished data).

In the last 10 years, neurologists working in Ethiopia have been alarmed at the magnitude of convulsive disorders seen in neurology clinics. Unfortunately health-workers in the country have not been alerted to the problem. In addition, facilities for the investigation and treatment of the disorder in the country are poor and limited. These deficiencies, coupled with faulty beliefs among epileptics about their disease and its medical management, render it an important medical and social problem in the country.

The purpose of this prospective study is to report on the pattern of epilepsy as seen in the neurology clinics in Addis Ababa in epileptics coming from within the city and in those referred from the countryside. A similar study has not been reported in the past from Ethiopia.

PATIENTS AND METHODS

Between November 1980 and November 1983, 468 consecutive cases of epilepsy

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been able to achieve drug control in most seen at the neurology referral clinic of the Black Lion Teaching Hospital and the private clinic of the author, both in Addis Ababa, were studied prospectively. The majority (70%) of the patients came from Addis Ababa, and the rest were from outside the city. A detailed history was taken from each patient and in most cases also from an eye-witness, with particular emphasis on the characteristics of the seizures as well as on information on complicated delivery, birth injury, cerebral infection and head injury. Enquiries were also made concerning any family history of epilepsy and the occurrence of febrile convulsions during childhood. Each patient underwent a complete physical examination, including a detailed neurological evaluation. The following investigations were carried out: haemogram, fasting blood sugar and skull X-ray.

Electroencephalographic examination was undertaken on 225 (48.1%) patients. The recordings were performed during the interictal period, while awake, after hyperventilation, and during photic stimulation.

In 50 patients, cerebrospinal fluid analysis was carried out. Carotid angiography was performed when a space-occupying lesion was suspected, or when the electroencephalogram (EEG) demonstrated obvious lateralizing abnormality.

RESULTS

This study was primarily concerned with adult epileptics. However, the age of our patients ranged from 2 to 75 years. The 11.5% of patients below the age of 10 years were either referred from the paediatric epilepsy clinic or attended directly.

The highest rate of incidence of epilepsy was seen in the age-group 11-20 years (35%), followed by the 21-30 (27%) and 31-40 (13.2%) age-groups (Table 1).

There was a striking preponderance of males in all age-groups: of the total number of epileptics, 60.3% were males and 39.7% females.

Febrile convulsions during childhood were reported in 7.7%. A family history of epilepsy was obtained in only 6.4%.

Clinical types of epilepsy

Of the 468 epileptics we studied, 73% could be classified clinically according to the classification adopted by the International League Against Epilepsy (5).

As shown in Table 2, the primary generalized epilepsy of the tonic-clonic type was seen most frequently (60.1%), followed by the partial complex (temporal lobe) epilepsy (19.3%), and secondary generalized seizures (11.6%).

Petit mal (absence) epilepsy was rarely encountered (2.1%). All were below the age of 20, the majority being in the 11-20 year age-group. Secondary generalized seizures were commonly seen below the age of 40 years.

The highest frequency of grand mal and temporal lobe seizures was seen in the 11-20 year age-group (31.3% and 38.7% respectively), followed by the 21-30 year age-group.

Aura was described by only 30% of the patients. The most common warning sensations observed were dizziness and vertigo as well as strange feelings in the body, hard to describe. Jacksonian attacks were commonly encountered in focal seizures with secondary generalization.

Associated disorders

Table 3 shows that a history of head trauma was obtained in 13.2%; 6.6% of the patients had associated cerebrovascular accidents with hemiparesis. Mental retardation seen below the age of 20 years was present in 4.7%. A history suggestive of meningitis or encephalitis was obtained in

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4.3% of the cases. Intracranial mass lesions were diagnosed in 3.8% of the patients investigated. Thirty patients showed evidence of severe burns due to a fall into an open fire during attacks.

Investigations

Of the 328 skull X-rays performed, 36 (11%) were reported abnormal; 15 showed skull fractures, mainly depressed; 5 showed evidence of increased intracranial pressure; intracranial calcification was revealed in only 2 cases (0.6%), of which one was associated with an oligodendroglioma. The 33 carotid angiograms showed subdural haematomas in 10; 8 angiograms were compatible with tumours; 15 were normal. Cerebral spinal fluid analysis in 50 patients proved normal, with the exception of 3 patients who had focal neurological signs, where protein was elevated. Haemograms and fasting blood sugar in 300 patients were also within normal limits, except for eosinophilia found in 15 patients.

EEG findings. The classification of Bental (6) was adopted in the analysis of the EEGs (Table 4). Well-developed regular activity, in most cases 10 H_z or above (cycles per second), was taken as normal; as borderline, more irregular theta-activity than expected for the corresponding age-group. Abnormality was considered established if irregular slow and sharp activity, as well as synchronized bursts of activity during rest, hyperventilation or/and photic stimulation were found. The EEG was normal in 19.6% of the patients who had the investigation; 22.2% demonstrated borderline abnormalities. Centrencephalic discharges were seen in 12%. Focal temporal abnormalities were encountered in 32%, and focal discharges other than in the temporal region in 12%. A petit mal pattern of spike wave discharges was discovered in only 2.2%.

Treatment

The majority of patients were treated with either phenytoin (Dilantin; USA) (40%), phenobarbitone (30%), or a combination of these two anticonvulsants (12%). Primidone (Mysoline: ICI Pharmaceuticals, UK), alone or in combination with Dilantin, was used in 10%. The rest of the patients received carbamazepine (Tegretol: Geigy, UK), ethosuximide (Zarontin: Parke, Davis, UK), or clonazepam (Rivotril: Roche, UK), either singly or in combination with the other standard anticonvulsants. Side-effects were generally uncommon except for gingival hypertrophy, skin changes and hirsutism associated with Dilantin. Only 5 cases of mild allergic skin rashes were encountered: 2 due to Dilantin and 3 to phenobarbitone.

DISCUSSION

If we accept the minimal incidence rate of epilepsy of 5/1000 as found by Giel (4) for the whole of Ethiopia, with an approximate total population of 35 million, there would be at least 175,000 epileptics in the country. This certainly makes the problem in Ethiopia quite significant.

In our experience, epilepsy constitutes 20% of out-patients visiting the neurology referral clinic.

The age and sex distribution of our patients is similar to that in previous African reports (1, 3, 7). The striking male preponderance, we believe, is due to the tendency in Africa for males to seek medical attention more readily than females; this is caused by both social and economic factors.

As in other hospital series in Africa (1, 8, 9), our results show that the disorder affects young patients. The onset of seizures in our series was below the age of 20 years in the majority (70%) of cases.

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TABLE 1: Age and sex distribution of epileptic patients

Age-group (years)	Male No.	Male %	Female No.	Female %	Total No.	Total %
0 – 10	82	6.8	82	17.4	164	35.0
11 – 20	88	18.8	76	16.2	164	35.0
21 – 30	76	16.3	50	10.7	126	27.0
31 – 40	42	9.0	20	4.2	62	13.2
41 – 50	30	6.4	10	2.1	40	8.5
51 – 60	6	1.3	4	0.9	10	2.2
> 60	8	1.7	4	0.9	12	2.6
Total	282	60.3	186	39.7	468	100.0

TABLE 2: Type of seizures in relation to age; no. of unclassifiable cases: 80 (17.1%); no. of classifiable cases: 388 (82.9%)

Type of seizure	AGE-GROUPS (YEARS) 0–10	11–20	21–30	31–40	41–50	51–60	> 60	Total patients No.	Total patients %
Primary generalized	31	78	64	35	21	8	6	243	62.6
Tonic-clonic (grand mal)	26	73	64	35	21	8	6	233	60.1
Absence (petit mal)	3	5	–	–	–	–	–	8	2.1
Myoclonic epilepsy	2	–	–	–	–	–	–	2	0.5
Partial epilepsies	9	48	45	27	12	4	–	145	37.4
Elementary symptoms	2	6	8	3	3	3	–	25	6.4
Partial complex (temporal lobe)	5	29	23	14	4	–	–	75	19.3
Secondary generalization	2	13	14	10	5	1	–	45	11.6
Total	40	126	109	62	33	12	6		
Percentage	10.3	32.5	28.1	16.0	8.5	3.1	1.5		

TABLE 3: Associated disorders

Disorder	No.	%
Head injury	62	13.2
Cerebrovascular accident (hemiparesis)	31	6.6
Mental retardation	22	4.7
Cerebral infection	20	4.3
Intracranial mass lesion: 10 subdural haematomas and 8 tumours	18	3.8
Migraine	10	2.1
Alcoholism (chronic)	8	1.7

TABLE 4: Electroencephalogram diagnosis: analysis of 225 EEG recordings

Electroencephalogram features	No. of patients	Percentage
Normal	44	19.6
Borderline	50	22.2
Abnormal	131	58.2
Centrencephalic discharges	27	12.0
Focal discharges (with or without secondary generalization)	99	44.0
Focal, frontal	18	8.0
Focal, temporal	72	32.0
Focal, frontotemporal	9	4.0
Petit mal	5	

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Because of the strong social stigma, our epileptics were reluctant to discuss the occurrence of the disorder in close relatives. We found during our study that a number of patients were concealing such information. Therefore, in spite of persistent and persuasive approaches, we found a positive family history only in 6.4%. This figure is low compared to those obtained by researchers in other regions of Africa (3, 9, 10).

As a result of inadequate information, the role of prenatal and perinatal factors in the incidence of epilepsy in our series could not be established. However, given poor antenatal care and home delivery in Ethiopia, we believe that birth injury has a definite contributory role in the development of epilepsy of the partial type, with or without secondary generalization.

Of the classifiable cases, idiopathic epilepsy of the grand mal type was commonest in all age-groups in our series. The prevalence rate was 60.1%, and the majority of patients were below the age of 40 years. On the other hand, petit mal was very rare (2.1%). The apparent rarity of absence seizures in Africa (1, 9, 10) is caused by underdiagnosis of the disorder, because patients as well as their relatives are often not bothered by the minor symptoms of the condition, and hence do not seek medical attention.

In contrast to the findings of Joshi *et al.* in India (11) and European experiences as reported by Gastaut *et al.* (12), we found partial epilepsy to be less common than the generalized type. However, the EEG recordings demonstrated a higher percentage of focal, predominantly temporal abnormalities, as compared to centrencephalic discharges. It is therefore conceivable that we may be clinically misdiagnosing many partial epilepsies as being primary generalized. History of febrile convulsions was obtained in 7.7% of our patients, much fewer than in other African studies (1, 2, 9). It is, however, interesting that even in our small figures we observed a higher proportion of febrile convulsion associated with temporal lobe epilepsy.

Myoclonic epilepsy and partial seizures with elementary symptomatology were not common in our series.

We found secondary generalized seizures quite significant in our study. The role of head injury in the causation of secondary symptomatic seizures is clearly demonstrated. There was a history of head injury in 13.2% of all our cases, a figure similar to that found by Joshi *et al.* (11) in India.

In the secondary generalized epilepsy there was a significantly higher incidence (30%) of head injuries. Post-traumatic epilepsy is thus a frequent and serious sequela of a traumatic head injury or an automobile accident, which are both common occurrences in Ethiopia. Only 4.3% of our patients gave a history of cerebral infection, and 6.6% gave clinical evidence of cerebrovascular accidents (Table 3). Both of these conditions must also have contributed to the partial epilepsies with secondary generalization.

In the epileptics without obvious neurological deficits of intracranial space-occupying lesions or head trauma, routine investigations, including haemogram, fasting blood, skull X-ray, were not contributory to diagnosis. They were, however, useful in excluding other clinical diagnoses. The negative results of our routine examinations and the valuable role of the EEG has been emphasised also in the study of Kellam in Zambia (13).

In Ethiopia our choice of anticonvulsants was limited to Dilantin, phenobarbitone and Mysoline, which are the drugs readily available to patients. With these cheap but effective agents we have

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been able to achieve drug control in most of our cases. Unfortunately we had a fairly significant defaulting rate of from 15% to 20%. In those who attended our clinics more regularly, we found that there were still some patients taking their anticonvulsants erratically. The patients whom we lose go to faith-healers, holy waters or traditional medicine men.

Serious side-effects of anticonvulsants were generally uncommon, and when they did occur they were not very troublesome. Some of those patients on phenobarbitone complained of impaired alertness and loss of power of concentration. Only a few of these patients required a change to another anticonvulsant, invariably Dilantin. Allergic skin reactions were rare; we encountered only 5 cases. Long-term use of Dilantin, however, caused gingivitis, coarseness of facial features and hirsutism, which sometimes created a problem, particularly in girls. We did not encounter megaloblastic anaemia due to Dilantin. It is interesting to observe that, in spite of the many defaulters, we found status epilepticus to be an extremely rare complication.

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Muramidase (Lysozyme) Findings in Sural and Radial Nerve Biopsies in Leprosy Patients After Varying Periods of Treatment[1]

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In tissues and secretions, Sir Alexander Flemming ([6]) was the first to show that lysozyme was the bacteriolytic element. Since the enzyme acts on muramic acid linkages in bacterial cell walls, the term muramidase has also been used as a synonym of the enzyme. Interest in this enzyme has remained high since the enzyme has been found to be raised in several diseases, indicating that it might be of diagnostic and/or prognostic value.

Recently, immunohistological techniques have been used to study the distribution of muramidase in tissues. Mason and Taylor ([12]) have thus shown that the enzyme could be found in serous salivary acinar cells, lactating mammary tissue, Paneth's cells, renal tubular cells, myeloid cells (including eosinophils), and histiocytic cells. In pathological tissues, they found marked positivity in reactive histiocytic cells such as found in granulomatous conditions like tuberculosis and Crohn's disease. The distribution pattern of the enzyme intracellularly was not described.

Other studies have demonstrated elevated serum muramidase levels in tuberculosis ([9, 11, 17]), sarcoidosis ([16]), inflammatory bowel diseases ([3, 4]), and myeloproliferative diseases ([20, 25]). Blennerhassett and Papadimitriou ([1]) studied the enzyme in several granulomatous reactions, and Rea and Taylor ([18]) studied its levels in serum and its distribution in tissues across the leprosy spectrum. In untreated leprosy patients, serum muramidase levels were elevated and particularly high levels were found in patients with severe reversal reaction or Lucio's phenomenon. These levels tended to decline with prolonged sulfone therapy. In tissues, two distinct staining patterns for intracellular muramidase were described. A granular pattern was seen in epithelioid and giant cells; whereas a saccular pattern was found in the lepromatous histocytes. These findings were later confirmed by Cologlu ([2]). In both studies, peripheral nerves were not included. Our study was therefore designed to study muramidase distribution in nerves and to compare the findings with those described in the skin of leprosy patients. We also stained several of the biopsies with Congo red to detect the presence of amyloid deposits in these nerves.

MATERIALS AND METHODS

Patients were randomly selected from among those admitted to the All Africa Leprosy and Rehabilitation Training Center (ALERT), Addis Ababa, Ethiopia. All of the patients had had oral sulfone (dapsone, DDS) 100 mg daily for varying periods of time, ranging from one month to 20 years, and others had received rifampin in addition to DDS (Tables 1 and 2). Patients with reversal reaction were given prednisolone. Compliance to drug treatment was difficult to assess, but a review of the patients' medical records indicates that many of them had almost certainly been irregular in their drug intake. We studied 34 Ethiopian patients, 24 males and 10 females, ranging in age from 15–60 years.

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TABLE 1. *Seventeen patients with lepromatous (LL) and borderline lepromatous (BL) leprosy.*

Biopsy no.	Sex	Age	Therapy		Bacilli		Histological diagnosis		Muramidase[b]	
			Drug(s)[a]	Duration (yr)	Skin	Nerve	Skin	Nerve	Skin	Nerve
1	F	46	DDS	1	NA[c]	0	NA	LL	NA	Granular +
2	M	31	DDS	10	Few	0	LL	LL	Saccular +	Saccular +
3	M	57	DDS	7	Few	0	LL		0	Doubtful
4	M	63	DDS	12	Many	Many	LL	LL	Saccular ++	Doubtful
5	M	38	DDS/RMP	1	Many	Many	LL	LL	0	Saccular +++
6	M	23	DDS/RMP	1	Many	Many	BL	LL[d]	Saccular ++	Saccular +++
7	M	38	DDS	15	Few	Few	LL	LL	0	Saccular +
8	M	23	DDS	10	Few	Many	LL	LL	0	Saccular ++
9	F	10	DDS/RMP	12	Many	Many	LL active	LL active	Saccular	Saccular +++
10	M	60	DDS	6	Few	Many	NA	LL	0	Doubtful
11	M	16	DDS	1	Many	Many	LL	LL	Saccular ++	Saccular ++
12	M	12	DDS/RMP	2	0	0	LL	LL	Saccular +	Saccular ++
13	M	31	DDS	1	Many	Many	LL relapse	LL relapse	Saccular ++	Saccular +++
14	M	42	DDS/RMP	16	Many	Many	LL relapse	LL relapse	Saccular ++	Saccular ++
15	F	26	DDS	17	NA	Many	NA	LL	NA	Saccular ++
16	M	51	DDS	10	NA	Many	NA	LL	NA	Saccular ++
17	F	60	DDS	20	NA	0	NA	LL	NA	0

[a] DDS = dapsone, RMP = rifampin.
[b] 0 = negative, + = faintly positive, ++ = positive, +++ = intensely positive.
[c] NA = not available.
[d] LLs = subpolar lepromatous.

TABLE 2. *Twelve patients with borderline tuberculoid (BT) and tuberculoid (TT) leprosy.*

Biopsy no.	Sex	Age	Therapy		Bacilli		Histology		Muramidase[a]	
			Drug(s)[a]	Duration	Skin	Nerve	Skin	Nerve	Skin	Nerve
18	F	25	DDS	3 yr	0	0	BT	BT	Granular +	Granular ++
19	M	16	DDS	2 yr	0	0	BT/TT	Normal	Granular ++	Negative
20	F	23	DDS/Pred.	2 yr	0	0	Not diagnostic	BT	Negative	Negative
21	F	40	DDS/Pred.	3 mo	0	0	Inadequate material	BT	Negative	Granular ++
22	M	28	DDS/Pred.	5 yr	0	0	Not diagnostic	BT	Negative	Granular +
23	M	37	DDS	2 yr	0	0	BT	TT	Granular +	Granular ++
24	M	24	DDS	3 yr	0	0	BT	TT	Negative	Granular +
25	M	60	DDS	15 yr	0	0	Normal	TT	Negative	Granular ++
26	M	33	DDS	10 yr	0	0	NA[c]	BT	NA	Granular/
27	M	20	DDS	2 mo	0	Few	BB[d]	BB	Granular/ Saccular	Saccular Vacuolated +++
28	M	22	DDS/RMP	2 yr	0	Many	Not diagnostic	BB/BT	Negative	Granular ++
29	F	23	DDS/Pred.	4 mo	0	0	NA	BT	NA	

[a] DDS = dapsone, RMP = rifampin, Pred. = prednisolone.
[b] 0 = negative, + = faintly positive, ++ = positive, +++ = intensely positive.
[c] NA = not available.
[d] BB = mid-borderline.

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TABLE 3. *Five patients with reversal (delayed hypersensitivity) reactions.*

Biopsy no.	Sex	Age	Therapy		Bacilli in nerve	Histology[b]		Muramidase[c]	
			Drug(s)[a]	Duration (mo)		Skin	Nerve	Skin	Nerve
30	F	33	DDS	1	Few	BB-BT	BB-BT	Granular ++	Granular ++
31	F	27	DDS/Pred.	2	Few	BB-BT	BB-BT	Granular +++	Granular +++
32	M	16	DDS/Pred.	9	0	BB-BT	BB-BT	Granular +++	Granular +++
33	M	17	DDS/Pred.	4	0	BB-BT	BB-BT	Granular +++	Granular +++
34	M	46	DDS/Pred.	1	0	BB-BT	BB-BT	Granular +	Granular +

[a] DDS = dapsone, Pred. = prednisolone.
[b] BB = mid-borderline, BT = borderline tuberculoid.
[c] 0 = negative, + = faintly positive, ++ = positive, +++ = intensely positive.

Skin biopsies were taken from active lesions; whereas the sural nerve biopsies were taken from either of the two legs, irrespective of the presence or absence of a cutaneous lesion over the course of the nerve. The technique of nerve biopsy, fixation, processing, and staining with hematoxylin and eosin, as well as with a Fite-Faraco modification of Ziehl-Neelsen staining, is described elsewhere ([8]).

The peroxidase-antiperoxidase (PAP) immunohistological staining technique ([22]) was used to demonstrate muramidase enzyme in tissues. Briefly, this included deparaffinization of sections and taking to water, blocking endogenous peroxidase with absolute methanol containing 0.3% hydrogen peroxidase, application of 1:5 diluted normal swine serum, followed by incubation with rabbit anti-human muramidase antibody. The antibody was used at a 1:1000 dilution. Swine anti-rabbit serum immunoglobulin at a 1:20 dilution was then applied before incubation with horseradish peroxidase–rabbit antiperoxidase (PAP) complex. The PAP complex was used as a 1:100 dilution. Localization of the enzyme activity was revealed by a reaction with diaminobenzidine-tetrahydrochloride (DAB) containing 0.01% hydrogen peroxide. This reaction gives a brown product at the site of the antigen-antibody reaction. Sections were counterstained with hematoxylin, dehydrated, cleared, and mounted in DPX. The substitution of normal serum for the specific anti-muramidase antibodies provided control sections. A few blocks of histologically normal nerves were retrieved from the histology archives and processed in a similar way as those from leprosy patients.

All dilutions were done in Tris buffer (pH 7.6), while washes were done in Tris-saline buffer (a 1:10 dilution of Tris buffer in normal saline). Antibodies were purchased from Dakopatts Immunoglobulin A/S, Copenhagen, Denmark; DAB was from Sigma Chemical Co., St. Louis, Missouri, U.S.A.

RESULTS

Using the Ridley-Jopling system ([19]), there were 16 lepromatous (LL), 1 borderline lepromatous (BL), 4 mid-borderline (BB), and 13 borderline tuberculoid (BT) or tuberculoid (TT) patients. Tables 1, 2, and 3 summarize our findings on the examination of nerve biopsies from these patients for muramidase. The criteria for describing the pattern as either saccular or granular were as close as possible to those described by Rea and Taylor ([18]) and by Cologlu ([2]) and as illustrated in their publications.

Two distinct patterns of muramidase staining were observed. In the saccular pattern, positive histiocytes and globi demonstrated a homogenous stain within vesicles or their lumen (Figs. 1 and 2). This form was characteristically seen in globi. On the other hand, the granular pattern consisted of uniformly distributed, intracytoplasmic, fine brown granules (Figs. 3 and 4), most intensely found in epithelioid cells and in giant cells when present.

In seven instances, skin material was not available for examination, and in a further three we found it impossible to use the terms



FIG. 3. Granular pattern of muramidase staining in a histiocyte (nerve biopsy from a tuberculoid leprosy patient).



FIG. 4. Granular pattern of muramidase staining in a histiocyte (nerve biopsy from a tuberculoid leprosy patient).

drug intake and, thus, even a long period of treatment is not equivalent to a reduction in bacillary load. In general, patients with high bacillary loads had a more intense muramidase staining. This finding is interesting in the light of our knowledge that even when bacilli are not detectable in the skin, solid-staining, presumably viable, bacilli can be demonstrated in the Schwann cells of peripheral nerves ([21]). Since we were not able to demonstrate muramidase activity in Schwann cells, it is tempting to suggest that a deficiency of muramidase enzyme in these cells could confer a survival advantage to *Mycobacterium leprae* in these cells. On the other hand, it has been shown that *M. leprae* antigens persist for long periods in peripheral nerves ([14]) and, therefore, it is possible that these antigens could induce muramidase activity in phagocytic cells found in the nerves. This could perhaps explain the persistence of muramidase-positive cells in the nerves from borderline patients, even though no bacilli were seen in a majority of those patients.

The irregular distribution of muramidase among the cells of the granuloma examined may reflect the observation of Mason and Taylor ([12]) and Gordon, *et al.* ([7]) that muramidase is synthesized predominantly in "reactive" histiocytes rather than in the "resting" histiocytes. The strong intensity of muramidase staining during reversal reaction would tend to support this concept. During these reactions there is an increase in lymphocytes transformable by *M. leprae*, indicating that the reaction is a delayed-type hypersensitivity to *M. leprae*. These sensitized lymphocytes could, through mediators, be activating resident cells like epithelioid cells. After such an activation, these cells could then become strongly positive for muramidase. This suggestion was first put forward by Rea and Taylor ([18]).

Our inability to demonstrate muramidase activity in cells of neuronal origin suggests

origin. Our results suggest that a high percentage of mononuclear cells infiltrating the peripheral nerves in leprosy are derived from blood monocytes.

The function of tissue muramidase in leprosy is not yet clear. Its peculiar intracellular distribution pattern in the different forms of leprosy, however, warrants further study to elucidate its role in the pathogenesis of the disease.

RESUMEN

Usando el método de la inmunoperoxidasa, se estudió la actividad de muramidasa (lisozima) tisular en 34 biopsias de nervios de pacientes con lepra y se comparó con la actividad encontrada en la piel. En la mayoría de los pacientes lepromatosos y lepromatosos-intermedios, la enzima se encontró con un patrón sacular dentro de las células, a diferencia del patrón granular encontrado en el extremo tuberculoide del espectro y durante las "reacciones reversas". De hecho, la más intensa actividad enzimática se encontró en 4 pacientes con reacciones reversas. Comparando con la piel, la actividad de muramidasa fue más intensa y persistió más tiempo en los nervios. El tratamiento antileproso exitoso redujo la actividad enzimática tanto en los nervios como en la piel pero ésto fue más marcado en la piel. Las células de Schwann y los axones no mostraron actividad de muramidasa, indicando que las células muramidasa positivas no son de orígen neuronal. Nuestros resultados sugieren que una alta proporción de las células mononucleares infiltrantes derivan de los monocitos de la sangre.

La función de la muramidasa tisular en lepra aún no está clara. Su patrón peculiar de distribución intracelular en las diferentes formas de lepra, justifican su estudio posterior para dilucidar su papel en la patogénesis de la enfermedad.

RÉSUMÉ

On a eu recours à la méthode de coloration par l'immunoperoxydase, pour étudier l'activité de la muramidase (lysosyme) des tissus dans 34 biopsies nerveuses prélevées chez des malades de la lèpre. On a comparé ces observations à celles faites au niveau de la peau. Chez la majorité des patients atteints de lèpre lépromateuse ou dimorphe-lépromateuse, on a constaté que l'enzyme présentait un profil en sac à l'intérieur des cellules. Par contre, un profil granulaire a été observé chez les malades atteints de lèpre tuberculoïde, qui se situe à l'autre extrémité du spectre clinique de la lèpre, de même qu'au cours des réactions de réversion inverse (reversal reactions). En fait, l'activité enzymatique la plus prononcée a été relevée chez 4 malades présentant de ces réactions inverses. Par comparaison aux observations faites au niveau de la peau, l'activité en muramidase était plus intense au niveau des nerfs; elle persistait également plus longtemps. Un traitement efficace contre la lèpre a permis de réduire l'activité enzymatique à la fois dans les nerfs et dans la peau. Cet effet était cependant plus prononcé dans la peau. Les cellules de Schwann, de même que les axones n'ont pas présenté d'activité typique de la muramidase, ce qui indique que les positives pour la muramidase ne sont pas d'origine nerveuse. Ces résultats suggèrent qu'une forte proportion des cellules mononucléaires qui infiltrent les nerfs périphériques au cours de la lèpre, sont dérivées des cellules monocytes du sang. La fonction de la muramidase tissulaire dans la lèpre n'est pas encore éclaircie. Les profils particuliers de la distribution intra-cellulaire de cette enzyme dans les différentes formes de lèpre soulignent cependant la nécessité de procéder à des études complémentaires, afin d'élucider son rôle dans la pathogénèse de la maladie.

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EXPERIENCE WITH TREATMENT OF WRITER'S CRAMP IN ETHIOPIA

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Resumé

L'auteur rapporte les aspects cliniques et la réponse au traitement concernant 32 patients éthiopiens, ayant une crampe des écrivains, suivis pendant 5 ans (1980 à 1985). Les signes sont principalment apparus pendant la troisième et quatrième décennie chez les hommes (sex ratio 16:1), et chez les individus ayant un engagement religieux.
Les thérapeutiques associant différents types de médicaments à une psychothérapie de soutien n'ont pas été efficaces.
Cette étude suggère que la crampe des écrivains peut être une manifestation focale d'un syndrome dystonique dont l'expression clinique est aggravée par des situations émtionnelles très anxiogènes.

SUMMARY

The clinical profile and response to treatment are described in 32 Ethiopians with writer's cramp, followed over a period of five years (1980-1984). The onset was mainly during the third and fourth decades, and males predominated by 16:1. Those engaged in clerical duties were more prone to develop the problem. Therapy with different types of drugs combined with counselling and reassurance was disappointing. The study suggests that writer's cramp may be a focal manifestation of a dystonic syndrome, with its clinical expression being aggravated by emotionally stressful situations.

Key words: Writer's cramp, dystonia deconditioning, biofeed back.

INTRODUCTION

The pathophysiology of writers's cramp is still obscure. Various explanations have been given insofar as its aetiology is concerned. There are those who regard it a neutrotic disorder and emphasise its psychosomatic nature (1-3), while others believed that it is a focal manifestation of a dystonic syndrome (4,5). As a consequence of these divergent views, the approach to its treatment has been influenced by each physician's bias and conviction.

This brief communication deals with a prospective study of the clinical profile and therapeutic experience of 32 Ethiopians with this perplexing and difficult neurological problem.

PATIENTS AND METHODS

Between 1980 and 1984 at the Neurology Clinics in Addis Ababa, Ethiopia, we saw 32 patients with clasical writer's cramp (30 males and 2 females), in whom other neurological disorders such as pyramidal or cerebeller diseases, Parkinsonism, essential tremors, and cervical spondylosis were ruled out. Most patients were referred to us by other physicians in order to rule out periopheral neuropathy or myopathy.

All the patients were interviewed by the author for possible emotional problems and experiences that either precipitated or contributed to the insidious onset of the disease. Their drinking habits were also looked into. However, psychiatric consultations or formal standardised and comparative pyschological assessments were not undertaken. Every patient underwent a detailed general and neurological examination.

In all patients, routine haematological tests (haemoglobin, white blood cell count and differential blood count, erythrocyte sedimentation rate) and biochemical tests (fasting blood sugar, liver function tests, uric acid, blood urea nitrogen), as well as VDRL serological investigations, were performed. Cervical spine X-rays were taken in 80% of the patients. X-ray of the shoulder on the affected side had to be taken in 10 patients who insisted that their problems was "definitely' at the shoulder.

Nerve conduction velocity measurements were carried out in 20 patients in whom peripheral neuropathy or carpal tunnel syndrome were suspected by the referring physician.

Different therapeutic approaches were employed. All patients were reassured by their physicians, and conselled whenever there was evidence of a stressful situation during the follow-up periods. The drugs that were used included diazepam, lorazepam, chlordiazepoxide, medazepam, bromazepam, thioridazine, fluphenazine, amitriptyline, haloperidol, benzohexol, L-Dopa, L-Dopa+carbidopa, carbam azepine, dephenyl-hydantoin and propranolol. These drugs were administered up to their maximum dose either singly or in combinations. For rheumatic pains and severe spasms in the hands and/or arms, simple analgesics and anti-inflammatory agents such as indomethacin were given together with physiotherapy.

RESULTS

As can be seen in Table 1 amongst the 32 patients with writer's cramp, the age at onset ranged from 20 to 50 years, with their peak at onset in the third decade ollowed bv the fourth. All patients were right-handed.

Neurological examination was normal in all patients, except in 2 who had the signs ot spasmodic torticollis,, and 10 patients in whom fine tremors were noticed in outstretched hands. Most of the patients exhibited shaking and tremors of the hand during attempts to write.

The haematogical, biochemical, serological, radiological and nerve conduction velocities were within normal limits in all the patients.

TABLE 1

AGE AT ONSET AND SEX DISTRIBUTION OF 32 ETHIOPIANS WITH WRITER'S CRAMP

Age (years)	20-29	30-31	40-41	50-59	Total	%
Male	3	13	12	2	30	93.8
Female	0	2	10	0	2	6.2
Total	3	15	12	2	32	100.0
%	9.4	46.9	37.5	6.2	100.0	

Insofar as the occupation of our patients (Table 2) was concerned, the majority were engaged in clerical duties that require a lot of handwriting. It was interesting to observe that there were proportionally more patients from the law-courts (2 iudges, 2 registrars and 3 lawyers). Ten clerks came from other administrative officers; of these, 4 were engaged in accounting. Four were teachers, 3 were university students, 2 held managerial posts, and 6 came from other walks of life (mechanic, drumer, pensioner, health officer, waitress and merchant).

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TABLE 2

OCCUPATION OF 32 ETHIOPIANS SUBJECTS WITH WRITER'S CRAMP

Clerical — duties related to Law-courts	7
Clerical duties — Administrative	6
Clerical duties —- Accounting	4
Teacher — Student —	4
Managerial Position —	3
Other —	2
	6
Total	32

Most patients presented with complaints of rheumatic-like pain and stiffness in the right hand, spreading or radiating to the arm and shoulder. Difficulties with writing came on and progressed very gradually. The symptoms of spasm in the hand-muscles resulting in the aches and pains grew worse with attempts to write.

Generally the difficulty with writing consisted of tremors or shaking in the hand, after a fairly good and easy start. Then the patient started to experience an inco-ordinated firm grip of the pen or pencil by the fingers, and the hand went into a flexion deformity of the fingers and wrist (Figures 1A and 1B). As writing was continued, the abnormal posturing of the hand and wrist became more pronounced, and there was an increase in the tremors and jerky movements of the hand. The writing grew more and more irregular and illegible (Figure 2). The writer then changed to a different grip of the pen (Figures 1C and 1D).

Different patients had developed different ways of holding their pen, resulting in some improvement of the handwriting, which unfortunately was short-lived. Still others used the left hand to steady the tremulous right hand during the active phase of writing. When writing eventually became impossible, most patients gave up in despair. The poor penmanship in almost all patients was aggravated by any type of emotional stress, when being watched by others and while being made to write or sign in a hurry.

Amongst our patients, only 8 either voluntarily or following our advice trained themselves to use the left hand. After one year of follow-up, 5 had developed similar problems in the left hand.

Over the four years of the study, we discovered 5 patients who from the start manifested or later developed evidence of dystonic writer's cramp, in which, beside the problem of writing, they also exprienced difficulties with fine motor tasks such as using a fork and knife, handling drum-sticks and tying laces. Two patients went on, after two years, to develop spasmodic torticollis which, in one patient, a health officer, was most disabling.

DISCUSSION

Writer's cramp is generally a comparatively rare disorder. This is true of our experience in Ethiopia. However, it is an interesting and intriguing neurological entity.

The age distribution and age at onset in our patients compare well with European (4) and African (6) published reports. Although males are supposed to be more affected than females by this disorder, the extreme male preponderance, 16:1, in our patients is probably an expression of the predominant role of men in clerical responsibilties in Ethiopia. The clinical features of our patients fit the classical description of writer's cramp.

The relatively high percentage of Ethiopian patients coming from a clerical background, particularly the law-courts, reflects the experience of Samuel Solly (1864), quoted by Sheehy and Marsden (4), that what he called "scrivener's palsy or the paralysis of the writers" was commonly seen in those that "... got their bread by the use of pen, either as the exponet of their own thoughts or the thoughts of others..." This British observation is certainly true of present-day Ethiopia, where aids such as typewriter, calculating or dictating machines are in most instances unavailable. As a result, judges, clerks, accountants and many others also engaged in strenuous mental duties have to document literally every word in their own handwriting, and in most situations with three or four carbon copies .

Sheehy and Marsden (4) argue that isolated writer's cramp is a focal dystonia rather than a psychosomatic disturbance. This view is also reflected by Meares (5). The dystonic cramps we observed in 5 patients and the development of overt spasmodic torticollis in 2 of our patients two years after the manifestations of writer's cramp tend to support the hypothesis.

The psychological mechanism of the disorder has been emphasised by others (1-3). Those who suffer from writer's cramp have been described as having obsessional personalities (1, 2), and suffering mental conflicts with some bearing on the act of writing (2). However, the role of psychotherapy in the treatment of writer's cramp has not been convincingly established. Crisp and Moldofsky (1) reported good respsonse from psychotherapy, but this was not the case in the experience of Bindman and Tibbetts (2), who suggested that biofeedbacks appeared to produce better results.

Management of writer's cramp has, in our experience, been most disappointing. In contrast to the findings of Osuntokun *et al.* (6) therapeutic response reassurance and the use of anxietolytic agents in optimal doses in our patients was unsatisfactory. Like Lang *et al.* (7), we did not register any benefit from anticholinergic drugs. Dopa preparations were likewise unrewarding. Propranolol, on the other hand, reduced tremors in 5 patients, of whom 2 also improved slightly in their writer's cramp. In conclusion, although we did not use deconditioning procedures (2) or biofeedback (3) on our patients, we did not find other therapeutic approaches successful in controlling or alleviating the symptoms of writer's cramp, which we found to be most distressing and frustrating handicap in our patients.,

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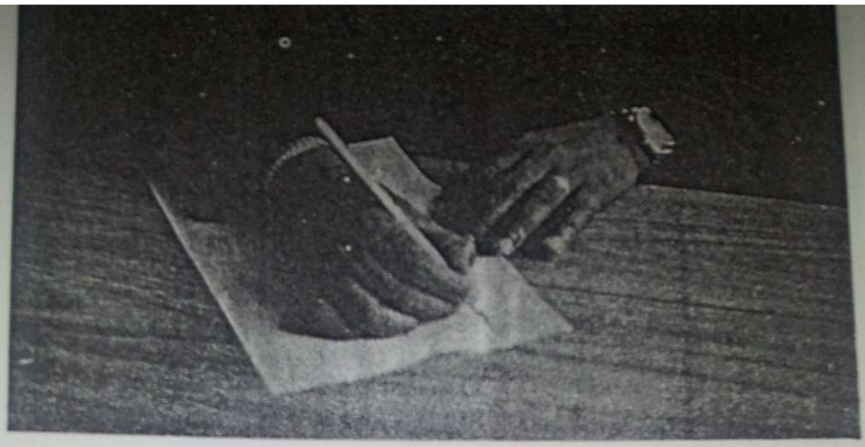


Fig 1.A Experience with treatment of writer's cramp in Ethopia



Fig 1.B Experience with treatment of writer's cramp in Ethopia



Fig 1.C Experience with treatment of writer's cramp in Ethopia



Fig 1 D Experience with treatment of writer's cramp in Ethopia

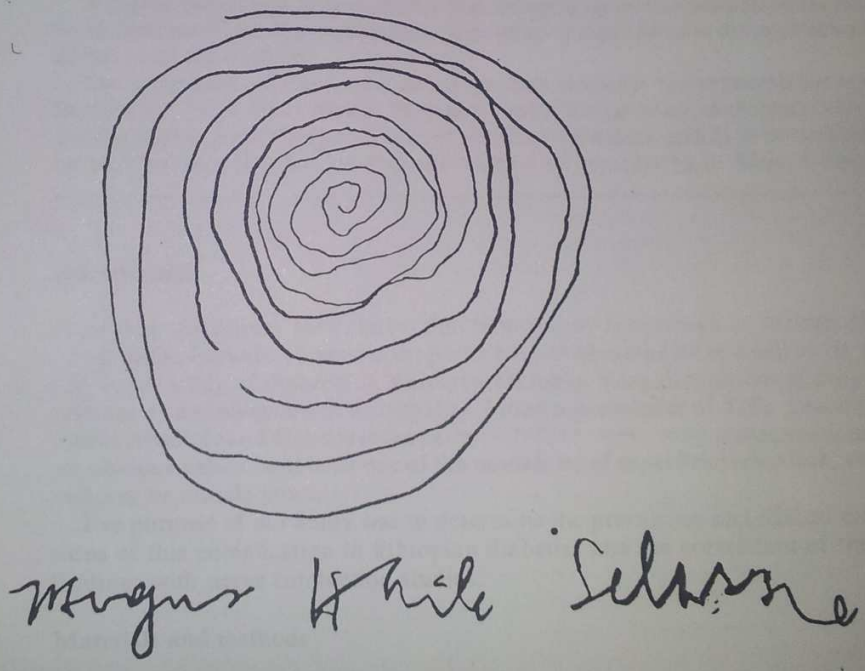


Fig. 2 Experience with treatment of writer's cramp in Ethiopia

45-year-old man with writer's cramp, photographed sequentially during the process of drawing and writing. Figures 1A and 1B show the abnomal posturing of the hand and wrist. 1C and 1D demonstrate a different grip of the pencil, which is tightly held in 1D. A drawing of an irregular Archimeds spiral, and illegible handwriting, are shown in figure 2.

Tropical and Geographical Medicine

NEUROPATHY IN ETHIOPIAN DIABETICS: A CORRELATION OF CLINICAL AND NERVE CONDUCTION STUDIES

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Abstract. A clinical and electrophysiological study of neuropathy in 215 unselected Ethiopian diabetics and 100 healthy controls was carried out at the Tikur Ambassa Teaching Hospital, Addis Ababa. The prevalence in diabetics was 54%, in controls 8%. The prevalence was significantly related to the duration of diabetes: 42%, 60% and 80% for a duration of respectively less than 5 years, 5 to 14 years, and 15 years and longer. There was no relationship of the prevalence to age. Diabetics with retinopathy (15%), nephropathy (12%) and liver cirrhosis (13%) had prevalences of respectively 70%, 76% and 71%; much higer figures than in patients without these complications.

A higher prevalence of neuropathy was detected by nerve conduction studies than by clinical methods. The mean conduction velocity diminished in direct relation to the duration of the diabetes.

The prevalence of neuropathy in our patients is similar to the prevalence reported from other countries in Africa. Poor nutritional background, inadequate control of the diabetes and the high prevalence of associated diseases such as liver cirrhosis may be partly responsible for the high prevalences of neuropathy in African diabetics.

Introduction

A number of studies have shown that neuropathy is common in African diabetics [1-4]. But in Ethiopia diabetic neuropathy has not been studied in detail so far. Belcher [5], in his study of diabetes in Northern Ethiopia, using diminution of deep tendon reflexes as an indication of neuropathy, found a prevalence of 47%. Lester [6] from Addis Ababa found diabetic neuropathy in 34% of cases, using as diagnostic criterium an obvious deficit in at least one of the modalities of superficial sensation, vibration, reflexes or muscle power.

The purpose of our study was to determine the prevalence and clinical manifestations of this complication in Ethiopian diabetics and the correlation of the clinical findings with nerve conduction studies.

Materials and methods

The study included 250 randomly selected Ethiopian diabetics from the Tikur Ambassa Teaching Hospital in Addis Ababa and 100 age and sex matched normal volunteers. Data pertaining to diabetes and its complications were recorded on a protocol prepared for the purpose and a complete neurological examination was performed.

Blood pressure was measured in the recumbent position and 15 seconds after the patient has stabilized standing upright. Light touch was tested with a wisp of cotton over the touch pad of the fingers and dorsum of the toes. Vibration was evaluated in the upper and lower limbs using a 128-Hertz tuning fork over the distal interphalangeal joints of the little finger and great toe in comparison with that of the examiner (RTH)

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For proprioception the patient was asked to indicate the direction of minimal passive movement of the distal interphalangeal joint of the little finger and the interphalangeal joint of the great toe. Muscle power was evaluated according to the Medical Research Council (MRC) scale [7].

Motor nerve conduction studies of the median, ulnar, peroneal and tibial as well as the sensory nerve conduction of the sural were performed on the right side in all patients. Pick up surface disc electrodes were placed over the motor points of the thenar, hypothenar, extensor digitorum brevis, and adductor hallucis muscles for the median, ulnar, peroneal and tibial nerves respectively. Sural sensory conduction velocity was determined antidromically by stimulating the sural nerve at a distance of 12 cm from the recording electrode which was placed behind the lateral malleolus.

Previous controlled studies in our EMG laboratory have shown that correction for temperature did not make a significant difference on the nerve conduction values obtained within the laboratory temperature range of 18°C to 20°C in the afternoon. Therefore surface temperature measurements were not made during this study.

Neuropathy was diagnosed if objective sensory deficits in the extremities, reduction or loss of deep tendon reflexes, autonomic disturbances or mononeuropathy without an obvious alternative cause were found singly or in any combination.

The statistical methods used in our study were the normal distribution test for significance (Z-test) and the arithmetic mean calculated from grouped data.

Results

There were 128 (59.5%) males and 87 (40.5%) females with an age range of 14 to 78 years ($\bar{x} \pm SD\ 42 \pm 2$). The age distribution is shown in *Table 1*. The duration of diabetes ranged from less than one year to 23 years with an average of 7 years.

Fifty-three per cent (53%) of the patients were on oral hypoglycaemic agents, 46% on insulin and 1% on diet alone. Diabetic control was unsatisfactory in the majority of the patients with irregular therapy and follow-up.

Neurological Findings. Of the 215 diabetics studied there were 116 (54%) patients, 70 males and 46 females, who had neuropathy with an age range of 14 to 77 years (mean 45 years). The duration of diabetes was less than 5 years in 35%, 5 to 14 years in 46% and over 15 years in 19%. Forty-six per cent (46%) of these patients were on insulin and 54% on oral agents.

The details of the clinical findings are shown in *Table 2*. 15 patients (7%) among the 215 diabetics examined exhibited a mixed sensorimotor polyneuropathy with gross atrophy and weakness of the muscles of the legs extending to involve the quadriceps. Mononeuritis simplex was encountered in seven cases: two oculomotor, two facial,

Table 1. Prevalence of neuropathy in relation to age

Age range in years	*Total*		*With neuropathy*	
	No.	*%*	*No.*	*%*
11 - 20	19	8.8	7	36.8
21 - 30	37	17.2	19	51.4
31 - 40	39	18.1	20	51.3
41 - 50	58	27.0	31	53.4
51 - 60	41	19.1	25	61.0
60 +	21	9.8	14	66.7
	215	100.0	116	54.0

Table 2. Frequency (%) of neurological symptoms and signs in 116 patients with neuropathy

Symptoms	Paraesthesiae distal legs	57.0
	distal arms	21.0
	Burning sensation soles	45.0
	palms	12.6
	Impotence (81 males)	48.0
	Bladder dysfunction	1.5
Signs	Reduced touch feet	52.0
	hand	20.0
	Reduced vibration feet	24.0
	Reduced position feet	1.0
	Reduced reflex ankle	60.0
	patellar	15.0
	biceps	10.0
	Orthostatic hypotension	10.0

one peroneal, one median, and one intercostal; mononeuritis multiplex, involving the oculomotor and facial nerves, was found in one case. The patient with intercostal radiculopathy had a sudden onset of right sided intercostal hyperaesthesia in the distribution of the eight intercostal nerve suggesting hepatobiliary or chest disease. All recovered after variable periods of time.

Autonomic Neuropathy (Table 2). Seventeen per cent of the patients gave a history consistent with orthostatic hypotension; measurement of the blood pressure established true orthostatic hypotension (a fall of 10 mm Hg in diastolic pressure) in 10%. Only three patients (1.5%), all below the age of 45 years, had bladder dysfunction in the form of difficulties with micturition and incontinence and only one case complained of nocturnal diarrhea. However 60% of all the diabetics studied were disturbed by constipation. Thirty of the 81 male diabetics (48%) interviewed reported impotence; the mean age of those affected (47.6 ± 1.6 years) was not different from that of the male diabetics (46.2 ± 1.4 years) who had no impotence.

Other Complications and Associated Diseases (Table 3). Cirrhosis of the liver, diagnosed at the diabetic clinic on the basis of clinical and laboratory data, was found in 13% and neuropathy was found in 71% of them. Retinopathy was discovered in 15%

Table 3. Prevalence of diabetic neuropathy in relation to the other complications and associated diseases

Associated diseases	*Total*		*With neuropathy*	
	No.	%	*No.*	%
Retinopathy	33 (215)*	15.3	23	69.7
Nephropathy	25 (215)*	11.6	19	76.0
Cirrhosis	28 (215)*	13.0	20	71.4
Hypertension	34 (190)*	17.0	17	50.0

* the numbers in brackets represent the total number of patients checked for the associated disease or relevant complication.

(33 patients) and nephropathy in 10% (25 patients). Neuropathy was found in 70% of those with retinopathy and in 76% with nephropathy.

Hypertension (a blood pressure greater than 150/95 in the recumbent position on more than one occasion) was discovered in 18% of the 190 diabetics in whom blood pressure was checked at the time of the neurological evaluation; no clear relation was seen between hypertension and diabetic neuropathy.

There were five patients with malignacies and five patients gave histories of exposure to a potentially neurotoxic agents (isoniazid and dapsone). But neuropathy was only found in one patient who had been on isoniazid for two years.

Nerve conductions studies in diabetics and normal controls. Table 4 shows the nerve conduction velocities in diabetics with and without neuropathy compared to normal controls. Motor nerve conduction velocity was slowed in the diabetics in comparison to the normal controls.

There were significant statistical differences in the neuropathic as compared to normal controls ($p < 0.01$). As is evident from the results diabetics without clinical neuropathy also exhibited slowed conduction velocities ($p < 0.01$) except for the sural nerve. *Figure 1* shows a progressive slowing of nerve conduction velocity of the peroneal nerve with increasing duration of the diabetes. Those with duration of less than 5 years had conduction velocities near that of normal controls. *Table 5* also shows the progressively increasing incidence of neuropathy in relation to the duration of the disease.

Table 4. Motor and sensory nerve conduction velocities in m/sec in Ethiopian diabetics

Nerve	*Normal Control*	*Diabetic without neuropathy*	*"p" compared to control*	*Diabetic with neuropathy*	*"p" compared to control*
Median	n = 100 58.8±6.2	n = 99 55.8±7.1	0.01	n = 116 51.0±7.2	0.01
Ulnar	n = 100 59.4±6.1	n = 99 56.7±6.2	0.01	n = 116 52.0±8.3	0.01
Peroneal	n = 100 50.3±7.3	n = 90 46.4±6.4	0.01	n = 110 40.0±5.1	0.01
Sural	n = 80 35.0±6.3	n = 70 34.7±6.3	0.30	n = 68 30.5±9.1	0.01

Table 5. Frequency of neuropathy in relation to duration of diabetes.

Duration of diabetes in years	*No. of patients*	*With neuropathy*	
		No.	*%*
<5	100	42	42.0
5 - 14	90	54	60.0
15+	25	20	80.0
Total	215	116	54.0

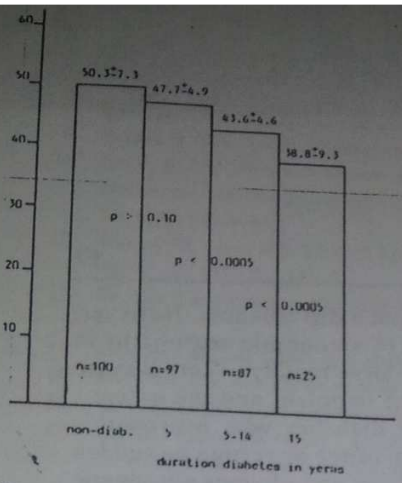


Figure 1. Average motor conduction velocity in the peroneal nerve in nondiabetics and diabetics with different duration of the disease.

Discussion

The prevalence of 54% of diabetic neuropathy found in this study was higher than the 47% reported by Belcher [5] and the 34% by Lester [6] from this country and is only surpassed by the findings from other African countries. There was no significant relation to age (*Table 1*) but the duration of diabetes was associated with a proportionally increasing prevalence of neuropathy (*Table 5*).

According to the criteria we adopted 8% of our normal controls also had neuropathy which is similar to the findings of Greenwood and Taylor [1] and Haddock [8] who detected some features of peripheral neuropathy in 15% and 17% respectively of normal controls. These findings support the view expressed by Haddock [2] that diabetes may precipitate neuropathy in a patient who has already borderline peripheral neuritis of nutritional origin; this may in part explain the high prevalence of neuropathy in our diabetics, the majority of whom are thin and malnourished, although some studies have revealed higher prevalences even in western countries where these factors are less prominent [9].

The commonest clinical manifestations of neuropathy (*Table 2*) were sensory symptoms of numbness or paraesthesiae in a 'stocking' pattern followed by burning pain in the soles of the feet. Involvement of the upper limbs in a 'glove' pattern was only seen in the severely afflicted.

Motor weakness was less prominent. Diabetic amyotrophy was not encountered and muscle atrophy was only found in 7% of those with neuropathy. As previously observed by Locke [10] many of our patients were unaware of their neuropathy up to the time of the study.

Mononeuritis simplex and multiplex were seen in 6% of our patients which appears to be higher than the 2.2% to 3.0% in Nigerian studies [4, 11].

Frequencies of autonomic neuropathy varying from 16% to 72% have been reported from Nigeria [4] and South Africa [12, 13]. In our study a complete battery of

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investigatory techniques was not used to detect autonomic disturbances. However, impotence came out as the most common (48%) form of autonomic neuropathy in spite of the reluctance of patients to discuss this problem readily. There was no significant difference ($p > 0.05$) in the mean ages of the impotent and the potent.

Orthostatic hypotension was found in 10% of our diabetics with neuropathic complications. These patients complained of dizziness, syncope or vertigo on sudden rising from a sitting or lying position. Nocturnal diarrhoea and obvious autonomic bladder dysfuhction were uncommon in this study. However we did not perform cystometrograms to detect early disturbance of bladder innervation which has been shown to occur in up to 40% of diabetics with impotence [14].

Liver cirrhosis is a common disorder which accounts for up to 12% of medical admissions in Ethiopia [15] and it was found in 13% of the 215 diabetics we studied. It is of interest that 71% of our cirrhotic diabetics had neuropathy (*Table 3*). It is therefore tempting to assume that the malnourished state of the cirrhotic diabetic may contribute to development of the neuropathy.

Unlike Osuntokun [16] we found a positive correlation between retinopathy and neuropathy particularly in those with a duration of diabetes exceeding 10 years. The same was true for nephropathy and neuropathy (*Table 3*). Since studies have shown a direct relationship between impairment of nerve conduction velocity and persistent hyperglycaemia [17] and improvement with good control of the diabetes [18] we feel that poor control in our diabetics, [19] due to ignorance and financial constraints, may play an important role in the development of neuropathy.

In diabetic neuropathy impairment of motor and sensory conduction velocity tends to parallel the degree of neurological deficit [20] and our findings were in accord with this observation (*Table 4*) [21, 22].

The detection of reduced nerve conduction velocity in diabetics without clinically detectable neuropathy ($p < 0.005 - 0.0001$ in comparison with controls) and the progressive reduction in conduction velocity in direct relation to the duration of diabetes (*Figure 1*) are in agreement with already established findings [21, 22].

In conclusion this study shows that neuropathy is common in Ethiopian diabetics probably due to a combination of adverse factors including a poor nutritional background, the common occurrence of associated diseases such as liver cirrhosis and poor control of the diabetes. Although the criteria we adopted for the diagnosis of diabetic neuropathy are not identical with those used in the other African studies referred to in this report, the similarity in the prevalence of neuropathy in general suggests a similarity in the contributory socioeconomic and environmental factors.

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CASE REPORT

MULTIPLE SCLEROSIS – A CASE REPORT ON AN ETHIOPIAN

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ABSTRACT. *The clinical presentation and diagnosis of multiple sclerosis in a 25-year-old Ethiopian female who died is described. The rarity of the neurological disorder in Ethiopia and the rest of Africa is briefly discussed.*

The demyelinating disease, multiple sclerosis is a very rare neurological disorder among Blacks. Acheson (1) has reported the low incidence of the disease in black Americans. Africa has been found a low-risk area for multiple sclerosis (2). In South Africa, where extensive epidemiological studies have been carried out, the disease has been described in only a very few cases of black Africans and Africans with mixed blood (3,4). In East Africa, 2 cases have been reported from Kenya (5), and 10 from Uganda (6).

The case reported is of a young Ethiopian female who presented with convincing signs and symptoms of multiple sclerosis, as also confirmed by laboratory and electrophysiological investigations.

CASE REPORT

A 25-year-old Ethiopian female left Addis Ababa for the United States in 1978 to pursue her studies in nursing. While in the United States she gradually developed reduction in visual acuity of the left eye, with intermittent double vision, as well as imbalance of gait with incoordinations. When evaluated in August 1978 she was found to be well developed, in no acute distress, but obviously anxious and depressed. Her blood pressure was 110/70, and pulse 80/min, regular.

Neurological examination disclosed full visual fields and sharp optic discs. The left optic disc was pale. Visual acuity was 20/30 in the right eye, and with the left eye she was able to count fingers at a distance of 0.6m (2 feet). There was a left esotropia and a Marcus-Gunn pupil. Extraocular movements revealed diminished abduction of the right eye. There was prominent nystagmus in the extremes of gaze. There were internuclear ophthalmoplegias, more pronounced on the left than on the right. A right ptosis was present. The remainder of the cranial nerves were intact.

Muscle strength was 5/5 in the upper extremities, and tone was normal. There was mild weakness in the dorsiflexors, evertors and invertors, and large toe extensors of the right foot, but strength was otherwise full in the lower extremities. The tone in the legs was markedly increased. Deep tendon reflexes were 3+ and symmetrical throughout. The plantars were upgoing. Jaw jerk was 2+, snout and Hoffmann reflexes were positive. Sensation

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was intact to primary and cortical modalities. Cerebellar examination showed marked dysmetria and dyssynergia with diadochokinesia bilaterally in the upper and lower extremities. Head and trunk were titubant, gait was broad-based and ataxic, and the patient was barely able to walk with the use of a quad cane (a support with four small legs, for balance).

The rest of the general physical examination was unremarkable except for a grade 2/4 systolic murmur at the upper left sternal border, and moderate tenderness to palpation in both lower quadrants without rebound tenderness.

Laboratory data during admissions in the United States. Haemogram and biochemistry investigations were normal. Venereal Disease Research Laboratory tests were non-reactive. Cerebrospinal fluid examination showed no cells, a protein of 29mg%, and a gammaglobulin fraction of 15.9%. Oligoclonal banding was strongly positive. The hot-tub test was also strongly positive. In the electrophysiological test, the visual pattern-evoked potential showed no response in the left eye and was normal in the right eye in August 1978. A follow-up examination in September 1979 showed a prolonged latency in the right eye.

The course of the patient's disease was that of a progressive deterioration, although she had occasional short-lived improvements. While she was admitted to the Harborview Medical Center in Seattle, Washington, USA, in December 1979, she was treated with 60mg prednisone daily for 10 days, with no apparent change in her symptoms. However, she showed some subjective improvement with physical therapy, which she continued to receive until her return to Addis Ababa, Ethiopia, in 1982.

In Ethiopia her condition further deteriorated. She was totally dependent in feeding because of ataxia of her upper extremities. She became bedridden, incontinent of urine and extremely depressed. She died in September 1983. Postmortem examination was not performed.

She was the third child and only girl in a family of seven children, born to Ethiopian parents. The father died in his late forties in a motor vehicle accident; the mother died from a cardiac disease. There was no family history of multiple sclerosis nor of any other neurological disease.

DISCUSSION

In the epidemiological studies of multiple sclerosis, such factors as latitude, climatic conditions and different types of infection, especially viral and genetic predispositions, have been directly or indirectly implicated. All these factors considered, the disease has been found to be extremely rare among Blacks.

Many of the detailed studies on the prevalence of the disease in Africa have been undertaken in South Africa. Bird and Satoyoshi (7) in their 1975 review of the subject observed that not a single proven case of multiple sclerosis had been diagnosed in 16,000.000 South African Blacks. To emphasise their observation, they appropriately stated, "If multiple sclerosis existed in the African community, one would expect to see some at least of the terminal bedridden cases which form a tragic part of the multiple sclerosis scene, even if early, difficult diagnoses were missed."

Indeed, after 17 years of practice in East Africa, Foster and Harries (5) diagnosed multiple sclerosis in only 2 endogenous Kenyans. Over a 10-year period, Kanyerezi *et al.* (6) reported 10 cases in Ugandans, of whom only 5 were studied prospectively by the authors.

In her review of the clinical details of 253 consecutive Ethiopian medical patients hospitalised primarily for neurological diseases, Lester (7) describes 2 male patients who were suspected on clinical grounds of

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having multiple sclerosis. The diagnosis in these patients was not confirmed by laboratory or electrophysiological means.

The patient reported here had her diagnosis established in the United States while she was a student. The diagnosis was based on the typical clinical presentation and progression of the disease, in addition to convincingly positive laboratory and electrophysiological investigations.

The patient had lived in the United States not more than a year when she developed the disease. It is a well-documented fact that persons who migrate from low-risk to high-risk areas above the age of 16 years maintain their low risk of developing the disease (9,10). It is therefore very unlikely that residence in the United States had anything to do with the patient's developing the disease.

Studies have also shown that genetic factors such as human lymph antigen (HLA) types are important in multiple sclerosis. Although the HLA type of this patient was not determined, a careful study of the family established that she was born from Ethiopian parents, without any evidence of mixed Caucasian blood.

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PARKINSON'S DISEASE IN ETHIOPIA:
A PROSPECTIVE STUDY OF 70 PATIENTS
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PARKINSON'S DISEASE IN ETHIOPIA: A PROSPECTIVE STUDY OF 70 PATIENTS

R.T. HAIMANOT

SUMMARY

The clinical manifestations, possible aetiological factors and investigatory findings in seventy Ethiopians with Parkinson's disease studied prospectively in Addis Ababa, Ethiopia, between 1980 and 1984 are presented. The mean age of the patients was 59.5 ± 8.1 years and 54.6 ± 8.4 years at the onset of their disease. These mean ages were lower than those from Europe and America. There was a male preponderance of 7:3. Most patients consulted a physician fairly late in the course of their disease when a significant disability had already occured. The inadequacy of management of the patients is discussed. As in the rest of Africa and the Black races, the disease was found to be rare in Ethiopia.

INTRODUCTION

Data from epidemiological and hospital-based surveys have shown that Parkinson's disease is very rare in the African (1,2,3) and the Black race in general (4,5,6).

Population-based studies are not yet available on neurological disorders in Ethiopia. One such study is, however, in preparation. As in the rest of Africa. Parkinson's disease is an extremely rare neurological disorder in Ethiopia, as indicated by analysis of hospital admissions (7,8).

In Addis Ababa, Ethiopia, the Department of Medicine of the Tikur Anbessa (Black Lion) Teaching Hospital has a neurology unit to which most of the neurological patients from the city and provincial medical centres are referred.

Occasionally neurological cases, particularly epileptics, are sent to psychiatric clinics. However, over the last four years, as a result of the strengthening of the neurology service, the majority of neurological diseases, including parkinsonism, have passed through the neurology unit of the teaching hospital.

This prospective study was undertaken to look in detail at the prevalence of Parkinson's disease, and examine the aetiological factors as well as the clinical presentations of the neurological disorder in Ethiopia.

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MATERIALS AND METHODS

Between 1980 and 1984, 70 Ethiopians with Parkinson's disease who were seen at the Tikur Anbessa teaching hospital and the private clinic of the author were studied prospectively.

The following data were obtained on each patient: age, sex, date of onset and initial symptoms of parkinsonism. Enquiries were also made about possible previous head injury, cerebral infection or syphilis, carbon monoxide poisoning and the use of neuroleptic drugs.

All patients were clinically and neurologically evaluated by the author. The following investigations were carried out: haematological indices, fasting blood sugar, blood urea nitrogen, liver function tests (transaminases and alkaline phosphatase) and VDRL. Sixty-three patients had skull X-rays. Diagnosis of Parkinson's disease was confidently made when a patient had the classical triad of bradykinesia, rigidity and tremor. In those patients in whom any of these major signs was absent, the presence of facial masking, abnormal postural reflexes, the typical gait, speech disturbance and autonomic dysfunctions were considered satisfactory additional evidence for the disease.

Two patients who, without the overall clinical picture of the syndrome, developed reversible transient parkinsonism following neuroleptic therapy, and another after carbon monoxide poisoning, were excluded from the study.

RESULTS

Patients with Parkinson's disease constituted less than one per cent of neurological hospital admissions for three years (Table 1), and 1.2% of the patients seen at the neurology clinics over the four-year period of the study (Table 2).

TABLE 1

Neurological admission to the medical wards of Tikur Anbessa Teaching Hospital, Addis Ababa

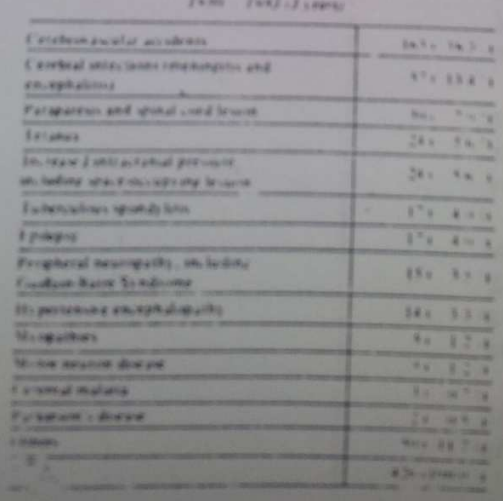


TABLE 2

Out-patient visits to the neurology referral clinics in Addis Ababa (December 1980 to August 1984)

	Number of patietns	% age
Parkinsonism	70	1.2
Neuropathy	381	6.6
Epilepsy	641	11.1
Lower back pain	901	15.6
Others	3,783	65.5
Total	5,775	100.0

A total of 70 patients with Parkinson's disease was identified; of these 47 patients (67%) attended our neurology referral clinics over the four years' study period although irregularly. Twenty-three patients (33%) were lost to follow-up. Five patients died during the study period, four from pneumonia and one from a histologically proven hepatoma.

The age and sex distribution of the patients is shown in Table 3. There was an obvious male preponderance of 7:3, and the peak frequency was in the age group 61 – 70 years, followed by 51 – 60 years, with a mean age of 59.5 ± 8.1.

TABLE 3

Distribution of age and sex in 70 Ethiopians with Parkinsonism

Age (years)	Male	Female	Total	% age
31 – 40	3	1	4	5.7
41 – 50	10	5	15	21.4
51 – 60	12	7	19	27.1
61 – 70	19	6	25	35.7
71 and over	5	2	7	10.0
Total	49	21	70	
Percentage	70	30	100	

The clinical presentation of the patients conformed to the classical description. The symptoms at the time of presentation are shown in Table 4. The mean age at onset was 54.6 ± 8.4. Tremor was the commonest initial symptom (90%), followed by bradykinesia (86%) and stiffness (71%).

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TABLE 4

Parkinsonism in 70 patients: Initial symptoms

Symptoms	*Number of patients*	*%*
Tremor	63	90.0
Gait disturbance	28	40.0
Slowness	60	85.7
Stiffness	50	71.4
Speech disturbance	30	42.9
Drooling	25	24.5
Myalgia/cramps	20	28.6
General fatigue/muscle weakness	49	50.0
Facial masking	53	75.7
Dysphagia	3	4.3
Irritability, depression, other psychiatric disturbances	7	10.0

Common associated conditions were hypertension (22%) and diabetes mellitus (10%). A history of head injury was obtained in 21 patients (30%) (Table 5). None of these patients had been engaged in the boxing profession.

Positive serum serology for syphilis was found in 6 of the 70 patients. One of these patients had also evidence of neurosyphilis (Argyll Robertson pupils and a positive VDRL test in the cerebrospinal fluid).

Only one patient gave a positive family history of Parkinson's disease: his father died at the age of 68 years of a similar illness, without receiving any treatment.

We were able to get a history suggestive of encephalitis in only one patient. Two other patients reported remote febrile illnesses which they thought were due to typhoid fever, but this could not be substantiated. None of the patients had a history of kernicterus.

The haematological indices were within normal limits in all except in 10 patients, in whom low haemoglobin levels were found. The liver function

TABLE 5

Associated conditions

Conditions	*Number of patients*	*%*
Hypertension	16	22.9
Diabetes mellitus	7	10.0
Cardiac lesion	3	4.3
Head trauma in remote past	21	30.0

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TABLE 6

Degree of disability in 70 patients with parkinsonism at the initial examination

Degree of disability	*Number of patients*	*%*
STAGE 1: Unilateral involvement only minimal, or no functional impairment	16	22.9
STAGE 2: Bilateral or midline involvement without impairment of balance	21	30.0
STAGE 3: Impairment of righting reflex, unsteady on turns; restricted in activity	14	20.0
STAGE 4: Severe disability; able to stand unassisted and walk but markedly incapacitated	12	17.1
STAGE 5: Confined to bed or wheel-chair unless aided	7	10.0

tests were also generally normal, except in one patient where the alkaline phosphatase was repeatedly elevated, this occurred in the patient who later died of hepatoma.

Of the 65 skull X–rays performed, only one was abnormal; this showed a remote depressed left frontal skull fracture.

Generally, most patients sought medical attention three to five years after the onset of their disease. The symptoms came on unilaterally in 70%, but later came to involve the other side. In the patient with depressed skull fracture, there was a fixed right hemiparkinsonism associated with hemiparesis.

In Table 5 we adopted the clinical staging for the degree of disability proposed by Hoehn and Yahr (9).

The patients were classified on the basis of their clinical findings at the time of presentation. The majority of patients (21%) came with bilateral or midline involvement without impairment of balance, but 19% were already severely disabled at presentation.

Treatment of our patients was rather difficult. Antiparkinsonian drugs were not readily nor continuously available, and when available, levodopa or the preparations with decarboxylase inhibitors were prohibitively expensive. Benzhexol hydrochloride (Artane) and levodopa (L-DOPA) were the commonest drugs used. Decarboxylase inhibitors, Sinemet (L-DOPA combin-

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ed with Carbidopa and Madopar (L-DOPA with benserazide) came into use in a few of our patients, only during the last ten months. In some patients amantadine (Symmetrel) was used with Artane. One patient underwent bilateral stereotactic operation abroad, with disappointing results.

DISCUSSION

Parkinson's disease is among the most prevalent neurological diseases. Prevalence rates as high as 112 to 187 per 100,000 population have been reported in the white races from various epidemiological studies (5,10,11). However, the disorder has been found to be much less prevalent in the Black races (5,6,12). Similar population-based studies are not readily available from Africa. Nevertheless, existing reports (1,3,8) also confirm the rarity of the disorder in Black Africans except in Senegal, where Collomb, Dumas and Girard (13), while discussing neurological disorders of that country, made the passing remark that Parkinson's disease was common.

It is now abundantly clear that there are racial differences in the predisposition to Parkinson's disease.

The Black races prove to be relatively protected from the disease. A significantly reduced frequency of the condition among Blacks was observed by Kessler in both his hospital-based and community-based surveys (5,6).

Rosanti, Granieri, Pinna, Aiello, Tola, Bastiani, Pirisi and Devoto (14), found a lower prevalence of the disease among the people of Sardinia, compared to North Europeans. They suggested that the low risk may be due to a possible negroid admixture among the Sardinians. They noted that Sardinians have high frequencies of HLA-Aw30 and HLA-B17 antigens, of which the latter is highly specific for the Black population (15).

There have been speculations whether the increase of body melanin pigmentation in Blacks is associated with the reduced risk (6), but this awaits further elucidation.

Although our study is not a population-based one, the material obtained comes from the single major neurological referral centre in Ethiopia, thus making it quite informative on the relative frequency of the disease in comparison to other neurological disorders. Tables 1 and 2 show how rare the disorder is in Ethiopia.

We have not gone into the detailed identification of aetiological factors because of the limitation of investigatory facilities and the difficulties of obtaining permission for postmortem examination. It is, therefore, very possible that we have grouped together some parkinsonism due to vascular causes with idiopathic Parkinson's disease (paralysis agitans). Postencephalitic parkinsonism, regarded as a sequela of Von Economo's type A encephalitis of the 1920s, has not been encountered in Ethiopia. In fact, findings do not suggest that encephalitis is in any major way responsible in the causation of the syndrome in this country. We had only one patient who gave a history suggestive of an encephalitis in the remote past.

It is interesting that 30% of the patients studied admitted to a remote

head trauma. This is much higher than the figure obtained by Osuntokun and Bademosi in Nigeria (16). In our patients, the injuries were associated with loss of consciousness in only five patients, one of whom was the hemiparkinsonian with depressed skull fracture. Our patients, eager to find an explanation for their disabling illness, try to relate it to even minor head traumas, particularly when a question suggesting this is put to them. We, therefore, do not think that head injury, though important in a few, can be incriminated as a causative or contributory factor in all the 30% of patients that gave such a history.

Syphilis, as a cause of Parkinson's disease was consistently considered in the patient with the other neurosyphilitic signs, although it is difficult to prove. It is interesting to observe that, like Vukotich and Giel (17), we have also been impressed by the rarity of neurosyphilis among Ethiopian patients. It is thus not an important aetiological factor in Parkinson's disease.

Compared to patients in previous reports, our patients on the whole developed the disease at a much younger age. The mean age at onset of the Parkinsonian symptoms in our patients was lower than those reported in the literature for Europe and North America (5,6,11) but similar to the findings in Sardinia (14). For cultural and social reasons, males in Africa tend to visit medical services more often than females. Even allowing for this situation, the male preponderance among our patients, a ratio of 7:3, is significantly higher than in other studies (5,6,11), but in accordance with findings in Nigeria (16).

As in most other studies, tremor was the most frequent initial symptom, and the most disturbing to our patients. Although rigidity and hypokinesia are more disabling symptoms, our patients gave undeserved concern to their tremors. This preoccupation was probably due to the social stigma associated with this obvious and easily observable symptom.

Neurological disorders, including epilepsy, are associated with strong social stigma in Ethiopia. Parkinson's disease is considered by many as a sort of a curse, although it does not entail being cast out by the community, as is commonly the case with epilepsy or leprosy. The poor parkinsonian sufferers often end up as beggars, whose tremor, fixed stooped posture and poverty of movement arouse spontaneous sympathy from the public.

The majority of patients had visited faith healers and holy waters before they came to us. This partially explains why, on the average, most of the patients came two to five years after the onset of their disease, when it was in a far more advanced and disabling stage (Table 5).

It is perhaps difficult to comment in detail on the response of long-term use of specific anti-parkinsonian drugs in our patients, as there was hardly any continuity in their administration. Nevertheless, on the whole, we can confidently observe that the majorty of patients responded favourably to the drug therapy. The response was often gratifying to both patient and physician. Artane, the most commonly available anticholinergic, was well tolerated except for occasional but transient hallucinatory experiences,

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particularly in the elderly. Levodopa was found to be best for rigidity and bradykinesia, but less so for tremors. We did not observe any on-and-off phenomena or dyskinesia with its use as a result of its intermittent administration in most patients.

The one experience of sterotactic operation, performed on a bank executive with a predominantly unilateral Parkinson's disease, was rather disappointing. He ended up with pseudobulbar palsy after his second operation. We felt that he should have remained on drug therapy after his successful first operation, which had achieved an excellent control of his severe right-sided tremors.

The irregular attendance at our follow-up clinics makes it difficult to predict the mortality rate. Some of our patients live in very remote and inaccessible areas. With these factors taken into consideration, the five deaths reported to us may be an underestimate; the figure may be much higher. With better and more regular drug treatment we might not only have improved the quality of life but also reduced the mortality, as documented in several studies (18, 19).

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SKIN DISEASES IN ADDIS ABABA
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SKIN DISEASES IN ADDIS ABABA

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SUMMARY

A descriptive, longitudinal and prospective study of 2000 consecutive new patients (between August 1980 and May 1981) seen in several dermatological clinics in Addis Ababa, Ethiopia is presented.

Besides the common diseases of temperate climates a number of tropical dermatoses are encountered. 162 different skin disorders were observed. Infectious diseases were the most frequent group of diseases accounting 38.5%.

Hyperpigmentation of the face, acne vulgaris, pyoderma, dermatophyte infections and scabies were the most frequently observed single diseases in our study. Out of every 5 patients one had a disease classified under the eczema group. High detection of leprosy was another important finding. Similar studies in Addis Ababa, Shoa and in other provinces would be useful in determining the incidence of skin diseases in the nation.

INTRODUCTION

The incidence of skin diseases in tropical countries has been discussed by a number of writers from Nigeria (1, 2), South Africa (3, 4), Senegal (5), Kenya (5, 6), and Ethiopia. Single, spot surveys are of limited value but may suggest lines for further investigation. Long term studies in which the variation in disease incidence can be considered against a changing environmental background are much more useful.

The objectives of the present study were:--

1. to determine the relative frequency of dermatologic diseases in 2000 consecutive new patients seen in different clinics in Addis Ababa.
2. to promote similar studies in Addis to deleneate the real incidence of dermatologic diseases in this city, and
3. to promote similar studies in other provinces of Ethiopia.

RESULTS

Table 1 is an analysis of the approximate age of the patients. The age fall between 15 and 34 years in more than 50%. Sex distribution was the same in Black Lion and VD centre. The difference between males and females shown in ALERT is due to the fact that most of the time the authors were

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TABLE 1

Age groups

Age groups	*No. of patients*	*%*
Less than 5 years	158	7.9
5 – 14	265	13.25
15 – 24	604	30.2
25 – 34	468	23.4
35 – 44	276	13.8
45 – 54	132	6.6
55 – 64	63	3.15
65 years and over	34	1.7
Total	2000	100

TABLE 2

Sex

Clinic	*Male*	*%*	*Female*	*%*
Black Lion	224	11.2	224	11.2
ALERT	541	27.05	218	10.9
VD Centre	387	19.35	406	20.3
Total	1152	57.6	848	42.4

TABLE 3

Patients and skin diseases diagnosed in the different clinics (2231 skin disorders in 2000)

Clinics	*No. of patients*	*%*	*Skin disorders*
Black Lion	448	22.4	499
ALERT	759	37.95	863
VD Centre	793	39.65	869

attached to the male section of the diagnostic clinic.

The difference between total number of patients and skin disorders is due to the fact that some patients had more than one skin disorder. A hindrance to the correlation of studies in comparative dermatology is the absence of a uniform system of classification and nomenclature. Many authors prefer to list all the dermatosis in numerical order of frequency.

The main categories listed covers a group of diseases according to our objectives and does not represent a classification of the diseases of the skin. Of the 162 different skin disorders observed 32 were the most frequent diseases (Table 5).

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TABLE 4

Skin diseases by groups

Group of diseases	*No. of patients*	*%*
Infectious diseases	770	38.5
Immunological disorders	568	28.4
Disturbances of pigmentation	279	13.95
Miscellaneous	241	12.95
Disorders of epidermal appendages	224	11.2
Metabolic, congenital and hereditary disorders	85	4.25
Tumours of the skin	64	3.2

TABLE 5

Most frequent diseases

Disease	*No. of patients*	*%*
1. Hyperpigmentation of face	188	9.4
2. Acne vulgaris	108	5.4
3. Pyoderma	104	5.2
4. Dermatophyte infections	98	4.9
5. Scabies	92	4.6
6. Pityriasis versicolor	86	4.3
7. Contact eczema	82	4.1
8. Neurodermatitis	79	3.95
9. Acneiform eruption (iatrogenic)	75	3.75
10. Pityriasis alba	72	3.6
11. Vitiligo	65	3.25
12. Papular urticaria-Strophulus	63	3.15
13. Seborrhoeic eczema	57	2.85
14. Leprosy	56	2.8
15. Lichen planus	51	2.55
16. Psoriasis	45	2.25
17. Unclassified eczema	44	2.2
18. Atopic eczema	39	1.95
19. Pruritus	39	1.95
20. Pediculosis	32	1.6
21. Onchocerciasis	30	1.5
22. Warts	29	1.45
23. Porphyria cutanea tarda	28	1.4
24. Photodermatitis	27	1.35
25. Fixed drug eruption	27	1.35
26. Syphilis	26	1.3
27. Elephantiasis	25	1.25
28. Naevus	23	1.15
29. Cheilitis & Cheilosis	20	1.0
30. Urticaria	20	1.0
31. Cutaneous leishmaniasis	18	0.9
32. Keloids	17	0.85

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Usually an urban population is more self conscious about such problems as hyperpigmentation of the face and acne vulgaris, explaining why these were the two most frequently diagnosed diseases.

DISCUSSION

Hyperpigmentation of the face was the disease found more frequently by the authors (9.4%). In Ethiopia, darkening of the face and hands is a common clinical feature of liver disease which in-turn accounts for about 12% of hospital admissions (9, 10). Tsega, et al (11), in a total of 25 patients with hyperpigmentation of the face and hands without blisters, that some of the clinical, biochemical and histological findings in the hyperpigmented group merge into those with PGT, the only difference being the absence of blisters in the former. Warndorff (12) reported several times on the evil effects of topical applications of preparation containing photosensitizing substances, such as chlorinated hydrocarbons, found in mineral oil and vaseline; promethazin; diphenhydramine; buclosamide; salicylanilides and hexachlorophene. The widely known clinical appearance of deficiency diseases such as kwashiorkor, pellagra, and phrynoderma may have contributed to the desire for a shiny skin. Daily application of oily substances, corticoid creams and so forth explains the growing number of patients with acneiform eruptions of the face and other complications (13).

The reason for such a high figure of bacterial infections is a subject for sympation but it is evidence that lack of hygiene and little access to antiseptics plays an important role. Health education and sufficient water supplies would help to lessen the infections more than any other measure on the other hand.

There is no satisfactory explanation for the preponderance of dermatophyte infections. The pattern of superficial dermatophyte infections differs from other countries.

Pityriasis versicolor is not uncommon. Scabies is a major public health problem and it is widespread in all age groups in Ethiopia. If neurodermatitis, contact, atopic, stasis, nummular, pyogenic, seborrhoeic and unclassified eczema are taken together, the incidence will be greater than 20%.

Pityriasis alba of the face shows up more distinctly in pigmented individuals for children are more affected than adults. This condition was very common (3.6%). Schaller (7) found a similar incidence, 3.1%. Vitiligo was quite common (3.25%). Prurigo-like rashes and papular urticaria were found frequently in infants. Leprosy was found in 56, patients (2.8%). Most of them Borderline tuberculoid and borderline expromatous.

Lichen planus is one of the frequent skin diseases in tropical countries and it is confirmed for Addis as the incidence is 2.55%. This agrees with other observations of (2, 6, 7). The eruption was usually widespread but few cases had buccal involvement. The incidence of 2.25% of all dermatosis indicates that psoriasis is one of the more frequent diseases. In relation with lichen planus and psoriasis, Schaller (7) found 1.10 and .74%.

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Unclassified eczema 2.2%, atopic eczema 1.95%, pruritus of unknown origin 1.95% were commonly seen but pediculosis, usually as a secondary was diagnosed in 1.6%. We found a high incidence of onchocerciasis, 30 patients, (1.5%). Warts were the most frequent viral infection.

Photedermatitis, 1.35%, fixed drug eruption; 1.35%, syphilis: 1.3% were shown to occur with the respective prevalence rates. As regards elephantiasis Schaller found 8.68%. I found only 1.25%. Naevi of ectodermal and mesodermal origin are regularly seen. Cutaneous leishmaniasis was found in 18 patients (0.9%) and Keloids 0.85%.

CONCLUSIONS

1. More than 50% of patients were in the age group (15–24) and (25–34).
2. There was no statistical difference between the sexes.
3. Infectious diseases were the most frequent group of diseases accounting 38.5%.
4. Hyperpigmentation of face was the most frequently observed single disease in our study.
5. Next to hyperpigmentation of face, acne vulgaris, pyoderma, dermatophyte infections and scabies were frequently observed.
6. Out of every 5 patients one had a disease classified under the eczema group.
7. High detection rate of leprosy is another important finding (56 new cases in only 7 months).

MATERIALS AND METHODS

This paper reports a descriptive, longitudinal and prospective study of 2000 consecutive new patients with dermatological diseases at the VD and skin clinic at ALERT, and the Black Lion Hospital.

A certain uniformity in the evaluation of the material is assured since all clinical examinations were done by the same person. Most of the patients were from Addis Ababa.

The percentages given are based on the number of patients and not on the number of diseases because some of the patients had more than one disease, and all diagnosed were recorded.

All new cases to the dermatologist were accepted. Some patients were included in the study although they had been seen previously in another clinic for some other reason. Venereal diseases were treated in separate clinics and only cases which had not been recognized and referred to skin clinics have been included. This makes comparison of these groups difficult. However, an attempt is made to group the diseases in order of frequency. The following data were recorded for each patient: sex, age, possible diagnosis and centre in which he had been seen. The more frequent dermatological diseases found in this study are presented.

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CASE REPORT

SHIGELLAEMIA IN ADULTS: CASE REPORTS AND LITERATURE REVIEW

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ABSTRACT. *Two cases of Shigella septicaemia are described. The first was a 59-year-old diabetic man with chronic renal failure who was admitted for dysentery and shock. Blood culture grew* Shigella dysenteriae *and* Enterobacter agglomerans, *thus indicating polymicrobial septicaemia. The second was a 39-year-old male patient admitted for abdominal cramps, diarrhoea, fever and chills.* Shigella flexneri *was grown from blood culture. The stool examinations in both patients showed many polymorphonuclear leucocytes and red blood corpuscles. Shigellaemia, particularly in adults, is apparently infrequent, with only a very few cases reported. Polymicrobial septicaemia involving Shigella is also not common. These conditions are discussed, with a review of the literature.*

Shigellosis has generally been accepted as an intra-luminal infection, mostly limited to the mucosa and lumen of the large bowel. Invasion of the bloodstream has also been recognised, but rarely encountered or reported (1-6). No Shigella has been incriminated in a 10-year study of bacteraemia in Sweden (7). Cronberg *et al.* (8), also from Sweden, did not isolate a single Shigella strain out of 564 blood isolates. From two studies in Ethiopia, at different times, no Shigella has been isolated out of 476 and 408 blood culture isolates, respectively (9,10). Similar findings have also been reported from the United States (11-13).

Polymicrobial bacteraemia or septicaemia, defined as a septicaemic episode due to at least 2 different organisms isolated from the same blood sample (14), is also relatively uncommon, but has been reported as far back as 1899 by Brill and Libman, as cited by Mackowiak *et al.* (15). Reported incidence varies between 6% and 13% (14-17). From the records of Tikur Anbessa (Black Lion) Hospital Microbiology Laboratory, Addis Ababa, of a three-year period, polymicrobial septicaemia accounted for only 2% of patients with positive blood cultures (unpublished data, M.G.).

There has been no Shigella septicaemia or polymicrobial sepsis in adults previously reported from Ethiopia. To our knowledge, this is the first report of both shigellaemia and polymicrobial septicaemia due to *Shigella dysenteriae* and *Enterobacter agglomerans*.

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CASE REPORTS

Case 1. A 59-year-old non-insulin-dependent diabetic male patient with chronic renal failure was admitted to the Medical Intensive Care Unit of Tikur Anbessa Hospital in May 1984. He had been on a regular oral hypoglycaemic drug for the previous 20 years. He was in apparently good health until a week before admission, when he developed a frequent bloody, mucoid diarrhoea with abdominal cramps and tenesmus, without vomiting. Two days before admission, he was noted to have an altered state of consciousness, and a day later went into coma.

The physical examination showed the patient to be in deep coma with Kussmaul's respiration. The blood pressure was unrecordable, carotid pulse was 96/min., respiratory rate 38/min., and the temperature 36°C (axillary). His tongue was dry and coated; he had a marked loss of skin turgor, and slightly sunken eye-balls. The jugular venous pressure was flat, with normal cardiac sounds and no murmur or gallop. He had diffuse rhonchi in both lung fields, and right basal crepitations. His abdomen was flat and soft with no mass or organomegaly. Bowel sounds were active. Rectal examination showed a loose sphincter tone and a bloody, mucoid stool on the examining finger. Laboratory results revealed a haemoglobin of 14.7g%, white blood cell count (WBC) of 39,000/mm^3, a platelet count of 138,000/mm^3, erythrocyte sedimentation rate (ESR) of 15mm in the first hour, a random blood sugar of 342mg%, and a blood urea nitrogen of 151.2mg%, with creatinine of 11.2mg%. Blood film for haemoparasites was negative.

Microscopic examination of stool showed many polymorphonuclear (PMN) leucoytes and red blood cells (RBC). Urinalysis gave Multistix colour gradation of ++ albumin, and a trace of sugar with no ketone. The chest X-ray showed patchy, fluffy, nodular right hilar and basal infiltration.

On the basis of the above findings, a diagnosis of diabetes mellitus, chronic renal failure and Gram-negative septic shock was made. Appropriate volume of hydration and electrolyte correction was attempted, and treatment with penicillin sodium and gentamicin was initiated, after collection of blood for culture. Despite these measures, the patient remained in coma and finally died of irreversible shock 20 hours after admission. Later, *Shigella dysenteriae* Type 1 and *Enterobacter agglomerans* were isolated. The Shigella isolate was resistant to ampicillin, carbenicillin, chloramphenicol, streptomycin, sulphadiazine and tetracycline, but sensitive to cephalothin, gentamicin, kanamycin, polymyxin, trimethoprim-sulphamethoxazole and cefotaxime. The Enterobacter was resistant to ampicillin, carbenicillin, cephalothin, chloramphenicol, gentamicin, kanamycin, streptomycin, sulphadiazine and tetracycline. It was sensitive only to polymyxin B, trimethoprim-sulphamethoxazole and carbenicillin.

Case 2. A 39-year-old male member of the university teaching staff was admitted to Tikur Anbessa Hospital for abdominal cramps and diarrhoea of 24 hours' duration, associated with fever, chills and headache of 5 hours' duration. The diarrhoea was watery, mucoid and frequent, with tenesmus and vomiting. He had no other symptoms pertaining to any specific organ system.

The patient had returned from Zway, a town 160km south of Addis Ababa, where he was conducting research among prisoners, many of them febrile. Since the place was a known malarious area, he was taking chloroquine prophylaxis.

On physical examination, he was sick-looking, but in no apparent distress. The blood pressure was 110/70mmHg, pulse 120/min., and the temperature was 39.6°C (axillary). He was not pale or icteric. The tongue was slightly dry. The chest was clear. Except for sinus tachycardia, the

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of better empirical therapy. It should be regular practice to take blood cultures in all cases of suspected or stool culture-confirmed bacillary dysentery associated with fever.

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Myopathies in Ethiopia

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Resume

Entre 1980 et 19086, soixante treize patients ayant une myopathie ont été hospitalisés dans l'unité de neurologie du département de médicine de l'hôpital Tikur Anbessa â Addis Abeba et ont fait l'objet d'une étude médicale prospective.

Ceas myopathies se répartissaient ainsi: 19 maladies le Duchenne, 1 maladie de Becker, 23 myopathies de ceintures, 5 atteintes facio-scapulo-humérales, 1 atteinte distale et 3 dystrophies myotoniques. Il y avait en outre 4 cas de myasthénie, 12 polymyosites, 5 dermatomyosites, et dans 1 cas il a été suspecté une myopathie mitochondriale. Les myopathies congénitales n'étaient souvent pas cliniquement reconnues, il était difficile de recueillir des antécédents familiaux précis et les patients étaient généralement vus â la phase terminale de leur affection, exceptés ceux qui présentaient une myopathie inflammatoire. Généralement, le diagnostic clinique a été confirmé par l'électromyographie, la biopsie musculaire, le dosage de la créatine phosphokinase sérique, ce qui a par ailleurs facilité la classification. Les problémes posés par l'élaboration d'un diagnostic précoce et par les soins de réhabilitation dáns le cas de ces patients éthiopiens est discuté dans cet article.

Summary

Between 1980 and 1986, seventy-three patients with myopathies referred to the Neurology Unit of the Department of Medicine of the Tikur Anbessa Hospital in Addis Ababa were studied prospectively. The pattern in the distribution of the muscular dystrophies was 19 Duchenne; one Becker; 23 limb-girdle; 5 facioscapulohumeral; one distal and there were 3 cases of myotonia distrophica. There were also 4 cases of myasthenia gravis, 12 of polymyositis, 5 of dermatomyositis, and one case of suspected mitochondria myopathy. Congenital myopathies were often missed clinically. It was difficult to get a reliable family history, and patients generally presented late in the course of their disease, except for those with inflammatory myopathies. Generally a thorough clinical assessment reinforced by electromyography, muscle biopsy and serum creatinine phosphokinase determination was found to be adequate in the diagnosis and classification of most cases of the myopathies. The problem of early diagnosis and deficiency in the comprehensive rehabilitatory and supportive care of Ethiopian patients with myopathies is commented upon.

Introduction

There are only scanty reports on the patterns and incidences of myopathies in Africa. Studies from some African countries (1-5) in the 1960s and 1970s have reported on the rarity of the disorder in the African. However, many of the neurologists working then in the African countries had rightly proposed caution in the problems of early detection of myopathies by parents and relatives (6), and also suggested that many cases might have been kept away from the attention of health workers (1). On the other hand pyomyositis has been found to be common in tropical Africa, particularly in Uganda (7) and Nigeria (8). This paper will present a five-and-a-half years' analysis of myopathies studied at a medical centre in Addis Ababa, Ethiopia.

Patients and Methods

Between 1980 and 1986, 298 patients from all over Ethiopia were referred to the Neurology Unit of the Department of Medicine at the Tikur Anbessa Teaching Hospital in Addis Ababa, with the diagnosis of myopathies. Among these patients those with non-specific rheumatic and myalgic pains, neuropathies, and motor neuron disease were excluded. Seventy three patients with myopathies were identified. These patients were examined and investigated according to a pre-set protocol.

A detailed history of the onset, progression of symptoms and family history of myopathy was obtained from each patient. All patients underwent general physical and neurological examinations on their initial presentation and on subsequent follow-up for periods of upto 5 years.

The following laboratory investigations were carried out: haematological indices, fasting blood sugar, blood urea nitrogen, liver function tests (transaminases and alkaline phosphatase) and serum creatinine phosphokinase (CPK). The majority of the patients had electromyographic examination which was also used to choos: the best

TABLE 2: INVESTIGATORY RESULTS IN 73 ETHIOPIAN PATIENTS WITH MYOPATHIES

	Creatinine phosphokinase		Electromyography		Muscle biopsy		
	% Normal	% Elevated	% Normal	% Myopathic	% Poor sample	% Normal	% Myopathy
Duchenne muscular dystrophy	10	90	——	100	20	——	80
Becker muscular dystrophy	——	100	——	100	——	——	100
Limb-girdle muscular dystrophy	39	61	22	78	22	26	52
Fascioscapulohumeral muscular dystrophy	40	60	20	80	20	40	40
Myotonia dystrophica	50	50	——	100	——	——	100
Late distal muscular dystrophy	100	——	——	100	——	——	——
Myasthenia gravis	——	——	——	100	——	——	——
Mitochondrial myopathy	——	100	100	——	——	100	——
Polymyositis	25	75	25	75	25	25	50
Dermatomyositis	30	70	20	80	40	20	40

One patient with Becker muscular dystrophy was diagnosed at the age of 18 years; the symptoms and signs were less severe and progressive than those of DMD. The high CPK and typical muscle biopsy were diagnostic.

The few cases of facioscapulohumeral muscular dystrophy were classical in their clinical presentation (Figure 3). Two of the cases were treated as Bell's palsy before their referral to us. The progression in this myopathy was very slow. Those with severe conditions demonstrated the typical lordotic posture.

Three patients with myotonia dystrophica were seen during our study period. Their age ranged between 35 and 42 years. Only one had a positive family history. Besides the typical myopathy and associated myotonia, all these patients showed frontal boldness (Figure 4) and testicular atrophy. One had cardiac involvement and some behavioural changes.

A 38 year-old woman recently presented to the Addis Ababa leprosy hospital with distal muscle weakness and atrophy in the upper and lower limbs, predominantly in the hands (Figure 5). The proximal muscles were quite normal and there were no fasciculations. The clinical picture was suggestive of symmetrical distal peripheral neuropathy, but her sensory examination was absolutely normal.

The distal weakness and atrophy had developed over a period of ten years. The serum CPK was normal, and so was the nerve biopsy, which showed no evidence of leprosy. However, the patient's muscle biopsy was obviously myopathic. An elder sister of the patient, who had similar early signs and symptoms, died from progression of her muscular weakness, which had involved the proximal parts. This case was diagnosed as late distal muscular dystrophy (Welander's distal muscular dystrophy).

A 12-year-old boy with muscle cramps and weakness following exercises, primarily running, was encountered during our study. He did not manifest any atrophy of muscles. Weakness in his proximal muscles was detected only after vigorous physical exercises. His serum CPK levels were elevated from 10 to 300 times the normal values at rest and after exercise respectively. The correct diagnosis of his myopathy has not yet been established, even after thorough and sophisticated investigations in the United States. A mhopathy associated with mitochondrial abormalities has been suspected. The condition of the patient is



Figure 2: Pseudohypertrophy of the calf muscles in a 5-year-old boy with Duchenne muscular dystrophy. Muscle biopsy demonstrates marked necrosis, hyalin fibres and excessive fibrosis (from Ref. 14)



Figure 3: Facioscapulohumeral muscular dystrophy. 21-year-old patient with typical distribution of muscle weakness in the face and shoulder girdle.

stable, as he has, in the meantime, learnt to live within his own exercise tolerance.

Myasthenia gravis was seen in four patients, three of whom were female. Two of the patients had the localized ocular form. The other two, one male and one female (Figure 6) who manifested generalized myasthenic weakness underwent thymectomy in Italy, and hyperplasia of the thymus was revealed. Subsequent to the surgery there was a good clinical response in both patients; and the pyridostigmine dosage was reduced and the prednisone which they were taking in fairly high doses, was discontinued. In both of these patients, the anti-striatal muscular and anti-achetecholine-receptor antibodies were positive, and the IgG was also elevated. One of the



Figure 4: Myotonia dystrophica: 50-year-old patient with elongated face and apathetic appearance, showing temporal and masseter wasting, mild ptosis and frontal baldness. His muscle biopsy shows variation in fibre size with atrophic and hypertrophic fibres and numerous internal nuclei, which also form a long chain on the longitudinal sections.

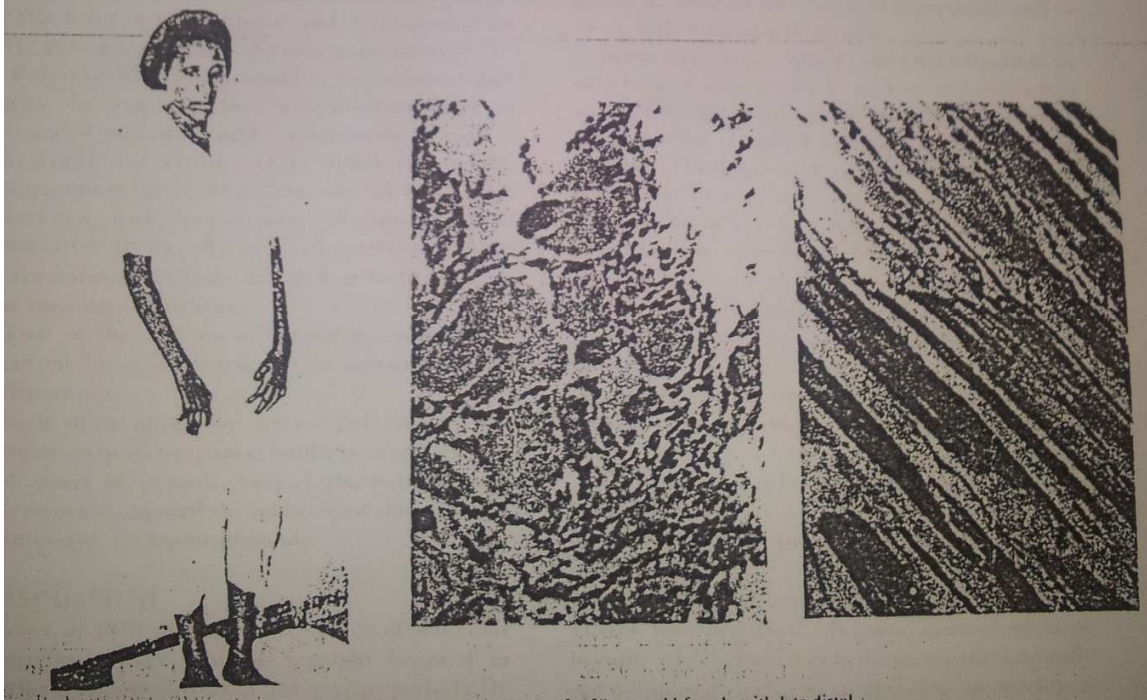


Figure 5: The atrophic hands of a 38-year-old female with late distal muscular dystrophy.



Figure 6. [illegible] Ataxic patient with opthalmoplegia.

two females had one successful pregnancy and delivery after her thyrectomy.

Pyomyositis as seen in Uganda and Nigeria (7, 8) is uncommon in Ethiopia. Only scattered cases have been encountered during our study period. However, autoimmune inflammatory myopathies in the form of polymyositis and dermatomyositis were detected in 12 and 5 cases respectively.

Polymyositis was commonly seen in young adult males. In some of these patients there was an associated preceding upper respiratory or gastro-intestinal infection. Our analysis of the inflammatory myopathies did not include those associated with an obvious diagnosis of the connective tissue diseases of systemic lupus erythematosis scleroderma, polyarthritis nodosa, and rheumatoid arthritis.

Two of the 5 cases of dermatomyositis which occurred in older females were associated with malignancies.

Eight of the idiopathic cases of polymyositis and dermatomyositis were successfully treated with very high doses of steriods; two of the patients with polymyositis required the addition of the immuno-suppressant, cyclophosphamide.

Discussion

Beleher in 1970 (9) saw only 3 cases of muscular dystrophy at the Gondar regional hospital in northern Ethiopia over a three-year period. He reported on 2 of the patients who were brothers with limb-girdle muscular dystrophy. Some scattered cases of myopathies have also been reported from other African countries (10-12). In their large analysis of 5327 children admitted to two Kenyan hospitals Odhiot and Shah (13) reported only 8 cases with muscular dystrophy.

In our experience, which comes from the analysis of 73 cases seen over a period of five-and-a-half years, limb girdle myopathy was the commonest. Although we received referrals from the major paediatric hospitals in the country, there may have been some degree of bias due to the attendance of our clinic by adult patients with the large number of cases with the limb-girdle dystrophy. Diagnosis of this myopathy was found to be difficult when patients presented in the initial phase of the disease, when it could be confused with neurogenic muscular atrophy. We had to use the CPK determination, electromyographic examination and muscle biopsy (Table 2), in combination with the clinical findings, to arrive at the correct diagnosis.

The diagnosis of DMD is often not difficult. The serum CPK levels were extremely high, and the electromyography and muscle biopsy were quite abnormal.

In our limited experience, the outcome in the DMD was disastrous, because affected children became wheel-chaired or bedridden at quite an early age compared to that of similar cases in developed

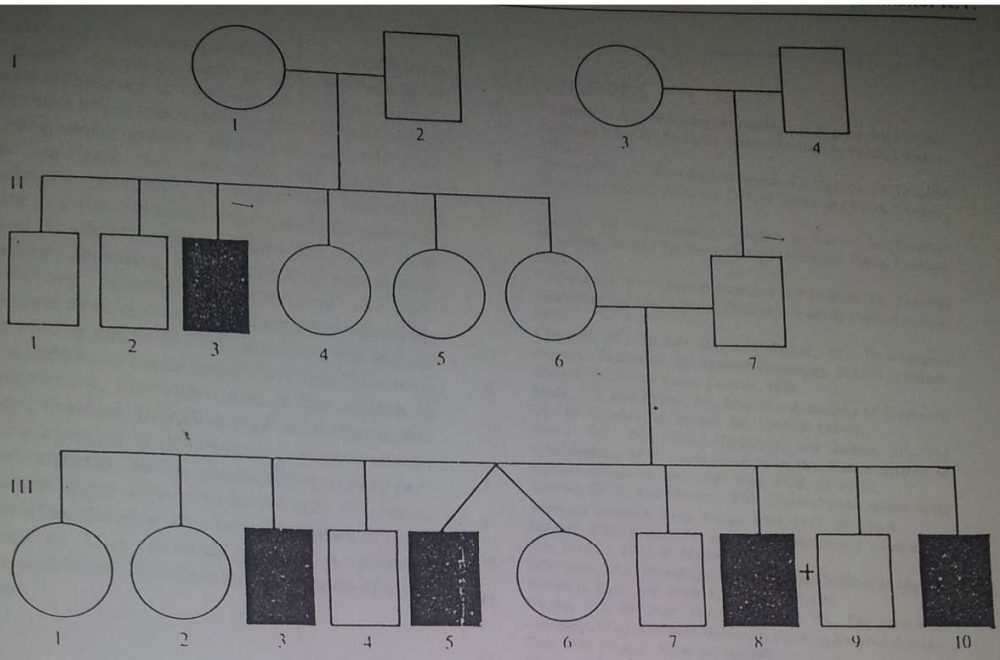


Figure 7: Pedigree of an Ethiopian Duchenne muscular dystrophy (DMD) family. Round symbol: female. Square symbol: male. large closed square: male DMD patient. + Deceased

countries, because of lack of rehabilitatory facilities in the Ethiopian situation.

As illustrated in the family pedigree shown in Figure 7, where 4 members in the same family are affected, the myopathy calls for early diagnosis and appropriate genetic counselling of the families involved about subsequent pregnancies. in this context it is interesting to observe that we often found it difficult to get a reliable family history in cases of myopathies. In Ethiopia, families tend to hide all information pertaining to other members afffected by hereditary diseases particularly myopathies. Only 5% of our 52 patients with genetic myopathies gave a positive family history.

Early diagnosis in inflammatory myopathies is also very important, as we have found treatment using steroids, with or without immunosuppressant drugs, to be most gratifying. Emphasis has to be given to the fact that, unlike the practice followed by many of our physicians, steroids have to be given in large doses and for prolonged periods in the inflammatory myopathies, tiltrating the dosage to the clinical response of the myopathic weakness and constitutional symptoms, as well as to the serum CPK levels.

Myotonia dystrophica is reported to be rare in the African (14). Dada in 1970 reported the first two Nigerian cases of myotonia dystrophica with the typical myopathic and cardiac abormalities. Our own 3 biopsy-proven cases were similar to those reported by him (15).

Myasthenia gravis is an interesting autoimmune myopathy which, in accord with our own experience, has also been found to be rare in the African (16, 18). In 1967 Greenwood and Francis (19) reviewed 11 cases in indigenous populations of South and Tropical Africa, 5 of which were their own cases from Nigeria. As in our cases the localized and more benign ocular form was the most common. Thymoma was rarely associated with these cases. Our cases had hyperplasia of the thymus. The response to anticholinergic agents was generally good, and thymectomy helped to achieve a better control of the myasthenic symptoms.

Except for the one case of suspected mitochondrial myopathy, metabolic and periodic paralysis myopathies were not encountered during our study; not were the rarer forms of congenital muscular myopathies identified. We think that these cases could have been missed because of lack of awareness on the part of parents and health workers and our inadequate diagnostic facilities, such as

sophisticated electrophysiological investigations and muscle biopsies, with proper histochemical staining techniques to evaluate suspected cases.

The most important aspect in the care of patients with progressive genetic myopathies is their close follow up and the provision of social and rehabilatory assistance, to make the life of the patients and their families much more meaningful. It is sad to observe that in Ethiopia, as in most developing countries, these comprehensive and rehabilatory services of physical therapy, orthopaedic devices and other supportive measures are not readily available. For instance, the lack of simple wheelchairs make many dystrophic patients non-ambulatory, bedridden and a big burden to their poor families. It is thus high time that health and social agencies in developing countries should pay more attention to the physically handicapped, who include those with neuromuscular disorders. The general public must also be made aware of these problems, so that patients can seek medical attention and better management by means of early diagnosis.

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NOTICE

The 23rd British Congress of Obstertics and Gynaecology

The 23rd British Congress of Obsterics and Gynaecology will be held in Birmingham, England from 12-15 July 1983. The scientific programme will comprise main sessions of invited papers, subsidiary sessions of free communications, posters and a film and video programme. A full and varied social programme is also planned.

The Preliminary Programme, Registration and Summary Forms may be obtained from the Congress Office, Royal College of Obstetricians and Gynaecologists, 27 Sussex Place, Regent's Park, London NW1 4RG.

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LOW-DOSE INSULIN IN THE MANAGEMENT OF DIABETIC KETOACIDOSIS IN A SUBOPTIMAL CLINICAL SETTING
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LOW-DOSE INSULIN IN THE MANAGEMENT OF DIABETIC KETOACIDOSIS IN A SUBOPTIMAL CLINICAL SETTING

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SUMMARY

Several studies in special centres have demonstrated that the low-dose insulin regimen, continuous intravenous (IV) or hourly intramuscular (IM), is safe, simple and effective in the management of diabetic ketoacidosis (DKA). The hourly IM regimen, 10 units IV and 10 units IM initially followed by 5 units IM hourly in 14 episodes of DKA in 12 patients, 4 males and 8 females, under suboptimal conditions was tried with limited biochemical monitoring using Dextrostix strips (Ames) for the hourly blood glucose determinations augmented by periodic spectrophotometric determinations. The mean initial blood glucose was 513.7 ± 135.3 mg/dl, the urine was strongly positive for ketones and the level of consciousness varied from drowsy to comatose. The mean insulin requirement before changing to subcutaneous injections at a blood glucose level of 250 mg/dl was 37.9 ± 13.1 units, IV fluid requirement was 2.5 to 6 litres and the duration of treatment was 4.6 ± 2.4 hours.

There was one death in the series, which was not due to insulin resistance, while all the others recovered uneventfully. This study shows that the small dose regimen is applicable in the treatment of DKA in circumstances with limited laboratory facilities and is possibly safer than the big dose regimen under such circumstances because of the lesser likelihood of the development of severe hypoglycaemia and hypokalaemia.

INTRODUCTION

Diabetic ketoacidosis (DKA) is a medical emergency that is still potentially lethal. In a review of the literature in 1977, Alberti (1) reported that the mortality in specialist centres still remained on the average between 5 and 10 per cent while in non-specialized centres it ranged between 20 and 30 per cent.

Successful treatment of DKA requires the administration of fluid and electrolytes, insulin and perhaps alkali under close observation. But the recommendations on the dose, route and frequency of insulin administration vary considerably. Until 1972, it had been traditional to use large doses of insulin (so-called conventional therapy). However, since 1973 several studies, conducted in different centres, demonstrated the effectiveness of much smaller doses given either by a continuous intravenous (IV) infusion or intermittent intramuscular (IM) injections (2-8). An editorial in the British Medical Journal in 1977 (6), after reviewing the experience with low dose

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regimens, concluded that they were simple, safe and effective. Kreisberg (2) also concluded that low doses of insulin were as effective as high doses and had fewer associated complications of hypoglycemia and hypokalemia but cautioned that the effectiveness of these regimens had been demonstrated only in metabolic or research units. In this study the low dose insulin regimen was applied under much less optimal conditions using dextrostix strips (Ames) for the hourly blood glucose determinations to treat DKA patients following the guidelines as recommended by Alberti (1).

MATERIALS AND METHODS

There were 22 episodes of suspected DKA during the study period from 9th November 1979 to 8th September 1980. Of these 14 episodes in 12 patients fulfilled the following criteria for the diagnosis of DKA and were included in the study.

a. Known history of diabetes mellitus or a history consistent with diabetes mellitus.
b. A blood glucose 300 mg/dl.
c. Urine sugar of 3+ or more and ketonuria of 2+ or more.
d. Depressed state of consciousness ranging from drowsiness to deep coma.
e. Evidence of metabolic acidosis as manifested by Kussmaul breathing with a respiratory rate of over 24 per minute.
f. Dehydration manifested by all or most of the following signs: diminished skin turgor, soft or sunken eye balls and dry tongue.

MANAGEMENT:

An IV infusion was started with a litre of normal saline and the rate of infusion adjusted according to the level of hydration.

A loading dose of 20 units of crystalline insulin (10 units IV and 10 units IM) was administered after taking blood for glucose determination. Five units of insulin were administered IM every hour thereafter until the blood glucose level dropped below 250 mg/dl. The initial dose of insulin was repeated if the blood glucose did not decrease by 10% or more of the initial value after one hour.

Blood pressure, pulse, respiration, level of consciousness and state of hydration according to the signs listed under (f) above and urine output were monitored every ½ to 1 hour.

Blood glucose levels were followed using the dextrostix strip (Ames) every hour with spectrophotometric determinations initially, 1 hour after initiation of insulin injections and when the dextrostix showed levels around 250 mg/dl.

Urine sugar and ketones were also checked hourly.

When the blood sugar level reached 250 mg/dl or less, the IV infusion was changed from normal saline to 5% dextrose in water or saline and crystalline insulin was given subcutaneously according to 4 hourly urine sugar determinations.

Potassium chloride was added to the IV in a dose of 10 to 20 mEq per litre after the urine output had reached 30 ml per hour until the patient was able to take food by mouth.

Fifty ml of 7.5% sodium bicarbonate (45 mmol) was added to the first bag in severely acidotic cases.

All the patients were managed in the general ward under close observation.

RESULTS

Initial clinical and laboratory findings (Table 1): The initial systolic blood pressure ranged from 0 to 120 mm Hg being 100 mm Hg or less in 11 of the 14 episodes, the pulse was 108 to 140 min. Two cases were comatose, 2 were stuporous and 9 were drowsy. Dehydration was severe in 5, moderate in 5 and mild in 1. The mean initial blood glucose (excluding the initial Dextrostix estimation of case 1) was 514 ± 135 mg/dl (370-750 mg/dl).

these workers, 46% were found to have skeletal fluorosis; usual radiological criteria were used for the diagnosis (A.R., Annual Report, 1977).

In August 1984, a medical board examined 300 persons from Wonji-Shoa with a presumptive diagnosis of skeletal fluorosis after complaints of pains and aches in the joints, limitation of movement, and progressive kyphosis. Radiological evidence of skeletal fluorosis was found in 65% of the 300 persons examined; 30 (10%) had crippling fluorosis *(figure 3)*. In these 30, cervical myelopathy and radiculomyelopathy seen in 15 persons was the commonest neurological complication followed by dorso-lumbar radiculomyelopathy detected in 10.

Ten persons were completely incapicitated and bedridden, the majority with paraplegia in flexion. Spasm of muscles in the lower limbs and the abdomen was extremely painful and troublesome in some patients. Sphincter disturbance was seen in 5 patients. Wasting and atrophy of muscle of the hands, especially the thenar eminence, and hypotonia in the upper limbs were seen in the advanced cases. Twelve patients of the 30 had sensory disturbance, predominantly a severe affection of the vibration sensation in the lower limbs.

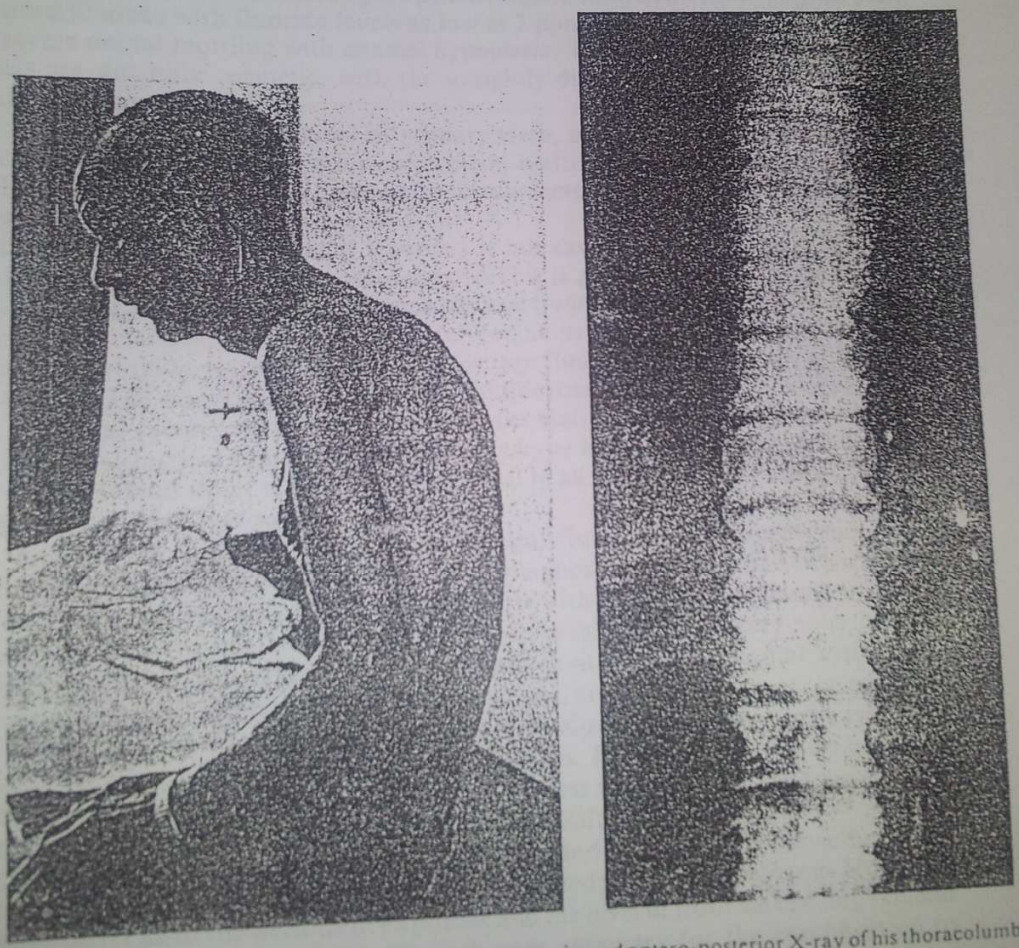


Figure 3 and 4. A patient with moderate skeletal fluorosis, and antero-posterior X-ray of his thoracolumbar spine, with calcification of intervertebral cartilage.

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Discussion

The accepted optimal and 'safe' concentration of fluoride is 0.8 ppm-1.0 ppm, with a maximum allowable limit of 1.5 ppm [14].

The Rift Valley groundwaters have very high fluoride levels, ranging from 1.5 ppm to 36 ppm. On the average, the water sources commonly used have fluoride contents of 3.5 ppm to 13.0 ppm. Studies from other countries [2, 5] and our own experience in Ethiopia have shown that these levels readily cause dental fluorosis in children, and over a prolonged period (8 to 10 years of consumption) skeletal fluorosis also.

Dental fluorosis of varying severity *(figure 2)* is a universal finding in the Rift Valley in children who were born and brought up in the region. Mild dental mottling has been recognized in areas with fluoride levels as low as 2 ppm. Higher levels, above 4 ppm, cause severe dental mottling with enamel hypoplasia. These adverse effects of dental fluorosis are not only cosmetic, with the unsightly discoloration of teeth, but also present a functional problem.

The presence of mottled enamel in primary teeth, observed during our survey in children residing in the Rift Valley since birth, reaffirms that placental transfer of fluoride [15] during pregnancy is also an important factor in the pathogenesis of dental fluorosis.

Unlike dental fluorosis, skeletal fluorosis is not easy to recognize, as it becomes clinically obvious in the far advanced stages. This is also true of our experience in Ethiopia. In the Wonji Shoa sugar estates, skeletal fluorosis was first identified only in the early 1970s. Its development occurred in Wonji over an exposure period of 15 to 20 years due to drinking-water containing an average fluoride concentration of about 8 ppm-10 ppm. The majority of cases of skeletal fluorosis were found in workers from within the sugar factory, particularly in the boiler stations, where temperatures were very high, resulting in the consumption of very large amounts of water. In the early 1970s, defluoridated water supplies were installed in all factories in the area, following the recognition of this problem.

The only means of early detection of skeletal fluorosis is by roentgenological examination. We used X-ray of the spine in the diagnosis and evaluation of the degree of skeletal fluorotic changes. The changes in those with end-stage, moderate to severe affection were often not difficult to identify. The bones showed increased bone density, with thickening and reduction of the medullary cavity. There irregular osteophyte formations, marginal lipping of the vertebral bodies, and calcification of the paravertebral ligaments. *Figure 4* shows a representative X-ray of the spine; this type was commonly seen in our patients with skeletal fluorisis. Early changes shown by X-ray are difficult to recognize as definitely fluorotic, unless the diagnosis is suspected in a patient coming from an endemic area such as the Rift Valley.

Our findings are consistent with the reports from India [2,3], where consumption of high-fluoride water for prolonged periods also resulted in skeletal fluorosis. However, experience differ as to the periods of exposure and the level of fluoride causing skeletal changes. Short [4] believed that 30-40 years were necessary for the complication to occur. Pandit [5], on the other hand, thought that 10-15 years was enough. Our own experiences seem to agree with the latter finding. In another observation, Siddiqui [3]

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found radiological evidence of skeletal fluorosis in 15.4% of subjects in a population using water with a fluoride concentration of only 2.5 ppm, after 14-15 years of residence. The subject is further complicated by the findings of Jolly [2], that crippling fluorosis was discovered in a village with a mean fluoride concentration of 3 ppm, but not in another village where a similar concentration had been consumed for the same period.

The age and sex distribution of both dental and skeletal fluorosis in our study is similar to that in most studies from India.

Although there is no doubt that the content of fluoride in drinking-water, and the period of consumption of that water, are very important factors for the development of fluorosis, other factors such as sex, occupation, climatic conditions, the chemical composition of the drinking-water, diet and nutrition states may also have significant contributory roles.

Cognisant of the gravity of the fluoride problem in the Rift Valley, the Ethiopian Government is intensifying its efforts and resources to find and provide alternative sources of drinking-water with low fluoride concentration, especially in densely populated areas, as the cost of defluoridation, in the present state of science, is prohibitive for a developing and economically hard-pressed country like Ethiopia. Existing estimates from the sugar estates show that it costs US $0.50 to defluoridate a cubic meter of water – an expensive measure when one considers water supply for large populations.

In isolated villages dependent on a high-fluoride ground-water supply and with no alternative sources, cheap methods of defluoridation need to be installed, and the collection of rainwater for drinking must be encouraged [16].

In preventive measures, it must be borne in mind that, in hot climates as in the Ethiopian Rift Valley, more water is consumed, and fluorosis may develop at rather lower levels of fluoride in drinking-water [17], particularly in people engaged in physically strenuous duties.

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OPTIC ATROPHY IN ETHIOPIANS

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ABSTRACT. *An analysis was made of 71 consecutive Ethiopian patients with optic atrophy seen at Menilek II Hospital's Ophthalmology Department and in the Neurology Unit of the Department of Internal Medicine, Tikur Anbessa Hospital, Addis Ababa, over a three-year period (1981-1984). There were 20 female and 51 male patients, with ages ranging from 4 to 68 years (average 36 years). In 20 (28.2%) patients, the optic atrophy was a result of antecedent infectious conditions; no definite cause was found in 15 (21.1%) cases. Other causes were optic neuritis in 8, toxic in 7, pituitary tumour in 6, post-syphilitic in 5, and post-traumatic in 5 patients.* Kosso (Hagenia abyssinica), *a local taenicidal preparation, was implicated as a possible toxic factor resulting in optic atrophy in the toxic group. The remaining patients had other sellar and intracranial lesions, and one was a case of ischaemic optic neuropathy. The response to systemic corticosteroid administration in 2 cases of optic neuritis was dramatic.*

A clinical diagnosis of optic atrophy is based on ophthalmoscopic findings of change in colour, structure of the optic disc, and disturbed function of the eye involved, evidenced by change in the visual acuity in the peripheral and central fields of vision (1,2). According to F.H. Budden, World Health Organization Consultant (unpublished report, 1981), the rate of blindness in Ethiopia was then estimated to be 1,500 per 100,000; that is, there were about 490,000 blind persons in the country, trachoma (200,000 blind) and senile cataract (140,000 blind) being the leading causes. In a study (3) made among 8,300 ophthalmic cases in Menilek II Hospital, Addis Ababa, the leading causes of blindness were cataract and trauma, in 25.8% and 15.8% respectively. Retinal and optic nerve lesions accounted for 4.9% of blindness in this group. Optic atrophy related to *kosso (Hagenia abyssinica)* toxicity was reported by Rokos in 1969 (4).

This study was undertaken in an attempt to find out the prevalence and aetiological factors involved in Ethiopian patients presenting with optic atrophy, since, to our knowledge, a detailed study has not previously been made.

PATIENTS AND METHODS

Sixty-seven patients who presented with optic atrophy, and 4 patients with disc oedema who subsequently developed optic atrophy, were included in the study. Patients with raised intraocular pressure were excluded. Medical history was recorded, including details of events leading to a reduction or loss of vision, previous use of drugs and traditional medicine, past history of head injury and ocular, cardiac or venereal disease, and family history of visual impairment or loss of sight, diabetes, syphilis and hypertension.

A complete physical examination, in-

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cluding a detailed neuro-ophthalmological examination, was made. Some of the patients were also admitted to the medical department for investigations. Visual acuity was tested using Snellen's chart. Visual field was examined, using a perimeter and Bjerrum's screen, whenever adequate vision and co-operation allowed it. Intra-ocular pressure was determined by Schiotz and Goldmann's appanation tonometry. Colour vision was tested, using Ishihara charts. Investigations included X-rays of skull, orbits, optic foramen and chest. Carotid angiography was performed when indicated. Complete blood count, erythrocyte sedimentation rate, fasting blood sugar, VDRL test and urine analysis were performed. A cerebrospinal fluid (CSF) examination was also made in some patients with a history of preceding infectious disease. Unfortunately, the 5 patients with reactive serum serology for syphilis refused lumbar puncture for CSF examination.

RESULTS

The male-to-female ratio was 2.6 : 1. Bilateral and unilateral optic atrophy occurred in 53 (74.6%) and 18 (25.3%) patients, respectively. The age and sex distribution is shown in Table 1. The age-group 10-29 years (49.3%) was the most affected.

A history of taenicide use was obtained in 23 (32.4%) patients; of these, 6 used niclosamide (Yomesan: Bayer, U.K.); 4 used aspidium (male fern); and one used dichlorophen. There was only one smoker, who also drank *araqi* (locally-brewed liquor). Antihypertensive treatment (reserpine) was used by 2 patients.

Local taenicidal preparations, *kosso (Hagenia abyssinica), enkoko (Embelia schimperi* or *Combretum aculeatum), mettere (Buddleja polystachya),* and *mekmeko (Oxalis anthelmintica)* were used by 12 (16.9%) patients. *Kosso* was the most frequently used, by 9 out of the 12 patients in this group.

Only 2 patients reported family visual impairment, in their respective fathers; it was suggestive of cataract in one, and trachoma in the other. A family history of diabetes and hypertension was obtained in 2 patients.

A history of sudden onset of blurring of vision was obtained in 25 (35.2%) patients; in the remaining 46 (64.8%), there was a progressive and insidious deterioration of vision. Associated sharp ocular pain was present in 10; headache, diffuse or of bitemporal localisation, was described by 20 (28.2%) patients.

Visual acuity was less than or equal to 6/60 in both eyes in 35 cases (49.3%) with bilateral optic atrophy, and in 16 cases (22.5%) with unilateral optic atrophy. Vision of 6/60 or better was obtained in one or both eyes of 18 (25.3%) with bilateral optic atrophy and in 2 (2.8%) with unilateral optic atrophy.

We were able to perform visual field testing in only 22 (31.0%) of our patients because of extremely poor vision and poor co-operation. The commonest defect was marked peripheral field constriction. Bitemporal hemianopsia was found in the cases with intrasellar lesions. Other findings were a caeco-central scotoma in a case of optic neuritis, and nerve fibre bundle defect in a post-infectious case.

Table 2 shows the aetiology of the optic atrophy as traced in our patients.

The diagnosis of sequelae to infectious or post-infectious disorders in 20 patients was based on a history of acute febrile illness, with or without loss of consciousness, preceding the development of the visual symptoms. Of the 20 patients so affected, 14 had their febrile illnesses between the ages of 1 and 14 years. Three who presented with systemic manifestations of tuberculosis (fever, night sweating and weight loss), high sedimentation rate and positive Mantoux test were treated with

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TABLE 1. Age- and sex-distribution of cases of optic atrophy

Age-group (years)	Sex M	Sex F	Total in each group	%
0 - 9	6	1	7	9.8
10 - 19	13	6	19	26.8
20 - 29	10	6	16	22.5
30 - 39	9	2	11	15.5
40 - 49	5	4	9	12.7
50 - 59	7	1	8	11.3
60 - 69	1	-	1	1.4
70+	-	-	-	0.0
All age-groups	51 (71.8%)	20 (28.2%)	71	100.0

TABLE 2. Aetiology of optic atrophy in Ethiopian patients

Aetiology	No. of patients M	No. of patients F	Total	%
Infection or post-infection	14	6	20	28.2
Idiopathy	9	6	15	21.1
Optic neuritis	5	3	8	11.3
Toxic	5	2	7	9.9
Pituitary tumour	5	1	6	8.5
Syphilis (positive serum VDRL)	4	1	5	7.0
Post-trauma	5	-	5	7.0
Ischaemic optic neuropathy	1	-	1	1.4
Other	3	1	4	5.6
Total	51	20	71	100.0

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a combination of systemic steroids and anti-tuberculous therapy of streptomycin, isoniazid and thiacetazone. None showed any appreciable improvement of vision.

In 15 (21.1%) of our patients, no definite cause could be attributed. Six patients had bilateral optic atrophy; and 5, with the typical visual field change of bitemporal hemianopsia, and skull X-ray findings of sellar changes, received the diagnosis of an intrasellar space-occupying lesion, presumably a pituitary tumour.

Toxic aetiology was presumed in 7 patients. In this group, patients with a history of regular ingestion (usually once every 2-3 months) of taenicidal medication (*kosso* and niclosamide in 2, *kosso* only in 3, *kosso* or *enkoko* and male fern in one, *enkoko* only in one) were included. One of these patients was a 4-year-old child, who was given *kosso* two weeks prior to the development of bilateral visual loss.

The diagnosis of optic neuritis was entertained in 8 patients with sudden loss of vision associated with sharp ocular and orbital pain. Aggravation of pain on ocular movement was described by 4 patients. Trauma was the cause of optic atrophy in 5 patients, 3 of whom had had motor vehicle accidents and had sustained head injury with loss of consciousness, prior to the development of the visual loss. The other 2 gave a history of trauma to the head. Ischaemic optic neuropathy was diagnosed in a middle-aged hypertensive man.

In most of our patients, the disease process was far advanced on presentation; the treatment offered the majority was therefore in the form of standard vitamin B complex tablets, one twice daily, intended primarily to satisfy the patients. All patients with reactive VDRL were treated with penicillin. Some of our patients still under follow-up have maintained visual acuity as on presentation. Fifteen (21.1%) patients with progressively deteriorating vision were put on high doses of systemic steroids, tapered off over periods of 2 to 3 months. Two patients with a diagnosis of optic neuritis showed a dramatic response to steroid therapy. None of our patients developed other neurological symptoms, with the exception of 2 with pituitary adenoma, who died from increased intracranial pressure and hydrocephalus. One patient with a chromophobe adenoma had a successful surgical removal of the adenoma in West Germany.

DISCUSSION

The male preponderance in almost all age-groups (male-to-female ratio 2.6 : 1) may suggest that optic atrophy is more common in the male population. However, this may well be because more male patients come to hospitals, as is true in most parts of Africa, making the male preponderance more apparent than real (5,6).

The post-infectious cases in our series comprised patients with meningitic or encephalitic-like illnesses, one case with measles and one case with typhoid. A comparison of our results to a similar study made in Nigeria (7) shows a higher rate of post-infectious and toxic aetiology in our series. In the Nigerian study, the idiopathic and optic neuritis group accounted for over 50% of the optic atrophies.

In almost a third of our patients, the aetiology was unknown. Even though biochemical tests were not performed, there was no strong clinical evidence to suggest nutritional factors. In Nigerians, chronic cyanide intoxication of dietary origin from cassava was implicated (8). In Ethiopia, cassava is not included in the staple diet of the different regions. Nevertheless, the role of as yet unidentified toxins in the causation of optic atrophy in Ethiopians needs further investigation.

Optic atrophy and neuritis may be associated with many diseases, metabolic and toxic disorders (9). In the majority of cases

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the cause may be unknown. Henderson (10) has reported optic nerve involvement in epidemic meningitis, enteric diseases, malaria and toxoplasmosis. Visual failure after viral infections and encephalitic illnesses is known to occur (11); it has also occurred after vaccinations for viral diseases (12,13).

Kosso ingestion was the presumed aetiological factor in the toxic group. Of the various taenicidal preparations, *kosso* seems to be the most commonly used (14). Rokos (4) claims to have seen 224 cases of bilateral optic atrophy in a period of 2 years while working in a hospital in Addis Ababa; in 9 of these cases, he made a presumptive diagnosis of *kosso* poisoning. The total number of cases of optic atrophy in his report is extremely high compared to our findings, but the lack of diagnostic criteria and clinical information he gives prohibits valid comparison. Nevertheless, we appreciate his drawing attention to the possibility of *kosso* toxicity in optic atrophy. The anthelminthic affect of *kosso* is ascribed to a *kosso* toxin related to filicic acid (found also in male fern) (15); and *kosso* has also been found, as quoted by Rokos, to contain derivatives of phloroglucin which, in an overdose or in hypersensitive individuals, may result in optic atrophy (4). What is difficult to explain, however, is the rarity of this complication in the Ethiopian population, where *kosso* is consumed so widely and frequently. It is quite possible *kosso* might be toxic to the optic nerve when consumed with other drugs or in an overdose, or against a background of other risk factors, such as age, nutritional deficiency, infective processes, or depressed immune state. In our paediatric patient, there was a strong cause-and-effect relationship.

A host of other taenicidal drugs are available, but aspidium oleoresin (male fern) and niclosamide (Yomesan) were frequently used by our patients. It is known that there are side-effects to almost all preparations, a few having hazardous effects. Male fern is known to produce optic neuritis (16) resulting in visual loss, sometimes associated with deep orbital pain or pain on eye movement. The symptoms are usually bilateral, but may occasionally be confined to one eye; recovery with residual optic atrophy occurs in the majority of cases. Our case was a 43-year-old man who was almost blind in both eyes after male fern ingestion.

According to Weiss (17), there are at least 49 drugs that are proven or presumed causes of optic atrophy, and of these a well-studied example is methyl alcohol, which results in optic atrophy 12-16 weeks after its ingestion. Aspidium (male fern), chloramphenicol, isoniazid, and ethambutol, for example, have been implicated in the causation of optic neuritis and optic atrophy (16). Kazarian (12) described optic atrophy after trivalent measles, mumps and rubella vaccinations. In general, the mode of action of the drugs and vaccine is not yet clearly understood.

In a review of 137 cases of optic neuropathies, Woods and Rowland (18) found 23 cases of syphilitic aetiology, the majority presenting with primary optic atrophy. Various forms of optic nerve involvement in syphilis were considered, including optic neuritis, chorioretinitis, papilloedema and primary optic atrophy, with optic neuritis being common in its late stages (18,19). The natural history and response to steroids in syphilitic optic nerve disease is controversial. Walsh (19) claims good visual prognosis with treatment involving penicillin and corticosteroid, the importance of the latter being to avoid the development of Jarisch-Herxheimer reaction. Due to lack of CSF serological confirmation, 5 cases of optic atrophy with strongly reactive serum VDRL were treated with a full course of penicillin, on a presumptive diagnostic impression of a syphilitic aetiology. However, there was no improvement of their visual impairment. This may be related to the

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severity of the visual loss on presentation, as has been suggested (19).

The apparent high figure of our pituitary tumour cases might have been due to the selection of cases referred to the neurology department. It is sad to observe that almost all of these cases presented at a time when they had reached an exacerbated stage of their disease, with almost total blindness.

The good response to steroids in 2 patients with optic neuritis might encourage early trials of steroid therapy when the clinical picture suggests the disease.

The finding of only a single case of ischaemic optic neuropathy in our series is suggestive of the rarity of this condition in our patients, as in other series (20).

In Ethiopians, aetiological diagnosis of optic atrophy, which is not uncommon, has been found difficult because of the nature of the disease, the limited diagnostic facilities, and the problems related to individual patients, such as inadequate history and lack of awareness, leading to a far advanced disease state.

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IDIOPATHIC FACIAL PARALYSIS (BELL'S PALSY) IN 167 ETHIOPIANS, WITH A CONTROLLED THERAPEUTIC TRIAL IN 59 PATIENTS

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ABSTRACT. *A prospective study was made of 167 consecutive Ethiopian patients with idiopathic facial paralysis (Bell's palsy) seen at neurological clinics in Addis Ababa during 15 months (1983-1985). Males and young persons aged between 11 and 40 years were predominantly affected. There was no seasonal variation in the incidence of the paralysis. Of the patients, 26% reported having a febrile illness during the 4 weeks before the occurrence of facial paresis. Hypertension and diabetes mellitus were found to be important predisposing factors. A controlled trial of steroid treatment carried out in 59 of the patients did not reveal a statistically significant difference between those who received prednisone and their controls on vitamins alone.*

Acute peripheral facial paralysis or Bell's palsy is a common neurological disorder encountered in Ethiopia. The pathogenesis of the illness is not yet resolved. Vascular ischaemia of the facial nerve (1,2) and viral infections (3-9) have been considered as possible aetiological factors.

Conflicting views are also held by different groups of workers on the use of corticosteroids in the management of the condition. This study was undertaken to determine the incidence, predisposing factors including viral infections, and the role of corticosteroids in the treatment of Bell's palsy in Ethiopia.

PATIENTS, CONTROLS AND METHODS

Using a pre-set prospective protocol, during the years 1983 to 1985, 167 consecutive patients with acute non-traumatic peripheral facial paralysis referred to our neurological clinic were examined over a period of 15 months. Anamnesis was sought from each patient concerning preceding viral and concurrent infections, as well as diabetes and hypertension. The presenting complaints were also noted. All patients underwent complete general, otorhinolaryngological and neurological examinations.

In accord with World Health Organization criteria (10), hypertension was defined as systolic pressure of 160mmHg or greater, or diastolic pressure of 95mmHg or greater, or both.

Determination of the fasting blood sugar and cholesterol was performed on the first 63 and 59 patients respectively, with an overlap. For viral serological tests, blood samples were collected at the first visit and 3 weeks later. Similar samples were taken from sex- and age-matched controls, though unfortunately the number of cholesterol controls was unavoidably smaller than that of the patients. These were patients attending the neurological referral clinics for complaints other than facial paralysis. The samples are currently being analysed at the

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Microbiology Laboratory of Ulleval Hospital, Oslo, Norway.

Electromyograph (EMG) studies were made on 25 patients, but the EMG machine then went out of order, and the protocol had to be modified to what was available.

All patients asked for and received electrical stimulation physiotherapy for a psychological placebo effect, although this was not part of the protocol.

Fifty-nine non-diabetic, non-hypertensive patients between the age of 10 and 50 years who presented during the first 4 days of onset of incomplete facial paralysis were then randomly allocated to the steroid or vitamin control groups by a single-blind procedure, using a block design of 10-year age-groups. Patients with advanced age, diabetes or hypertension were exluded from the steroid trial, because of the well-documented influence on outcome.

The prednisone treatment consisted of 40mg daily for the first 5 days, and was then tapered to 5mg per day over 5 more days; for children the dosage was adjusted to age and body-weight. The vitamins used were B complex (B1, B6 and B12), one tablet twice daily. Most patients were seen at least twice during the average follow-up period of 10 months; those on the steroid trial were seen more frequently.

Five months after treatment, the facial motor recovery was assessed. Complete recovery was considered to have occurred when there was no difference between the involved and the normal side during closing of the eyes tightly, wrinkling of the forehead, blowing out of the cheeks, and grinning. "Fair return" implied incomplete recovery, with minimal functional motor deficit. Little or no improvement, and complications of faulty recuperation, were taken as "poor return" of function. This grading system was adopted from the work of May *et al.* (11).

RESULTS

The study comprised 167 patients: 97 males (58.1%) and 70 females (41.9%). Within the wide-ranging age distribution, peak incidence was in the age-groups 11-20 and 21-30 years; 9.6% of the patients were below the age of 10 years. Slightly more males than females were affected (Table 1).

The commonest presenting complaints were deformity of the face, with crooked mouth, inability to close the eye, and numbness and pain in the retroauricular area on the affected side. Taste disturbance and hyperacusis occurred in only 3 patients.

The facial paralysis occurred on the left side in 83 and the right in 79 of the patients. A history of recurrent paralysis on the same side was obtained in 3 patients. Bilateral affection was encountered in 5 patients, either at the same time or within a period of 10 months.

Analysis of the seasonal distribution of 126 consecutive patients seen over a year did not reveal any significant variation of incidence.

Forty-four of the 167 patients (26.3%) reported having had a preceding infection, mainly in the forms of coryza or sore throat. Of the controls, 11% had had a preceding infection. Hypertension was discovered in 21% of 100 adults with Bell's palsy, as compared with 6.8% of the controls. There were 12 of 63 adult patients (19%) with elevated fasting blood sugar levels, as compared to 4.0% of the control group; of the 12, 8 had frank diabetes and were already on treatment when they developed Bell's palsy. Cholesterol was elevated in 20.3% of 59 adults (Table 2).

As shown in Table 3, those treated with prednisone did slightly better than those on vitamins alone, but the difference was not statistically significant.

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TABLE 1. Age- and sex-distribution of 167 patients with Bell's palsy

Age-group (years)	No. of patients	%	%, general Ethiopian population*
0 - 10	16	9.6	33.9
11 - 20	42	25.1	21.6
21 - 30	40	24.0	13.7
31 - 40	28	16.7	11.1
41 - 50	16	9.6	8.1
51 - 60	14	8.4	5.3
61 - 70	10	6.0	3.5
70+	1	0.6	2.8
Total	167	100.0	100.0

*Central Statistical Office, Addis Ababa, 1984

TABLE 2. Conditions associated with Bell's palsy

Condition	No. of patients examined		No. of patients	%	No. of controls	%
Hypertension	100 (adults above 20 years)	above 95mmHg diastolic	21	21.0	15/220	6.8
		below 95mmHg diastolic	79	79.0	205/220	93.2
Preceding viral or concurrent infection	167 (all patients)	present	44	26.3		
		absent	123	73.7		
Fasting blood sugar	63 (adults above 20 years)	above 110mg%	12	19.0	3/75	4.0
		below 110mg%	51	81.0	72/75	96.0
Serum cholesterol	59 (adults above 20 years)	above 250mg%	12	20.3	9/49	18.4
		below 250mg%	47	79.7	40/49	81.6

TABLE 3. Comparison of treatment of Bell's palsy with vitamins and steroids

Treatment	No. of patients	Return of facial function					
		Complete		Fair		Poor	
		No.	(%)	No.	(%)	No.	(%)
Vitamins	29	18	(62.1)	6	(20.7)	5	(17.2)
Steroids	30	19	(63.3)	7	(23.3)	4	(13.3)
Total	59	37	(62.7)	13	(22.0)	9	(15.3)

From the overall analysis, 57% of all our patients who could be followed up had recovered fully when examined 6 months after the onset of their illness, on supportive therapy of vitamins and physiotherapy; 11% had fair return of facial motor function; 12% showed very little or no recovery.

Young patients and those with incomplete facial paralysis at the onset had, on the whole, a better prognosis. It is noteworthy that patients who were overtly tense and extremely worried about their paralysis did poorly, even when all other factors were predictive of good outcome. A significant proportion of such patients with psychoneurosis exhibited synkinesis even after an apparent full recovery of facial motor function had been recorded.

DISCUSSION

This study reaffirms that Bell's palsy is a common neurological disorder, also in Ethiopia. The presenting complaints and clinical manifestations in our patients were similar to those reported elsewhere (12).

The aetiopathology of this neurological affection is not very well understood. There are two predominant hypotheses. A possible viral cause has been studied extensively (3-9) without conclusive results, but the commonly reported history of a preceding infection makes this theory attractive. Interestingly, 26% of our patients gave such a history. We have therefore decided to pursue this further, with serological tests for neurotropic viruses. Like Adour and Wingerd (13), we found no seasonal variation in the distribution of our cases, although Berg *et al.* (4) discovered an increased incidence during early autumn, with the suspicion that enteroviruses may be important in the causation of the paralysis.

The vascular factor in the form of thrombosis or spasm leading to ischaemia of the facial nerve has also been hypothesised, particularly in older patients (1,2). Korczyn *et al.* (3) further suggest that viral or other diseases may predispose to vascular lesions leading to the nerve damage. Thus far, the pathogenesis of Bell's palsy is evidently still poorly understood. However, there are accepted predisposing factors: our study is in accord with previous observations that diabetes (2,14) and hypertension (2,14-16) are important factors in the development of acute facial paralysis: we found elevated blood sugar levels in 19% of 63 of our patients, and hypertension in 21% of 100 patients.

Screening of 933 Ethiopian bank employees in Addis Ababa detected high blood pressure in 5% of males and 0.8% of females (16). In another study, 12% of 2103 medical out-patients in an Addis Ababa clinic were hypertensive (17). In our 100 adult patients with Bell's palsy, there is a significantly higher incidence of hypertension. It is believed that hypertension is the most important single discriminating variable (15) in acute facial paralysis.

With or without steroid therapy, the return of facial function was poorer in those with advanced age and hypertension. In our experience, diabetes also presented a poor prognostic effect on recovery from Bell's palsy in young and old, but particularly when associated with hypertension and old age - perhaps a foregone conclusion. Generally, diabetics took longer to show signs of recovery than non-diabetics, an outcome recorded in other studies (14,18).

Most Ethiopian patients react with profound shock when they develop acute facial paralysis. This may be a reflection of the superstitious belief, commonly held, that this affection is a sort of curse, often associated with the devil.

The use of steroids in the management of acute facial paralysis is controversial. May *et al.* (11) did not find it useful, while Adour *et al.* (19) concluded that the results of prednisone treatment were superior. Ing (12) goes as far as to recommend that all

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patients with Bell's palsy presenting within one month of onset of the illness should be given a trial of treatment with steroids; unfortunately, this recommendation was based on an experience of only 8 patients.

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CASE REPORT

AMYLOID CARDIOMYOPATHY – A CASE REPORT

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ABSTRACT. *A 43-year-old male presented with cardiomegaly, aortic and mitral valve incompetence, bilateral heart failure and the nephrotic syndrome. Rectal and kidney biopsy showed amyloidosis, and echocardiography confirmed cardiomyopathy. The available evidence was diagnostic of amyloid cardiomyopathy, which is discussed in the report with consideration of the differential diagnoses.*

In addition to rheumatic heart disease, which is still common in Ethiopia, and the much less common degenerative and hypertensive categories, cardiomyopathies have also been reported in recent Ethiopian medical literature (1-3). But to our knowledge this is the first report of amyloid cardiomyopathy from this country, and the purpose of the report is to stimulate efforts to determine the underlying cause in patients suffering from this type of cardiac disease.

CASE REPORT

A previously healthy 43-year-old Ethiopian male was admitted with complaints of abdominal distension of 3 months, cough productive of scanty, whitish, occasionally blood-tinged sputum of 3 weeks, and severe dyspnoea and orthopnoea of 2 weeks' duration. The abdominal swelling had progressed within a few weeks to oedema involving the whole body. But he had no angina, syncopal attacks, history of rheumatic fever, syphilis, diabetes mellitus, hypertension nor cigarette-smoking, and alcohol intake was only one to two bottles of beer per week. He had lost weight, although he could not state how much, and complained of severe weakness.

On physical examination, the man looked ill and wasted, and was in moderate respiratory distress. The pulse was 100 per minute with regular rhythm, the blood pressure 100/40mmHg, the respiration 24 per minute and the temperature 37°C. The jugular venous pressure was 7cm above the sternal angle at 45 degrees, and the praecordium was quiet, with the cardiac apex palpable in the seventh left intercostal space at the anterior axillary line. A third heart sound was audible at the apex, and there were a pansystolic grade 3/6 mitral murmur and a high-pitched grade 2/6 aortic diastolic murmur. The lung bases were dull to percussion, with diminution of the breath sounds and moist crepitations.

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The abdomen was grossly distended with ascites; the liver was ballottable, with the edge at 4cm below the right costal margin. There was marked pitting bilateral ankle oedema, and the skin was dry and scaly over the extremities.

Laboratory results were as follows: haemoglobin 15.6g%, white blood cells 9200, erythrocyte sedimentation rate 90mm in the first hour, urine protein 4+ with Albustix, pus cells 10-12 per high-power field (HPF) and granular casts 2-3/HPF. Twenty-four hour urine protein was 4.8g. Bence-Jones' protein was negative. Total serum protein was 5.6g, albumin 1.3g, alpha-1 globulin 1.4g, alpha-2 globulin 0.3g, beta globulin 1.9g and gamma globulin 0.6g per decilitre; alkaline phosphatase was 148 and the fasting blood glucose was 80%mg. The blood urea nitrogen, bilirubin transaminases and serum electrolytes were normal. Cell test was negative. The sputum was negative for acid-fast bacilli, and ascitic fluid analysis showed characteristics of transudate. Chest X-ray showed cardiomegaly, pulmonary congestion and bilateral pleural effusion; spine and thoracic cage X-ray showed no osteoporosis nor osteolytic lesions. Electroeardiogram (ECG) showed sinus rhythm, low voltage in all leads, poor progression of the R wave in the right precordial leads, and a PR interval of 0.18 second. Lung spirometry revealed a restrictive pattern.

On these bases, diagnostic possibilities considered were rheumatic heart disease and cardiomyopathy, with nephrotic syndrome secondary to heart failure or nephropathy caused by the cardiomyopathic aetiology. Conventional treatment for heart failure and further investigations were undertaken. Rectal biopsy and subsequently kidney biopsy were positive for amyloid. Echocardiography showed normal ventricular cavities, with marked thickening of the interventricular walls. However, ventricular contractility was significantly diminished. The aortic root was dilated slightly, with its deformed valves vibrating in systole, and the mitral valves vibrating in diastole. There was also mild to moderate pericardial effusion not detected clinically. These findings were found to be compatible with cardiomyopathy and aortic valve disease. Thus, although endomyocardial biopsy could not be performed to confirm the diagnosis, the cumulative evidence indicated primary amyloidosis as the most likely cause of the cardiomyopathy as well as of the nephropathy.

Histochemical examination of amyloid specimens was performed in Glasgow Infirmary laboratories. The microscopical report on a rectal biopsy showed amyloid resistant to permanganate pretreatment, proving that the amyloid protein was of the AL (light chain) type.

DISCUSSION

In a patient presenting with heart failure combined with nephrotic syndrome, one possible mechanism for the development of the latter is related to the severity of the heart failure itself (4, 5). The nephrotic syndrome may also occur in constrictive pericarditis due to a similar mechanism (6). In this patient, the ventricular thickening, evidence of mitral and aortic valve incompetence, and the left-sided heart failure precluded serious consideration of constrictive pericarditis (7).

Rheumatic heart disease could not be ruled out entirely, but the simultaneous occurrence of right and left heart failure rather than a' right-on-left sequence of events, together with refractoriness of response to conventional failure regimen in a patient without complications such as active rheumatic carditis or bacterial endocarditis, reduced the likelihood of this aetiology (8). On the other hand, a possibility of idiopathic

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cardiomyopathy could not be dismissed, short of demonstration of another aetiology for the cardiac disease (9).

An alternative explanation for the concurrent manifestations of heart failure and the nephrotic syndrome is a pathological process independently affecting both the heart and kidneys. Collagen and metabolic diseases and sarcoidosis are in this category. Among them, diabetic cardiomyopathy with nephrotic syndrome due to diabetic nephrology is excluded in the present case, by absence of evidence of diabetes mellitus. Sarcoidosis can be a challenge when the classical bilateral hilar lymphadenopathy with a negative Mantoux test is not present (10). In addition to the myocardium heart involvement, this condition may include the valves and pericardium, sometimes with effusion, just as in primary amyloidosis. Incomplete forms of haemochromatosis and disseminated lupus erythematosus without clinical evidence in other systems would also be difficult to exclude (11). But the demonstration of amyloid in the rectal and kidney biopsies in this case either ruled out these alternatives or rendered their further pursuit unnecessary. In addition, the small pericardial effusion (7), elevated alkaline phosphatase and alpha and beta globulins, and diffuse low voltage in the ECG, are all compatible with primary amyloidosis.

Amyloidosis of the heart can present as restrictive, congestive (as in this case), or as obstructive-hypertrophic, or any combination of these (8, 12-15). The restrictive type is difficult to differentiate from constrictive pericarditis (7, 13-17). Amyloid cardiomyopathy may also present with valvular lesions. Mitral incompetence is the most common finding, but aortic incompetence, though rare, may also occur (13, 17, 18). Extensive myocardial infiltration is the main cause of cardiac dysfunction, but valvular lesions may contribute to the haemodynamic disturbance.

The spectrum of tissues involved in primary amyloidosis include skin, gastrointestinal tract, skeletal muscle, heart, parenchymal organs and peripheral nerves. But the number of tissues and systems affected varies considerably, and in some cases only the heart may be involved (19).

In this patient, there was no clinical evidence of tongue or peripheral nerve involvement. Biopsy of liver, kidney, intestine, rectum, skin or gum may be used for diagnosis. Rectal biopsy is the most common means, because of relative safety, easy accessibility and good yield (20). Isolated cardiac amyloidosis is difficult to diagnose, because the technique for myocardial biopsy (transvenous right ventricular endomyocardial biopsy) is available only in specialised centres.

The prognosis in amyloid cardiomyopathy is poor, since no mode of treatment has been shown to be effective, and death commonly ensues within 2 years of the development of heart failure (19, 21).

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AFRICAN HISTOPLASMOSIS IN ETHIOPIA: A CASE REPORT
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AFRICAN HISTOPLASMOSIS IN ETHIOPIA: A CASE REPORT

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SUMMARY

A nineteen-year-old boy presented with papulo-nodular cutaneous lesion with abscess formation and multiple lytic bone involvement. He was ill-managed for several months for various dermatologic conditions until a biopsy from the nodule proved to be consistent with *Histoplasma Duboisii* infection. He had disseminated disease with involvement of the reticuloendothlial, skeletal, cautaneous and respiratory systems. The disease though reported from both East and West Africa, seem to be uncommon. It is emphasized that the presence of multiple papulo-nodular lesion with or without discharging sinuses in a chronically seriously sick looking patient warrants a histopathologic study and a radiologic survey of the bones.

INTRODUCTION

Ever since Duncan identified *H. duboisii* in 1943 (1) the number of patients seen over the past 40 years remains quite small. The largest series ever analyzed by Lucas in 1964 (2) included 56 cases for the whole of Africa and only two were from East Africa. Lucas (3) has also described a personal series of 52 cases in 1970 from West Africa. In 1977 Mugerwa (4) from Uganda described 15 cases diagnosed over a period of 19 years, the largest series for East Africa. Reports from other East African countries are scanty and most come in the form of case reports (5-11). To our knowledge there has been no report on African Histoplasmosis from Ethiopia. The purpose of the present communication is to describe a patient found to have *H duboisii* infection in Ethiopia and bring an awareness to look for the disease which otherwise could easily be misdiagnosed, short of histolopathologic examination.

CASE REPORT

P.K., a 19-year-old male, has been living in a small village in Southern Ethiopia for the past 3 years. He has been healthy until 4 months prior to the diagnosis when he first noted an itching painful papulo-nodular lesions over the extremities and trunk coming and disappearing in crops. The lesions progressed to form abscesses and later ulcerated. He also developed discharging sinus at the radial end of the left forearm. He had constitutional symptoms of mild fever, anorexia and marked weight loss. He was repeatedly seen in a rural hospital, and failing to respond to various topical and oral medication, he was finally referred to us.

On admission, he looked ill and debilitated. He had papular lesions over the face, multiple fluctuant abscesses, ulcers and crusts over the scalp, trunk and extremities. He also had generalized lymphadenopathy. He, however, had no fever, hepatosplenomegally or gibbus. There was no sign of chest infection.

Investigation on admission showed Hgb = 11.2 gm% WBC = 4800 mm^3 and ESR = 82 mm/hr

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1st hr. Urinalysis, BUN, serum transaminases and fasting blood sugar were all normal. Alkaline phosphatase was elevated 4 times the upper normal. VDRL was non-reactive. Rose Waaler and L.E. cell prep. were negative. The total serum protein was 9.9 gm% and albumin was 2.87 gm%. Gamma globulin was 4.4 gm%. Mantoux test and sputum for AFB were both negative. The chest X-ray on admission had bronchopneumonic infiltration at the right (R) lung base. This finding, however, resolved without treatment.

Skull X-ray showed multiple lytic lesions. X-ray of left (L) forearm showed cortical erosion of distal ulna and bony destruction and osteolysis of the adjacent radius. However, there was no sequestrum. X-ray of ribs and spine were all normal.

Histopathologic examination of a biopsy taken from a nodule showed findings consistent with *H. duboisii*. Subsequent culture from the pus and scrapping from the ulcer grew Histoplasma which was later speciated as *H. duboisii*.

Treatment: Patient was started on amphotericin B at 0.6 mg/kg/day and was later changed to 1 mg/kg every third day. He had side effects of pain, fever and chills with the initiation of medication. It was otherwise tolerable.

RESULTS

Two weeks after the start of the treatment, he had less pain and better appetite. There were no new skin lesions. At two and half months on treatment he is much better. He has an almost complete resolution of skin lesions. He has gained weight and is ambulating. To date, he has taken a total of 1.6 gm amphotericin B.

DISCUSSION

Our patient presents a classic description of African Histoplasmosis with cutaneous and bone involvement. He had X-ray evidence of pulmonary lesion which disappeared without treatment. We have not confirmed the chest involvement by sputum culture nor Giemsa stain. Culture proven pulmonary involvement, though rare, has been described both ante-mortem and post-mortem (5, 6). In many cases, however, it is suspected when it occurs together with other foci of infection. Certainly in our patient, it was not tuberculosis. The possibility that this could have been a bronchopneumonia cannot be excluded.

Radiological bony changes occur in about 2/3 of patients. The skull is the commonest site for granuloma deposition followed by the ribs, forearm etc (2). Our patient confirms this observation. The cutaneous manifestations being the earlier ones to appear, dominate the clinical presentation and we believe most patients appear to a dermatology clinic. We emphasize that the presence of painful papulonodular lesions or multiple abscesses with or without discharging sinuses in an ill-looking patient warrant a biopsy study from the lesion and a radiological survey of the bones.

A disturbance in serum albumin globulin ratio has been documented in some studies. Our patient had an elevated total protein with a reversed albumin globulin ratio. The abnormally elevated alkaline phosphatase is probably due to the bony lesions. However, the presence of granulomas in the liver must be considered, too.

The epidemiology of *H. duboisii* infection remains far from clear. This deficiency is partly due to the scanty numbers of patients observed and the disease seems never to occur in epidemics — a situation which favoured epidemiologic study in *H.* [illegible] believes the incubation period could be as long as several [illegible]

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years. Our patient has been living at the Ethio-Sudan border for the past 3 years. It is difficult to sort out where he contracted the disease. Perhaps more important is the awareness that the disease occurs here like elsewhere in East Africa and health personnel should be on the look out.

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SERO-EPIDEMIOLOGICAL SURVEY OF CYTOMEGALOVIRUS INFECTION IN ETHIOPIA

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ABSTRACT. *A sero-epidemiological survey of the prevalence of antibodies to cytomegalovirus (CMV) was carried out in two cities and three towns of Ethiopia. Sera from 500 people were investigated for immunoglobulin G antibodies by the enzyme-linked immunosorbent assay (ELISA) technique. Of 100 infants under 12 months of age, 62 were seropositive; among children 1-5, 6-10, and 11-15 years of age, 82%, 90% and 92% were seropositive respectively. Of 100 adults, 98 were positive for antibodies against CMV. Both sexes were equally affected, and financial status did not affect the acquisition of infection; nor did environmental hygiene influence the prevalence of seroimmunity. As in most developing countries, antibody prevalence is shown to be high among the study population at an early age, and the size of a family is an important determinant of the rate of seropositivity.*

Cytomegalovirus (CMV) is one of the 5 human herpes viruses. It can be transmitted from person to person by various routes, but requires intimate contact (1).

The infection is acquired by oral, congenital, parenteral, and sexual routes. Breast milk, saliva, semen, urine, cervical secretion, blood transfusion, organ and marrow transplants are sources of CMV infections. The most important mode of transmission is across the placenta and during passage through the birth canal. The inability of maternal immunity to prevent transplacental transmission of CMV makes it a unique virus and a leading cause of congenital viral infection (2-4).

In developing countries, the prevalence of antibodies to CMV is known to be high, strongly influenced by socioeconomic factors (1,3,5,6). The status of seroimmunity of our population is not known as regards CMV, as no previous study has been made. No clinical case of CMV infection was ever reported in Ethiopia.

Tsega *et al.* recently described the demographic characteristics of Ethiopia in relation to viral hepatitis (7). With an infant mortality rate estimated at about 150-200 per 1000 live births, Ethiopia is one of the poorest countries in the world (8). The objective of this study was to document the seroimmune profile of our population, in such poor socioeconomic conditions, and if possible to identify factors that are important in acquisition of CMV infection. In addition, as this was part of a broader

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study of liver diseases in Ethiopia, it was thought relevant to identify any association that CMV might have with jaundice and hepatitis.

SUBJECTS AND METHODS

The study population was drawn from Asmara, Yirgalem, Harar, Nekemt and Addis Ababa, 5 major urban centres which represented the northern, southern, eastern, western and central parts of Ethiopia, respectively. These geographical areas also happened to include the 3 major ethnic groups.

For logistic and financial considerations, we limited our study population to 500, and obtained 100 sera from each of the 5 regions. Subjects were seen in hospitals and health centres in the urban centres, and for this reason the great majority were urban dwellers, although we were able to include some people from the outlying areas. Patients or subjects who came to hospitals and health centres were randomly taken, without regard to their complaints or diagnoses.

In each region we obtained 20 blood specimens for each of the age-groups under 12 months, 1-5, 6-10, 11-15 and above 15 years of age. Using a prospectively prepared protocol, we obtained relevant epidemiological and clinical data on each subject just before blood was drawn. These included age, sex, address, marital status, occupation, financial status, number of people in the household, number of rooms inhabited by each household, source of water supply and mode of excreta disposal. An arbitrary operational poverty line was drawn at 350 Ethiopian birr per month, below which a person was considered poor; a person with a monthly income above 350 and below 500 birr was defined as average, and one above 500 birr was considered rich (7). (One US dollar is officially equivalent to 2.07 birr.) Each patient was asked about any clinical history of jaundice and/or liver disease.

Blood samples, collected by venous puncture in vacuum containers numerically coded, and sera, separated by centrifugation, were kept frozen in ice at 4°C until transported, in a day or two, to Addis Ababa, where they were stored at −20°C. Blood was drawn from femoral veins from children below the age of 6 years. Sera were finally sent by air in CO_2 ice in a portable freezer to the Virology Department at Malmö General Hospital, Malmö, Sweden. Immunoglobulin G (IgG) antibodies against CMV were determined by the enzyme-linked immunosorbent assay (ELISA) technique. The data were analysed by computer at the International Livestock Centre for Africa (ILCA), Addis Ababa.

RESULTS

The study population comprised 258 (51.6%) males and 242 (48.4%) females (male-to-female ratio 1.1 : 1); the same ratio was found in all the regions. The 3 major ethnic groups, Amhara (154: 30.8%), Oromo (127: 25.4%), and Tigre (116: 23.2%), were included, although their number is not proportional to the blend in the general population. The remainder comprised minorities. Christians constituted 83%, Moslem 15%, and others 2%. Because of the design of the study, children were over-represented in the survey population. Out of 500, 400 (80%) were under 15 years of age, and of these 40% were in the pre-school age-group. Adults above the age of 15 numbered only 100 (20%), distributed into the following occupational groups: 4% farmers, 4% nurses, 3% housewives, and 9% others.

Analysis of the economic status of the population studied was 8% rich, 28% average and 64% poor. Other indices of economic status were also considered. Family household size ranged from 2 (0.8%) to 17

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(0.2%); with a mean of 5 people per household. The majority of the households had a single room, in which about 5 persons lived (Table).

DISCUSSION

Like most serological surveys conducted in developing countries, this study indicated

TABLE. Conditions and number of persons per household in a cytomegalovirus infection survey, Ethiopia

No. of rooms per dwelling		No. of persons per household	
1	294	1 - 3	42
2	87	4 - 5	123
3 - 4	80	6 - 7	155
5 - 9	31	8 - 10	123
		11 - 17	26
Total	492*	Total	469*

*The data were incomplete for 8 and 31 respectively.

Environmental hygiene, taken as an index of economic and social wellbeing, indicated that 206 (41%) of the population drew water from unsafe sources, such as rivers, pools and wells; 294 (59%) had piped water. Excreta disposal data revealed that 200 (40%) of the population defecated in open fields, 184 (37%) in protected pits, and 31 (6%) in unprotected pits; 85 (17%) used modern toilet facilities.

Of the population studied, 7.2% had a previous history of jaundice, although none had liver disease at the time of the survey. Only 2 had hepatomegaly, and these were suspected of having schistosomiasis.

The assessment of seroprevalence of antibodies to CMW showed that 62%, 82%, 90%, 92% of those under 12 months, 1-5, 6-10, 11-15 years of age respectively were seropositive. Children under 12 months of age may have passively acquired antibodies, and the 62% seropositive may not indicate a true infection rate. Adults (over 15 years of age) were 98% seropositive. Both sexes were equally affected, and there was no difference in the distribution of seropositivity in the different regions.

that there is a high prevalence of seropositivity in our population in general, and in children in particular. In their survey of CMV antibodies in mothers and children in 19 countries, Krech and Tobin (5) amply demonstrated the often-stated fact that CMV infection is common worldwide, but much more so in the developing countries in Africa, Asia and Latin America. They showed that children of from 4 months to 4 years of age were 2.8% seropositive in England, while in Entebbe, Uganda, 95% already had antibodies to CMV at that age (5). Various reasons are given for such obvious disparity in CMV infection.

In their study of congenital CMV infections from 2 different countries but 3 socioeconomic groups, Stagno *et al.* (6) showed that socioeconomic factors are important, and determine at which age infection is acquired. Paradoxically, in contrast to the situation with other viruses such as rubella, congenital infection with CMV is higher in populations with a higher rate of seroimmunity. This contradiction is explained by the known fact that CMV has a long latency in the host, and reactivation of

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this endogenous virus in immune pregnant women results in more congenital infections in their offspring than in those of sero-negative mothers (2-4). Thus, congenital CMV infection may be one of the factors contributory to the early acquisition in most developing countries, in which congenital infection is estimated at about 0.25% to 2% of newborns. However, in developed countries where seroimmunity is relatively lower among child-bearing women, congenital CMV infection is about 0.2 to 1% (4). The newborns may also acquire infection during parturition, as seropositive mothers are known to excrete the CMV in cervical secretion.

It is also believed that a high rate of seropositivity in the first few years of life can be due to the breast-feeding habits of a people. This mechanism of CMV transmission has been shown to be important (9,10). In Ethiopia, 100% of rural, 97.3% of urban poor, and 91.4% of rich urban mothers breast-feed their babies (11). Moreover, the number of Ethiopian mothers who continue to breast-feed until the end of the first year was found to be 41%, 85% and 99% for urban rich, urban poor and rural mothers, respectively (11). In a population where the CMV seropositive rate is high, the infection rate from breast-milk alone can also be high in such circumstances. Some mothers continue to breast-feed for nearly 2 years. and they may also continue to be the source of infection during that time (12).

The social factors that go with income are considered to be significant factors in CMV infection (1,3,6), as clearly shown by antibody prevalence worldwide (5) as well as in a given community (3). However, in our study we failed to show a statistically significant difference in antibody prevalence between the rich and the poor, judged by family income (χ^2 : 4.13; P = 0.126). On the other hand, we found a statistically significant difference in antibody prevalence between those with large and small-sized families (χ^2: 18.96; P = 0.083).

A sensitive index of socioeconomic well-being may be the number of persons in a room, or the number of square metres per person. Our study showed that, on the average, 5 people lived in a single room, and this was true for about 60% of the study population. The population was drawn from major urban centres of the 5 regions, and may not be representative of a given region. However, the style of life of most urban centres is not much different from rural life in many respects. although overcrowding in cities and towns might be greater. Crowded living conditions have been postulated as an important determinant for the transmission of CMV both in the west and in the east (13,14). After the age of 20 years, sexual contact may also contribute to CMV transmission (15). In our study, other socioeconomic factors, such as source of water supply, mode of excreta disposal, sex and ethnic group, were not shown to influence the prevalence of antibodies to CMV.

Of 36 subjects with a history of jaundice, we found 32 with antibodies to CMV. To what extent CMV contributes to jaundice and hepatitis is difficult to judge, and needs further study.

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SEROLOGICAL SURVEY OF HUMAN IMMUNODEFICIENCY VIRUS INFECTION IN ETHIOPIA[1]

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ABSTRACT. *More than 26 countries, many of them in Central and East Africa, have been experiencing epidemics of human immunodeficiency virus (HIV) infection and acquired immunodeficiency syndrome (AIDS) since 1981. Yet, AIDS started to appear in Ethiopia in 1986. This serological survey was conducted on a total of 1754 sera collected from different parts of Ethiopia starting in late 1982. Sera were tested for HIV antibodies using the ELISA, ENVACOR HIV 1 EIA and the Western Blot methods. There was no positive serum during 1982 and 1983. The first 2 positive sera were detected in the 1984 collection.*

The reason for the delayed appearance and the source of HIV infection in Ethiopia are not clear. There is a trend towards a rapid rise in the rate and spread of infection. The reuse of inadequately sterilised hypodermic needles is emphasised as a possible major mode of transmission. Screening of blood before transfusion must be mandatory and the existing policy of health education should be pursued with more vigour than ever at this critical time.

The acquired immunodeficiency syndrome (AIDS) was first described in homosexual men and intravenous drug abusers in the United States of America in 1981 (1, 2, 3). During the following three years, epidemiological studies indicated that AIDS was a blood-borne and sexually transmitted disease caused by a virus either called lymphadenopathy-associated virus/immunodeficiency associated virus (LAV/IDAV) or human T-cell lymphocytotropic virus III (HTLV-III) (5); henceforth referred to as human immunodeficiency virus or HIV. By 1986 another human immunodeficiency virus (HIV 2) was described in West African patients with AIDS (6). At present, HIV infection is a major world wide social, economic and health problem. Although the problem of AIDS reached epidemic proportion in North America and Central Africa in the early 1980's, retrospective clinical and serological studies suggest that HIV infection probably occurred *de novo* and started to spread in the late 1970's. While the geographic origin remains a controversial subject there is a trend of eastward propagation of HIV infection within the African Continent.

In Ethiopia, the first few cases of clinical AIDS were diagnosed in 1986. Since then, 21 more cases of AIDS and 65 carriers of HIV antibodies have been reported by the

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AIDS Task Force of the Ministry of Health (Dr. Getachew Gizaw, personal communication). This study is a serological survey of antibodies to HIV in sera obtained from different parts of Ethiopia beginning in December 1982.

SUBJECTS AND METHODS

Subjects and origin. There were 4 groups of subjects from which sera were collected. The first group, collected between December 1982 and February 1983, consisted of 500 patients, 100 from each of the following cities (provinces): Asmara (Eritrea), Harar (Hararge), Addis Ababa (Shoa), Yirgalem (Sidamo) and Nekemte (Wollega). The age range was between less than 1 year and 53 years. The overall male to female ratio was approximately 1 : 1 and was comparable between provinces except for Sidamo, where there was a male predominance. These patients came from different parts of each province to the main hospitals and satellite health centres located in or near the capital cities for different and often minor complaints. There was no selection of patients on the basis of their presenting problems.

The second group, collected between February and November 1983, consisted of 459 healthy, volunteer blood donors seen at the Ethiopian Red Cross Blood Bank in Addis Ababa. With the exception of 19 donors, who came from different administrative regions of Ethiopia, all subjects were from Addis Ababa and its vicinity. The average age was 30 years with a range of 18 to 53 years. There were 409 (89%) men and 50 (11%) women, their occupations being civil servants, students, merchants, drivers, mechanics, military personnel and farmers.

The third group, collected throughout 1984, consisted of 167 patients with Bell's palsy and 100 normal controls. The 267 subjects, mostly under 50, were predominantly men and came from different parts of Ethiopia, referred to the neurology Clinic of Tikur Anbessa Hospital for serological screening for viral infections.

The fourth group, collected during the years 1985, 1986 and 1987, consisted of 528 patients seen and followed for a variety of liver diseases at the Liver Clinic of Tikur Anbessa Hospital. The mean age was 39.5 years, with a range from 14 to 70 years. There were 317 males and 211 females referred from different parts of Ethiopia, most from Addis Ababa and its vicinity.

Serological tests. All sera were stored at -20°C until they were shipped by air in CO_2 ice to the appropriate laboratories. Sera from groups 1, 2 and 4 were tested for HIV antibodies at the Department of Virology, Department of Medical Microbiology, University of Lund, Sweden, and from group 3 at the Ulevål Hospital, Oslo, Norway, using the enzyme linked immunosorbent assay (ELISA) method (Viromostika anti-HTLV-III, MICROELISA SYSTEM, Organon Teknika B.V. Boxtel, Holland) as a screening test for anti-HIV. The positive sera of the third and fourth group were confirmed by the Western-Blot and of the fourth group only by the ENVACOR assay (Abbott, B.V., North Chicago, Illinois, U.S.A.) for the detection of antibodies to envelope and core antigens of HIV.

RESULTS

There was no anti-HIV positive serum detected among the 959 subjects studied between December 1982 and November 1983 (Groups 1 and 2). The first 2 positive sera appeared in the group collected during 1984 (group 3) in a 26 year old man and a 20 year old woman, both with Bell's palsy. They both were from Addis Ababa but unfortunately were lost to follow-up. Subsequently there was no positive serum until September 1986. Since then, 13 patients examined for liver and gastrointestinal conditions were found to be positive for HIV antibodies (group 4) (Table 1).

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TABLE 1. Results of serological survey of HIV antibodies

Subject group	Time of sera collection	Number of sera tested		Sera positive for HIV			
				ELISA	ENV/CORE*	Western blot	
1	Dec.1982-Feb.1983	500		0	-	-	
2	Feb.1983-Nov.1983	459		0	-	-	
3	1984	267		41	-	2	
4	1985	36	528	0	0/0	-	13
	1986	77		1	1/0	1	
	1987	415		14	12/11	12	
Total	1982-1987	1754		55	13/11	15	

*ENVACOR HIV EIA assay for envelope (ENV) and core (CORE) proteins

These 13 HIV carriers were patients seen between September 1985 and October 1987 at Tikur Anbessa Hospital for gastrointestinal complaints, aged between 17 and 52 years (Table 2). There were 8 men and 5 women. Nine patients came from Addis Ababa and its vicinity, 1 each came from Dese and Mekane Selam (Welo), Bahr Dar (Gojam) and Aseb, respectively. Five of the patients were civil servants, 1 was a lorry driver, 1 an orderly, 1 a merchant, 1 a factory worker, 1 a student, 1 a farmer and 2 women were unemployed. Ten of the patients had never received blood transfusions, while the three others had a well documented history of transfusion of between 2 and 10 units. Eleven patients reported that they had received one to several injections for various conditions. Clinically, 8 patients had histologically confirmed liver cirrhosis, associated in two cases with primary hepatocelullar carcinoma, and in 1 case each with hepatic tuberculosis, non-Hodgkin's lymphoma, and multiple myloma. Four patients had vague right upper quadrant pain and non-ulcer dyspepsia. The thirteenth patient had marked weight loss, fever, excessive sweating, hepatomegaly with steatosis, and disseminated tuberculosis without lymphadenopathy; she was also positive for HBsAg.

DISCUSSION

According to the results of this serological survey, the earliest appearance of HIV antibodies in 4 different study populations in Ethiopia was in 1984. Also, the first clinically overt case of AIDS was diagnosed in 1986. Considering the long incubation time of HIV infection, from 6 months to five years and probably more, it is reasonable to assume, that HIV infection was introduced into the community of Addis Ababa by 1984. Since then, a high prevalence of HIV antibody carrier state among prostitutes (7%) in Addis Ababa has been reported (8). As was also observed in this survey, there is a rising trend in the prevalence of HIV carriers starting from early 1987 and, by January 1988, 21 cases of AIDS have been reported to the AIDS Task Force of the Ministry of Health. Two of the patients with HIV antibodies detected by this survey during 1987 (Code No. 183 and 268) fit the diagnosis of AIDS or AIDS-

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TABLE 2. Demographic and clinical data on subjects positive for HIV

Code No	Date of hospitalisation	Age	Sex	Residence	Occupation	Blood transfusion	Needles	Diagnosis
31	Sept. 1986	27	M	Addis Ababa	Civil servant	No	Often	Right upper quadrant pain without specific diagnosis.
49	Oct. 1987	18	F	Nazareth (Shoa)	Unemployed	2 units when admitted to hospital	Occasional	Marked weight loss, macronodular cirrhosis and hepatic tuberculosis, HBsAg positive with Anti-HDA. Died.
61	March 1987	50	F	Bahr-Dar (Gojam)	Divorced, unemployed	2 units before hosp.	Once	Macronodular cirrhosis
86	Sept. 1987	33	M	Addis Ababa	Civil servant	No	Often	Vague abdominal pain, dyspepsia
123	Nov. 1987	52	M	Dese (Welo)	Civil servant	No	No	Cirrhosis with hepatoma. Died on 3rd hospital day.
128	Sept. 1987	37	F	Addis Ababa	Civil servant	No	Occasional	Dyspepsia, cause unknown.
136	Sept. 1987	26	M	Addis Ababa	Orderly	No	No	RUQ pain, cause unknown.
162	Jan. 1987	17	F	Addis Ababa	Student	Over 10 units in 3 years	Several	Macronodular cirrhosis. Died from bleeding varices.
173.A	Oct. 1987	48	M	Aseb	Post administrator	No	Often	Cirrhosis and multiple myeloma.
183	Nov. 1987	51	M	Addis Ababa	Lorry driver	No	Often	Marked weight loss, macronodular cirrhosis, non-Hodgkins lymphoma. Died.
203	Feb. 1987	32	M	Addis Ababa	Merchant	No	Often	Cirrhosis, type?
268	Sept. 1987	23	F	Akaki (Shoa)	?actory worker	No	Occasional	Marked weight loss, fever, sweating. Fatty liver, disseminated tuberculosis, no lymphadenopathy, HBsAg pos.
271	Jan. 1987	52	M	Mekane Selam (Welo)	Farmer	No	Several	Macronodular cirrhosis, hepatoma

complex (9, 10).

What is the source of HIV infection in Ethiopia? Since epidemics of AIDS are claiming thousands of lives in Central and East Africa, it may be speculated that the new and delayed introduction of HIV infection into Ethiopia is part of the trans-continental spread (7). Migration of refugees across the borders, frequent visits to existing harbours by sailors, the fact that Addis Ababa is the seat of many international organizations hosting several international meetings annually and the frequency of prostitution in this capital city all favour HIV introduction and spread.

What could be the most likely mode of transmission among this population? In North America and Western Europe, homosexual promiscuity and parenteral transmission account for the majority of cases while in Africa, heterosexual promiscuity is believed to be the predominant means of transmission (11, 12). Considering the high prevalence of HIV infection among prostitutes (8), promiscuity might be the major mode of transmission in this population. However, the multiple use of inadequately sterilised hypodermics so widely practised in this country needs serious attention. "Medically promiscuous hypodermics" are known to have caused viral infections of epidemic proportions in the past (13, 14) and may be the cause for the high prevalence of hepatitis B virus infection in this country (5). Among the 13 subjects found to have HIV antibodies in their sera, 7 had several injections at different places, often for minor reasons. Until very recently, blood transfusion was carried out without screening. It is likely that at least one of the 3 blood recipients (Code No. 162) acquired HIV infection from multiple, unscreened blood transfusions. At present, with the knowledge of spread of HIV outside Addis Ababa (Bahr Dar, Dese, Mekane Selam (Welo), Aseb, Akaki and Nazareth), it is unethical to limit the screening of blood for transfusion to Addis Ababa alone. Therefore, the current efforts to extend screening facilities to other parts of Ethiopia should be pursued urgently.

In summary, this serological survey suggests the HIV infection was probably introduced to this country by 1984 and that there is a rising trend in the rate and spread of infection. We suggest that the existing health policy for the prevention of HIV infection should be pursued more vigorously than ever at this opportune moment.

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PREVALENCE OF PARALYTIC POLIOMYELITIS IN RURAL AND URBAN POPULATIONS IN ETHIOPIA: REPORT OF A HOUSE-TO-HOUSE SURVEY

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Abstract. A house-to-house survey was carried out to determine the prevalence of poliomyelitis. During the survey 37,219 households were visited and 17,941 children 5–9 years old were found. Of 231 lame children, lameness compatible with paralytic poliomyelitis was found in 131, of these 91% had their condition before the age of 3 years. Nineteen percent needed a stick support for walking while 12% were unable to walk even with support. This problem was more common in rural populations. The prevalence of paralytic poliomyelitis was 7.3/1,000 children 5–9 years old.

In recent years poliomyelitis has been recognized as a major public health problem in developing countries. Recent lameness surveys have shown prevalence rates ranging from 1.0–7.5/1,000 children, higher than initially suspected.[1–4]

Poliomyelitis is presumed to be endemic in Ethiopia, however, no reliable data on the size of the problem exists. A house-to-house survey was carried out to determine the prevalence of the sequelae of poliomyelitis.

MATERIALS AND METHODS

Children aged 5–9 years were surveyed to gain information on the incidence of the disease over the previous 5 years.

In the Gondar region a random selection was not possible; 30 clusters were drawn from communities accessible to health services. The communities chosen represented urban, urban-rural, and rural populations. An urban cluster had a population >2,000 and some piped water, electricity, a clinic, and elementary and high schools. An urban-rural cluster included a town with a population <2,000 and the people living in the surrounding area. A rural cluster is one where the population lived in homesteads in scattered areas. Of the 30 clusters, 10 were urban, 8 were urban-rural, and 12 were rural. A house-to-house survey was done from February to July 1983. The number of children in the 5–9 year age group was determined and information was obtained on any children in that age group with lameness from any cause.

All instances of lameness in 5–9-year-old children were investigated by a pediatrician, an internist, and an experienced health officer. The criteria for inclusion in the category of residual paralysis from poliomyelitis included: asymmetrical muscle weakness, atrophy and flaccid paralysis or paresis, diminished or absent tendon reflexes, normal sensation, and history of nonprogressive lameness following an acute febrile illness.

RESULTS

In the survey of the 30 population clusters 37,219 households were visited and 17,941 children aged 5–9 years were found. Of these children 231 were lame (1.3%). Residual paralysis compatible with poliomyelitis was the most common cause (131) of lameness (Table 1). The second common cause was lathyrism (43), a spastic paraplegia caused by excessive consumption of the beans of *Lathyrus sativus*. Children with this disease were found in 3 clusters near Lake Tana which had been affected by severe flooding resulting in a severe food shortage in 1974. Other causes of lameness were cerebral palsy, trauma of all kinds, and congenital deformities.

Fifty-four percent of the 131 cases of poliomyelitis with residual paralysis was in males. The rate by age showed a stable endemic situation (14.8, 18%) for all the age groups, except for the

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TABLE 1

Causes of lameness in children 5–9 years old in the Gondar region, Ethiopia

Cause	No. cases	Percent
Poliomyelitis	131	56.7
Lathyrism	43	18.6
Cerebral palsy	21	9.1
Trauma, including burns	16	6.9
Congenital deformity	11	4.8
Other	9	3.9
Total	231	100.0

TABLE 2

Age at onset of paralytic poliomyelitis

Age at onset (months)	No. cases	Percent	Cumulative percentage
≤6	22	16.8	16.8
7–11	40	30.5	47.3
12–23	39	29.7	77.1
24–35	18	13.7	90.8
36–47	7	5.3	96.1
48–59	1	0.8	96.9
≥60	4	3.1	100.0
Total	131	100.0	

5–6 year group where the prevalence rate was 34.4%.

Age of onset of poliomyelitis was <2 years in 77% of the children and <3 years in 91%. About 97% of the children had poliomyelitis at <5 years (Table 2).

Degree of disability was assessed by ability to walk with or without support. Sixty-nine percent of the lame children managed to walk without support, 19% required a stick support to walk, and 12% were unable to walk. The most common paralysis was of the left lower limb (45%); the right lower limb (36%) was the second most frequently affected extremity (Table 3).

The prevalence rate was estimated to be 7.3/1,000 for children aged 5–9 years. The incidence rate is estimated to be 1.8/1,000 in the 0–4 year age group. The prevalence rate was 3.5 for urban clusters, 10.5 for urban-rural, and 6.5/1,000 in rural clusters (Table 4).

DISCUSSION

Although our study involved a limited population sample in the Gondar Administrative Region, we believe the results are indicative of the magnitude of the disease throughout Ethiopia. It was assumed that paralytic poliomyelitis was the only cause of nonprogressive residual paralysis marked by asymmetric muscle weakness, atrophy and hypotonia of muscle, diminished deep tendon reflexes, normal sensory examination, and onset following an acute febrile illness. However, such paralysis has been described with Coxsackie and Echo virus infections.[5] Paralytic poliomyelitis was the most common (57%) cause of lameness in the 231 lame children. In India poliomyelitis was found to be responsible for 34% to 70% of lameness.[4, 6]

In our study the disease showed no predilection for males (54%). Similarly, Gharpure et al.[7] found no gender bias, but investigators from India[8–11] have found male preponderance.

The age distribution of residual paralytic poliomyelitis showed a lameness rate of 34.4% in the 5–6 year age group, while rates for the other age groups ranged from 14.8% to 18.5%. The higher rate in the 5–6 year olds might be the result of an isolated epidemic of poliomyelitis that occurred 6 years earlier. Seventy-seven percent of the cases had onset of disease at <2 years of age; in 91% of the cases, the onset was at <3 years of age. These findings reflect those found in other studies.[6, 12–14]

Degree of disability was assessed by the ability to ambulate with or without a mechanical support. Nineteen percent required a stick support to walk and 12% were unable to walk. The result was similar to that found by Basu[6] in India. The degree of disability in different countries was variable.

Estimated prevalence rates of poliomyelitis reported in studies from Ghana, Egypt, and Bangladesh[1–4] ranged from 1.0 to 7.5/1,000 for 5–14-year-old children. Our estimated preva-

TABLE 3

Distribution of residual paralytic poliomyelitis cases according to site of paralysis

Site of paralysis	No. cases	Percent	Cumulative percentage
Left leg	59	45.0	45.0
Right leg	47	35.9	80.9
Both legs	16	12.2	[illegible]
One leg + one arm	6	4.6	[illegible]
One lower leg + trunk	2	1.5	99.2
Both lower + upper limbs	1	0.8	100.0
Total	131	100.0	

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TABLE 4

Prevalence rates of residual paralytic poliomyelitis by degree of urbanization

	Urban	Urban-rural	Rural	Total
No. of clusters	10	8	12	30
No. of children surveyed	3,946	6,497	7,498	17,941
Children with residual paralytic poliomyelitis	14	68	49	131
Prevalence rate per 1,000 children	3.5	10.5	6.5	7.3

lence rate of 7.3/1,000 for the 5–9 year age group was similar to that found in rural Ghana[1,2] but lower than rates from Egypt[3] and rural Bangladesh.[4] The significance of this difference is difficult to assess.

The effect of urbanization on the prevalence rate was assessed. Estimated rates for the urban, urban-rural, and rural areas were 3.5, 10.5, and 6.5/1,000, respectively. Studies in India by Jhala et al.[9] showed prevalence rates for residual poliomyelitis of 4.23 for the urban and 5.78/1,000 for the rural areas. Basu[6] in 1981 reported a prevalence rate in India of 3.7–6.18 for urban and 4.4–8.6/1,000 children aged 5–9 years in rural areas. These data also suggest that poliomyelitis is more of a problem in rural than in urban populations. The high prevalence rate for the urban-rural population in our study may be due to a high population concentration in an extremely unhygienic environment, the absence of piped water, and the lack of health service facilities.

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Altered State of Consciousness in Adult Ethiopians: Analysis of Aetiological Factors

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ABSTRACT

A PROSPECTIVE STUDY to determine the relative incidence of diseases causing altered state of consciousness in patients admitted to the medical wards of the Tikur Anbessa University Teaching Hospital, Addis Ababa, Ethiopia was undertaken. 300 consecutive patients with altered state of consciousness were included in the study. The majority of patients were below 40 years of age. The causes for altered state of consciousness were metabolic in 125 (41.7%), infectious in 101 (33.7%) and neurological diseases in 64 (21.3%) patients. Hepatic encephalopathy, found in 74 patients (24.7%) was by far the commonest medical cause of altered state of consciousness. In 10 patients (3.3%) no definite diagnosis could be reached. 173 (57.7%) patients died. The age and disease patterns were found to be different from those seen in Europe and North America.

INTRODUCTION

ALTERED STATE of consciousness is a medical and surgical emergency which has to be dealt with urgently. Knowledge of the relative incidence of diseases causing this condition in a particular area can be most informative to physicians, whose approach to the management of the condition in patients can be likewise facilitated. To our knowledge there has been only one study[1] which has addressed itself to prognosis in non-traumatic coma in a tropical environment. Our prospective study was undertaken at the Tikur Anbessa University Teaching Hospital, Addis Ababa, to determine the relative incidences of diseases causing altered state of consciousness in patients admitted to the medical wards.

MATERIAL AND METHODS

ALTERED STATE of consciousness is defined as a clinical state manifested by conditions ranging from confusion and disorientation to person, place and time to stupor and deep coma[2].

From March 1984, up to September 1985, 300 consecutive patients that were admitted to the medical wards of the Tikur Anbessa Hospital with a diagnosis of altered state of consciousness, and patients who developed such condition while in the hospital and stayed in the same or worse state for at least 24 hours were included in the study.

According to a preset protocol, history was obtained from the closest relative available and from the patient

Age in Years	Metabolic Diseases		Infectious Diseases		Neurological Diseases		Unknown		Total	
	No. of Patients	No. of Deaths	No. of Patients	No. of Deaths	No. of Patients	No. of Deaths	No. of Patients	No. of Deaths	No. of Patients	No. of Deaths
0 - 9	-	-	-	-	-	-	-	-	-	-
10 - 19	18	6	24	10	1	-	-	-	43	18
20 - 29	20	12	35	20	6	3	2	-	63	35
30 - 39	23	15	21	10	9	5	3	2	56	32
40 - 49	23	10	9	3	13	10	2	1	47	24
50 - 59	22	19	10	8	8	5	1	1	41	33
60 - 69	12	8	1	-	13	10	1	1	27	19
70 - 79	6	4	1	-	11	3	1	1	19	8
80+	1	1	-	-	3	3	-	-	4	4
Total	125 (41.7%)	77 (44.5%)	101 (33.7%)	51 (29.5%)	64 (21.3%)	39 (22.5%)	10 (3.3%)	6 (3.5%)	300 (100%)	173 (100%)

Table I. Altered state of consciousness in 300 Ethiopian medical patients. The age pattern, major groups of diseases and their outcome.

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	No. of Patients	Mortality
Metabolic Diseases	125 (100%)	77(61.6%)
Hepatic Encephalopathy	74 (59.2%)	57
Renal Failure	18 (14.4%)	11
acute	2	1
chronic	16	10
Poisoning	14(11.2%)	4
Organophosphate compounds	7	2
Chlorpromazine	2	1
Phenobarbitone	2	-
Carbonmonoxide	1	-
Unknown	2	1
Diabetic Ketoacidosis	13(10.4%)	4
Others	6(4.8%)	1
Infectious Diseases	101(100%)	51(50.5%)
Relapsing fever	20(19.8%)	12
Cerebral malaria	16(15.8%)	8
Septicemia	16(15.8%)	11
Typhoid fever	14(13.9%)	6
Tuberculous meningitis	11(10.9%)	8
Pyogenic meningitis	8(7.9%)	3
Others	16(15.8%)	3
Neurological Diseases	64(100%)	39(60.9%)
Intracranial bleeding*	24(37.5%)	21
Atherothrombotic stroke	17(26.6%)	9
Cerebral emboli	8(12.5%)	6
Others	15(23.4%)	3

Table II - The different diseases and their outcome.

* The diagnosis of intracranial bleeding include hypertensive intracerebral bleed and subarachnoid hemorrhage.

after he or she got better. Detailed general and neurological examination was performed on every patient. Determinations of hemoglobin, white cell count, sedimentation rate, urinalysis, fasting blood sugar, blood urea nitrogen, serum creatinine, serum transaminase levels, alkaline phosphatase, bilirubin, serum sodium and potassium and examination of the blood film for haemoparasites were done. Lumbar puncture for cerebrospinal fluid analysis was performed in patients with suspected infections of the central nervous system and those with cerebrovascular accidents. A bloody cerebrospinal fluid was taken diagnostic for both intracerebral bleeding secondary to hypertensive cerebrovascular accident as well as subarachnoid hemorrhage from other causes.

Hepatic encephalopathy		Septicemia	
Liver cirrhosis	48	Septic abortion	5
Primary hepatocellular carcinoma	13	Post-delivery	1
Cholangiocarcinoma	1	Malingnancy (Hematological)	3
Acute viral hepatitis (1 pregnant)	10	Diabetes mellitus	2
Chronic active hepatitis	1	Ascending cholengitis	1
Reye's syndrome	1	Acute pancreatitis	1
		Unknown	3
Total	74	Total	16

Table III - Underlying Diseases in hepatic encephalopathy and septicemia

RESULTS

OF THE 300 patients included in the study, there were 186 males and 114 females. 83.3% of patients were below the age of 60 years, 54.0% were below the age of 40 years and 35.5% were below the age of 30 years. 173 patients died (57.7%) (Table 1).

The major groups of diseases encountered were metabolic in 125 (41.7%), infectious in 101 (33.7%), and neurological in 64 (21.3%) patients. No definite diagnosis could be be reached in 10 patients (3.3%). Hepatic encephalopathy was the single most common disease and 59.2% of the metabolic diseases (Table 2). Table 3 shows the underlying diseases in patients with hepatic encephalopathy, and septicemia. The precipitating factors for hepatic encephalopathy were upper gastro-intestinal bleeding, infection, hepatotoxic drugs and for diabetic ketoacidosis mainly infection (Table 4).

Out of 13 patients with diabetic ketoacidosis diabetes mellitus was diagnosed for the first time in 6 patients. The ingestion of poisons or overdose of drugs was intentional in 11 patients and accidental in three patients. Jaundice was present in 14 of 20 and 12 of 16 cases of relapsing fever and cerebral malaria respectively.

The cerebrovascular accidents accounted for 49 of the 64 patients (76.6%) with neurological diseases. History of hypertension was obtained from 14 of 24 and five of 17 patients with intracranial bleeding and thrombotic stroke respectively. In all patients, treatment of the hypertension was irregular and follow-up poor and erratic. Out of eight patients with cerebral emboli, six patients had atrial fibrillation. In three of the six patients, the cause of atrial fibrillation was mitral stenosis secondary to rheumatic heart disease.

Hepatic Encephalopathy	
Upper Gastrointestinal Bleeding	21
Infection	8
Hepatotoxic drugs	3
Undetermined	42
Total	74

Table IV - Precipitating Factors of hepatic encephalopathy.

DISCUSSION

IN A prospective study of non-traumatic coma done in Europe and North America, Bates *et al.*[3] and Levy *et al.*[4] found that diffuse hypoxic ischemia due to cardiac arrest, profound hypotension, and respiratory arrest accounted for the majority of the cause of coma, which is in contrast to our finding where hepatic encephalopathy and infectious diseases were the major aetiologic factors.

The majority of our patients were young reflecting the population structure of our society. This age distribution pattern was also noticed in other similar studies reported from different parts of the country[5-10]. But in the European study[3] the majority of patients were

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between the age of 50–79 years with a mean age of 58 years. Hepatic encephalopathy was the most common single diseases encountered (24.7%). This reflects the common occurrence of liver disease in Ethiopia as shown in previous studies where it accounted for up to 12% of diagnoses of medical admissions to hospitals in Ethiopia[5–9]. This is in contrast to findings in Europe and North America where hepatic encephalopathy was found in 10.7%[3] and 10.2%[4] of patients with altered state of consciousness.

Infectious diseases were the cause in 33.7% of our patients while it was only found in 13.2% and 3.2% patients reported by Bates *et al.*[3] and Levy *et al.*[4] respectively. Jaundice was present in the majority of patients with relapsing fever and cerebral malaria. Thus examination of the blood film for haemoparasites, repeatedly if need be, should be one of the first investigations in the unconscious and jaundiced patients in the African setting. This prevents further delay in diagnoses and management of these curable diseases, which is the major factor for unfavourable outcome[13,14]. As shown in previous studies, the absence of fever does not rule out the presence of these diseases[15].

Organophosphate compounds were the most common poison used. Similar findings were reported from Kenya[11] and Uganda[12]. These compounds are used as pesticides in farms and are also available at low cost in the open markets for use as insecticides at home. Appropriate measures to control the availability of these compounds for use other than the one they are intended for is necessary.

In the six patients with septicemia, and two patients with acute renal failure, septic abortion was the underlying illness. A similar finding was reported previously in patients with acute renal failure[16].

The reasons for inadequate treatment and poor follow-up of patients with hypertension and cerebrovascular accidents are not well studied. From our clinical observation, the lack of adequate facilities for early diagnosis, treatment and follow-up of patients and the lack of aggressive effort by medical practitioners to set up a programme for control of hypertension are the main reasons at this stage. Other contributing factors include the low socio-economic status of patients to afford long term drug therapy, return of patients to their native villages after diagnosis where no further follow-up is possible and their low education status to comprehend the long-term complications of the disease. These problems have also been encountered in other African countries[17,18].

Thus there is a need to intensify our efforts in the early diagnosis of hypertension in the community and inform the public through mass health education programmes the dangers of hypertension and the value of treatment and regular follow-up. Several studies have shown that there is a definite favourable effect of control of hypertension in the prevention of stroke[19–23].

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was part of an epidemiological study of hookworm endemicity in the area. The study area is located at an altitude of 1900m, about 45km west of the city of Gondar in a small town called Mizaba in North-west Ethiopia.

RESULTS

The highest rate of infection was observed in April 1985 and the lowest in February and July of the same year (Figure 1). There are apparently two peaks, although not well defined, per year, one in March-May and the second one in August-October.

Figure 1

The monthly rates of infection of 103 school boys and girls who were examined monthly for 14 consecutive months beginning in August 1984 and ending in September 1985.

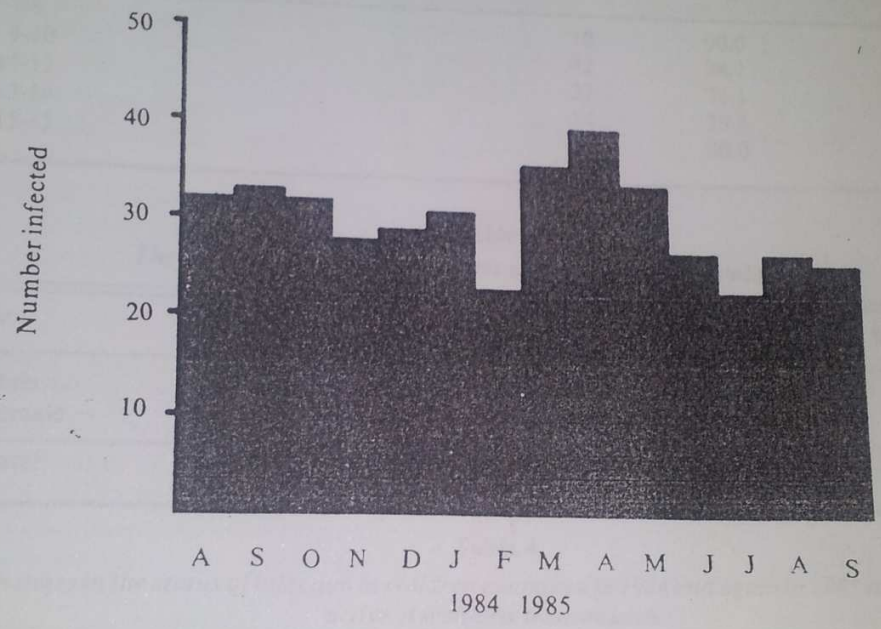


Table 1

Frequency of appearance of eggs in stool of 103 school children who were examined every month for 12 consecutive months (August 1984 to July 1985). Frequency is defined as the number of months in which eggs of "A. lumbricoides" were recovered in the year.

Frequency	*No. of pupils*	% of total
0	17	16.5
1-3	39	37.8
4-6	26	25.2
7-9	14	13.6
10-12	7	6.8

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The frequency of appearance of ova of *A. lumbricoides* in stool during a period of one year varied from 0 to 12 (Table 1). Most stool specimens did not have ova for most of the year (Table 1).

The highest rates of infection as measured by period prevalence were observed in children below 11 years of age (Table 2). The frequency of appearance of eggs appears to be independent of the period prevalence observed in each age group (Table 2).

Table 2

The relationships of age and rates and frequency of infection by "A. lumbricoides". Frequency here denotes the number of times (months) in which eggs were found in stool of any one individual. (Frequency ranges from 0-12). One slide per stool sample per month was examined for consecutive 12 months (August 1984 to July 1985).

Age groups (yrs)	*No. exam.*	*% + ve*	*Frequency*
7-8	10	90.0	3.5
9-10	42	88.1	4.2
11-12	27	74.1	3.7
13-14	14	78.6	3.9
15-18	10	80.0	3.0

Table 3

The relationships of sex and rates of infection by A. lumbricoides

Sex	*No. exam.*	*No. infected*	*% + ve*
Male	30	23	76.7
Female	73	63	86.3
Total	103	86	83.5

Table 4

Changes in the status of infection in children examined in 1984 and again in 1985 in an area of active Ascariasis transmission.

Month	*Age (yrs)*	*No. Exam. (both yrs.)*	*No. +ve 1984**	*Conversion+*	*Reversion*	*No. +ve 1985*
August	7-18	103	32 (29.9)	20 (28.2)	25 (78.1)	27
September	7-18	103	33 (32.0)	13 (18.6)	20 (60.6)	26

*Number of parenthesis are percentages
+Number in parenthis indicated percentage incidence.

There was no significant difference between the rates of infection of males and females (Table 3).

There appears to be a reduction in incidence of infection as measured by the ratio

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DISCUSSION

The overall infection rate by *A. lumbricoides* at any one time is low compared to previous studies (1, 7). A more reliable picture of infection patterns can be obtained by examining more than one slide per specimen per month; this was not possible in the present study.

There are apparently two peaks in the monthly rates of infection, one in March-May and the second in August-October. These peaks may be associated with the rainy seasons in the year. The region normally receives rain twice a year, once during February-April (small rainy season) and the second in June-September (the heavy rainy season). The availability of moisture which is required for the survival of Ascaris ova in soil may have reflected itself in the transmission pattern observed in this study. The infection that occurred during the rains, leaving a couple of weeks for larval development in soil at the beginning of the rains, appears to manifest itself about 8 weeks after the beginning of the rains. About six weeks after infection were required prior to the detection of ova in stool. The results obtained may indicate continuous loss and gain of parasites.

Some pupils were apparently free from infection throughout the year, while most were free for most parts of the year (Table 1). It is likely that low levels of infection may have been maintained throughout the study period and still remaining undetected due to the resultant low level of the number of eggs in stools.

The highest period prevalence is 90%, 7-8 year old group and the lowest 74.1%, 11-12 year old group (Table 2). The frequency of appearance of ova in stool of each age group may indicate an apparently low rate of infection in the community. It must, however, be noted that the number of pupils examined in each age group is small, and comparisons based on such small numbers are not reliable.

It is surprising to note that the frequency of appearance of eggs and the period prevalence do not show any association (Table 2). One would have expected the highest period prevalence to occur in age groups in which the highest frequency of appearance of ova is recorded. One possible explanation for the present observations may be that period prevalence indicated susceptibility to infection, while frequency of appearance of ova indicated resistance to infection.

It is not surprising to note that there is no difference in the period prevalence of infection in males and females, since most studies in Ethiopia have shown similar results (7).

The incidence of infection was declining during the study period (Table 4). In the absence of any known direct man-made intervention that affects the prevalence of the parasite in the community, it is suspected that the reduction may be due to environmental changes. The overall dry conditions of 1985 may have contributed to the apparent reduction in transmission. The reduced moisture level may contribute towards the reduction in transmission, by detrimentally affecting the development of the infective stage.

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A HOUSE-TO-HOUSE SURVEY OF NEONATAL TETANUS IN URBAN AND RURAL AREAS IN THE GONDAR REGION, ETHIOPIA

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Abstract. A house-to-house survey of neonatal tetanus was performed in 30 population clusters in Gondar, Northwestern Ethiopia. At the end of the survey 37,219 households were visited and 2010 live births were recalled. Out of the 2010 live-born children 127 had died. Eighty died during the neonatal period. Nine of the neonatal deaths were due to tetanus, giving a neonatal tetanus mortality rate of 4.5/1000 live births. The problem of neonatal tetanus in developing countries, particularly that of Ethiopia, is discussed.

Key words: Neonatal tetanus; house-to-house survey; Ethiopia

Introduction

Recent community surveys have shown that neonatal tetanus is a serious health problem in developing countries. The high prevalence of this preventable disease is due to lack of education and inadequate antenatal care of the mother and immediate postnatal care for the infant.

In Ethiopia the Expanded Programme on Immunization was started in urban areas in 1980. The antenatal and postnatal care is still rudimentary and inadequate. The mortality and incidence rates of neonatal tetanus are unknown.

In order to save resources and to test the feasibility of a combined survey method, a house-to-house survey in the same population was performed to determine the mortality and the annual incidence rates of neonatal tetanus and the prevalence of the sequelae of poliomyelitis.

Methods

In most fatal cases of neonatal tetanus, the history obtainable from the mother is precise enough for the causes of death to be diagnosed with reasonable accuracy. In a survey performed in Ivory Coast, it was shown that the accuracy of recall deteriorated after seven months [1]. An effective survey may therefore be carried out by a house-to-house enquiry into the fate of all children born over a period of six months. Because children born in the month leading up to the date of the survey were still in their neonatal period (and therefore were still at risk of dying as neonates), they were excluded from the survey and enquiry was made only of those live-births occurring in the six months period which ended one month before the date of the survey.

In the conditions prevailing in Gondar administrative region, northwestern Ethiopia, a truly random selection was not possible. Therefore selection of the 30 population clusters was made from communities

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which are currently accessible to the health services. The communities for the survey have been chosen to represent urban and rural populations as well as high land and low land areas.

In the 30 population clusters selected a house-to-house survey was carried out from February to July 1983. Using pretested survey forms a number of clinical and epidemiological data were collected on 67 live births in each cluster population. During the same household visits, the number of children in the age group of 5 to 9 years was determined. Information was obtained on any children in that age group with lameness from any cause (reported elsewhere). Well-known national and local events as well as religious holidays were used to assist parents in recalling the date of birth, death and onset of the disease. The survey was carried out by 12th grade school leavers who were trained for the purpose and supervised by the investigators. The possible causes of death were determined by the investigators. The criteria for accepting a neonatal tetanus death as due to tetanus were: death occurring between the third and the thirtieth day of life of a child who was breast fed and behaved normally for the first two days after birth, and failure to suck at the onset of illness, followed by trismus, spasm, rigidity and convulsions before death.

Results

At the end of the survey 37,219 households were visited and 2010 live births were recorded. Out of the 2010 live-born children 127 had died. Eighty of the deaths occurred within the neonatal period. The main causes of death were bronchopneumonia, prematurity, tetanus, asphyxia and sepsis. In 20.5% the cause of death could not be ascertained. Nine infants died of neonatal tetanus. Seven out of the nine died within 15 days after birth. Eighty-nine percent of the 127 infants who died were delivered at home. Of these, 104 were delivered by untrained traditional birth attendants (TBA). The umbilical cords were cut in all cases with new blades. The nine neonatal cases were delivered by untrained TBA. Three of them had surgical procedures by a local healer.

Out of the 2006 mothers 452 (22.5%) had two vaccinations with tetanus toxoid. When this was analysed by locality it was found that only 245 (36.6%) of the urban, 133 (22.1%) of the urban-rural, and 74 (10.1%) of the rural mothers were vaccinated. All the mothers of the neonatal tetanus patients were unvaccinated.

The overall annual incidence of neonatal tetanus was 4.5/1000 live births. The incidence for the urban clusters was zero, while that of the urban-rural areas and rural areas were 6.6 and 6.8/1000 live-births respectively. The incidences for the clusters with altitudes below 2000 meters and above 2000 meters were 3.7 and 5.0/1000 live births respectively.

A retrospective study of the paediatric admission records of the Gondar Hospital from January 1977 upto January 1983 showed the average case fatality rate for neonatal tetanus to be 71% and the annual incidence 4.4/1000 paediatric admissions.

Discussion

Neonatal tetanus is a major health problem which is associated with high morbidity and mortality. In Ethiopia the magnitude of the problem has not been defined. The case fatality rate of neonatal tetanus from our hospital admissions was 71% which is comparable to that found by Anu Gupta *et al.* [2] and Seghal *et al.* [3] which ranged between 70-80%. The fatality rate is also high in other parts of the world [4-7].

The mortality rate of neonatal tetanus from our survey was 4.5/1000 livebirths, which we think is a gross underestimination of the real situation. The high rate (89%) of home delivery, the high delivery rate (81.8%) by untrained TBA, the low maternal vaccination rate (22.5%) and the frequent traditional surgical interventions, such as tonsillar scrabbing, circumcision and avulectomy, favour a high neonatal tetanus infection rate. However the reluctance of mothers to give information about dead

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infants and the inability to diagnose 20.5% of the cases might have contributed in reducing the neonatal mortality rate.

The result is, however, similar to that of recent surveys which showed neonatal tetanus mortality rates of less than 5/1000 live births [8]. The mortality rates in Bangladesh, India, Somalia [8] and Pakistan [9] were more than 20/1000 live births.

The survey also showed that neonatal tetanus is more of a problem in rural than in urban areas which is similar to the results of surveys done elsewhere [8-11]. Clusters with altitudes above 2000 meters had a higher neonatal tetanus mortality rate than those below 2000 meters, which is contrary to the findings of Mazzefero *et al.* [12] who reported the highest incidences in subtropical regions, intermediate rates in temperate and the lowest rates in cold regions.

As expected tetanus occurred more frequently among babies delivered at home by untrained TBA than those delivered in hospitals or clinics, which is similar to the findings of Chen [13] in rural Malaysia. The maternal vaccination rate in our study was only 22.5% and the mothers of the nine neonatal tetanus cases were not vaccinated. The value of using trained TBA and maternal immunization with tetanus toxoid in reducing the neonatal tetanus mortality rate was clearly demonstrated by Berggren *et al.* [14] in a rural area of Haiti in 1972. Newell *et al.* [15], in 1966, used toxoid vaccine for the prevention of neonatal tetanus in a double controlled field trial. Not a single case of neonatal tetanus occurred in the babies of mothers given two or three doses of tetanus toxoid.

Neonatal tetanus is a serious public health problem in Ethiopia and it can only be controlled if measures are taken to train TBA and immunize all expectant mothers with two or more doses of tetanus toxoid.

Our study also demonstrated that the combined survey method is a relatively cheap and effective epidemiological tool.

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THE USE OF HAEMOGLOBIN A_1 IN THE EVALUATION OF DIABETIC CONTROL IN ADULT ETHIOPIAN DIABETICS

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ABSTRACT. *In 69 non-insulin-dependent (NIDDM) and 54 insulin-dependent (IDDM) consecutive diabetics and 70 healthy controls, all Ethiopians, diabetic control was initially assessed in an Addis Ababa hospital by the traditional method (TM), and later glycosylated haemoglobin (Hb) A_1 was checked, to assess the diabetic control and also to evaluate the TM's usefulness. There were 65 NIDDM patients on oral agents, and 4 on diet control. The majority of the IDDM patients required more than 40 units of Lente insulin. The mean HbA_1 for the IDDM, NIDDM and controls was, respectively, 11.3% ± standard deviation 3.1, 9.6% ± 1.9 SD, and 6.9% ± 1.6 SD. The overall concordance rate between the two methods of assessment was 57%; concordance was better in the IDDM (66.7%) than in the NIDDM (49.3%). Of 74 diabetics judged as poorly controlled by the TM, only 51 (68.9%) had HbA_1 over 10%, and 9 of 17 patients who had good control according to the TM had normal HbA_1, indicating that the TM is not always reliable, and thus confirming other studies' observations. It is suggested that HbA_1 assay should be available at least in major teaching and research centres, where many diabetics are being followed up.*

Although glycosylated haemoglobin has been available for the assessment of diabetic control for over a decade, its clinical application has been limited to specialised laboratory centres until fairly recently. However, with the introduction of the micro-column chromatographic techniques, using kits, the determination of glycosylated haemoglobin has become much simpler for wider clinical use.

There are various types of chromatographically separable minor haemoglobins in the red blood cell haemolysates of normal adults. But the ones used to monitor diabetic control are Hb (haemoglobin) A_1 and HbA_1c (1-3). HbA_1 is composed of HbA_1a, HbA_1b and HbA_1c. Although all the fractions are increased in poorly controlled diabetics (3), HbA_1c accounts for about 70% of the total HbA_1.

Glycosylated haemoglobin is an important tool in assessing the state of diabetic control over the previous several weeks. At the Tikur Anbessa (Black Lion) Hospital Diabetic Clinic, Addis Ababa, we have been relying on the traditional method (TM) (i.e. patient history, and urine and blood glucose measurements, at the time of clinic visits) to evaluate diabetic control. Although the limitations of the TM are well known (4-7), there was formerly no objective way of evaluating its worth in our circumstances. Thus, in this study, HbA_1 was checked in diabetics, firstly to assess the state of diabetic control, and secondly to compare the result with that of the TM in order to evaluate the latter more objectively, and then to find out the extent of

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usefulness under our conditions.

PATIENTS, MATERIALS AND METHODS

Patients. A total of 123 consecutive Ethiopian diabetics was included in the study. The details of the clinical data are given in Table 1. Each patient was examined for evidence of complications, and the fasting blood sugar (FBS) was determined on at least 2 occasions before checking the HbA_1 2 to 3 months later. In addition, the patients were interviewed for symptoms of diabetes, particularly nocturia, thirst and blurred vision, which are better recalled, and so give more reliable information. Urine sugar was checked less frequently.

Of the non-insulin-dependent diabetes mellitus (NIDDM) patients, 65 were on oral agents, and 4 on diet control. A majority of the insulin-dependent diabetes mellitus (IDDM) patients required over 40 units of Lente insulin, taken as single injection; split doses were less frequently accepted. None of the NIDDM or IDDM patients had excessive blood loss, alcoholism, renal failure or haemolytic anaemias. There were 8 NIDDM and 4 IDDM patients who had liver cirrhosis, but without decompensation. The diagnosis of liver cirrhosis was made on the basis of clinical findings and abnormal liver function test results.

The patients were divided into 3 groups according to the degree of diabetic control as judged by the HbA_1 level or by TM: (a) poor control, when the HbA_1 was over 10%, or when the FBS was more than 10mmol/L (> 180mg/dl), nocturia of more than 3 times, presence of blurred vision, and moderate to severe thirst (drinking 3 litres or more daily); (b) fair control, if the HbA_1 was 8.1%-10%, or if the FBS was 7.8 to 10mmol/L (140 to 180mg/dl), nocturia up to twice, and mild thirst (drinking up to 2 litres daily); (c) good control, when the HbA_1 was equal to or less than 8%, or when the FBS was below 7.8mmol/L (< 140mg/dl), nocturia of nil to once, and no thirst.

Other tests performed included urine protein, blood urea nitrogen, liver function tests and creatinine.

Neither patients nor controls were screened for haemoglobinopathies, since the conditions were extremely unlikely to be present.

Controls. Seventy consecutive healthy Ethiopian individuals (38 females and 32 males) with a mean age of 38.4 ± 15.8 years (± standard deviation) participated in the study.

HbA_1 assay. Blood drawn from each person was assayed for HbA_1 on the same day by the microcolumn chromatography technique (Boehringer Mannheim GmbH Laboratories, West Germany). The method used was modified from Schnek and Schroeder (8), and all observations were meticulously carried out in accordance with the manufacturers' directions. Briefly, 0.05ml of whole blood was mixed with 0.2ml of 0.1% borate buffer (eliminator for labile HbA_1) reagent, pH 7.0, and the mixture, shaken thoroughly once or twice during that time, was kept at room temperature for 30 minutes. Then 0.05ml of the haemolysate was applied to a weakly acidic cation-exchange resin in a disposable column. To this, 0.2ml of phosphate buffer, pH about 6.7 (the elution reagent), was added; the eluate was allowed to drain completely, and was then discarded. Another 4ml of the phosphate buffer was added to the column; the eluate, collected over a period of 30 to 40 minutes, was thoroughly mixed, and the absorbance A_1 was measured by the Beckman spectrophotometer (Du-50, USA) within 5 minutes. Finally 4ml of sodium chloride was added to the column, and the eluate was collected in 10 minutes. Fifteen millilitres of redistilled water was added to this eluate, and, after thorough mixing, the absorbance A_2 was measured within 30 minutes. HbA_1 was then calculated, using

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the following formula:

$$\% HbA_1 = \frac{A_1}{A_1 \pm (4.75 \times A_2)} \times 100$$

According to the manufacturers, HbA_1 value of 5%-8% indicates normal metabolism, while a value over 10% indicates poor metabolic adjustment.

The unpaired T-test for independent means with pooled variance was used for statistical analysis. The chi-square test was used to check for differences between proportions.

RESULTS

The mean HbA_1 in the IDDM patientswas 11.3% ± 3.1(± SD), significantly different ($P < 0.001$) from the mean HbA_1 of 9.6% ± 1.9 SD in the NIDDM patients. In the control group, the mean HbA_1 was 6.9% ± 1.6 SD (range 5.6 to 7.9), and this was significantly different ($P < 0.001$) when compared with that of the IDDM and NIDDM. Furthermore, the finding in this group of healthy individuals was similar to that in the Caucasians catered for by the manufacturers of the materials for the assay (5%-8%). The overall concordance rate between the evaluations by the HbA_1 and the TM was 66.7% in the IDDM and 49.3% in the NIDDM patients.

The relations between the TM of evaluation and the HbA_1 level are given in Tables 2 and 3. Among the NIDDM group (Table 2), 26 patients (37.7%) had HbA_1 greater than 10%, and, of these, 19 had poor metabolic control when they were assessed by the TM. Of the 21 NIDDM patients (30.4%) with normal HbA_1, 7 had good metabolic control and 3 poor control, according to the TM. In the IDDM group (Table 3), 36 patients (66.7%) had HbA_1 over 10%, while 12 (22.2%) had normal HbA_1; 32 of the former and 5 of the latter had poor control, as judged by the TM.

Five of the 8 NIDDM and 3 of the 4 IDDM patients who had liver cirrhosis had HbA_1 over 10%.

DISCUSSION

The pathogenesis of the long-term diabetic complications, such as the microvascular disorders, still remains a controversial issue. One of the hypotheses that has been advanced is the presence of poor diabetic control over a long period of time (9). Indeed, there are studies which indicate the usefulness of good metabolic control in the prevention of long-term complications (10,11).

Thus, while good metabolic control is believed to prevent long-term diabetic complications, good control *per se* requires an objective means of long-term assessment. Traditionally, clusters of symptoms and signs, with urine glucose and blood glucose values at the time of each visit, have been and are still being used to assess diabetic control. The inaccuracy of urine glucose in some patients, and the poor specificity of historical data, are well known (4-7); hence these parameters are not wholly dependable. In addition, sporadic FBG determinations, as practised in different hospitals and clinics in Ethiopia as well as in other developing countries, reflect no more than the metabolic state at single points in time, chosen from a frequently changing continuum of blood glucose control; hence these cannot give information about the previous metabolic state. (The gap in time between the FBG tests and the HbA_1 assay was unavoidable.) Certainly, home glucose monitoring is important in properly assessing diabetic control, but the cost is high for use in our circumstances, while spot blood glucose determinations are important for the im-

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TABLE 1. Clinical data of non-insulin-dependent diabetes mellitus and insulin-dependent diabetes mellitus patients

Clinical data	NIDDM[1]	IDDM[2]
Total number	69	54
New patients[3]	23	14
Old patients[4]	46	40
Male	33	27
Female	36	27
Age (years)		
Range	23 - 75	15 - 46
Mean ± standard deviation	47.9 ± 12	28.5 ± 10.9
Complications		
Neuropathy	29	15
Retinopathy	17	17
Nephropathy	9	12
Peripheral vascular disease	3	2
Haemoglobin A_1 (%)		
Range	6.2 - 16.3	7.3 - 20
Mean ± SD	9.6 ± 1.9	11.3 ± 3.1
Fasting blood glucose (mmol/L)		
Range	5.9 - 13.7	9.7 - 16.4
Mean ± SD	11.4 ± 2.1	12.8 ± 2.9

[1]non-insulin-dependent diabetes mellitus; [2]insulin-dependent diabeter mellitus; [3]duration of diabetes less than one year; [4]duration of diabetes more than one year

TABLE 2. Relation between traditional method of evaluation and HbA_1 value in 69 NIDDM patients

HbA_1 value (%)	Traditional method of evaluation			Total
	Good	Fair	Poor	
8	7	11	3	21
8.1 - 10	3	8	11	22
> 10	2	5	19	26
Total	12	24	33	69

TABLE 3. Relation between traditional method of evaluation and HbA_1 value in 54 IDDM patients

HbA_1 value (%)	Traditional method of evaluation			Total
	Good	Fair	Poor	
8	2	5	5	12
8.1 - 10	0	2	4	6
> 10	3	1	32	36
Total	5	8	41	54

mediate management of the diabetic.

In this study, the usefulness of the TM in the evaluation of long-term diabetic control was studied, using HbA_1. The overall concordance rate between the TM and the HbA_1 level was about 57%; concordance rate between the NIDDM and TM versus the IDDM and TM was not different ($\chi^2 = 3.74$, $P > 0.05$) (Tables 2 and 3). It should be noted that this finding was not affected by the inclusion of the 12 patients with liver cirrhosis. Of the total 74 patients (60.2%) who were judged as poorly regulated by the TM, 51 (68.9%) had HbA_1 over 10%; the concordance rate between the two methods was better for the IDDM group than for the NIDDM group (32/41 vs 19/37), the difference being significant ($\chi^2 = 6.12$, $P < 0.025$). Of the total 17 patients who had good control according to the TM, only 9 had normal HbA_1 level. These findings indicate that judgements made by using the TM are not always reliable. The non-specificity and poor sensitivity of the TM in assessing diabetic control has been reported by Nathan *et al.* (12) and Gonen *et al.* (13).

On the other hand, the usefulness of the glycosylated haemoglobin assay in the long-term assessment of diabetic control has been studied by different authors (14-16). Indeed, currently there is no single assessment that is as informative as the glycosylated haemoglobin assay about the long-term metabolic control of the diabetic. The technique is simple, and the cost per test is about 7 Birr (1 US$ = 2.07 Birr). The cost of HbA_1, as it stands, may appear expensive, but, when compared with the costs incurred in making sporadic blood glucose and urine glucose determinations, together with the limitations these tests have (4-7), it may in fact be relatively cheaper. Therefore, for a better long-term assessment of the diabetics, it is suggested that the HbA_1 assay should be available at least in the major teaching and research centres, where the course of diabetes in many patients is being followed up.

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ADDENDUM. Reference 8, above, should read as follows:

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INCIDENCE OF RENAL AMYLOIDOSIS IN ADULT ETHIOPIAN TUBERCULOSIS PATIENTS

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INCIDENCE OF RENAL AMYLOIDOSIS IN ADULT ETHIOPIAN TUBERCULOSIS PATIENTS.
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INCIDENCE OF RENAL AMYLOIDOSIS IN ADULT ETHIOPIAN TUBERCULOSIS PATIENTS.

M. MENGISTU

SUMMARY

In a study of 120 adult Ethiopian tuberculosis patients who were admitted to the Black Lion Teaching Hospital (BLTH) in Addis Ababa, Ethiopia, there were 9 patients who had significant proteinuria. Of these, 6 had renal amyloidosis which was proven by renal biopsy; this makes an incidence of 5%. Two patinets had renal failure of which one died. The difficulties in following patients to assess the effect of anti-tuberculous therapy on the renal lesion is discussed. Renal amyloidosis is almost always fatal and the only way to prevent it is by controlling tuberculosis.

INTRODUCTION.

Secondary amyloidosis has been reported in connection with tuberculosis. In 1974, it was reported that 75% of 200 cases from India, 54% of 37 cases from a Scottish series and about 33% of 22 patients from an American series had secondary amyloïdosis due to tuberculosis (1). In Iran tuberculosis was the main cause of renal amyloidosis (2,3).

In Ethiopia, tuberculosis, in its various forms, is still prevalent; and indeed, it is estimated that 2% of the population or 600,000 people suffer from the disease and of these only very few patients get the proper treatment.

The incidence of renal amyloidosis in tuberculosis patients in Ethiopia is unknown. A study was conducted in 120 patients who were consecutively admitted to the BLTH, in order to find out the incidence of renal amyloidosis. The results of this study are described in this paper.

MATERIALS AND METHODS

Of 120 tuberculosis patients who were admitted to the medical department between April 1980 and December 1981, 67 were females and 53 males. The age ranged from 14 to 70 years (mean 28.2 years). The diagnosis of tuberculosis was

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established by radiology, positive acid fast bacilli in the sputum or visceral fluid, biopsy and a positive Mantoux test. The types of tuberculosis and the distribution by sex are given in Table 1.

Table 1

Type of tuberculosis according to sex and incidence of renal amyloidosis in 120 Ethiopian tuberculosis patients.

Type	Male	Female	Total	Number of Renal amyloidosis	Incidence (%)
Pulmonary tuberculosis	33	37	70	2	1.67
Disseminated tuberculosis	6	14	20	0	0.00
Tuberculous peritonitis	4	10	14	1	0.83
Tuberculous lymphadenitis	5	4	9	3	2.50
Tuberculous spondylitis	4	1	5	0	0.00
Tuberculous pericarditis	1	0	1	0	0.00
Renal tuberculosis	0	1	1	0	0.00
Total	53	67	120	6	5.00

Nine of 120 patients (7.5%) had significant proteinuria in 24 hours urine specimen on different occasions. Renal biopsy was performed in 6 of these patients who consented to the procedure.

In the remaining 111 patients renal biopsy was not considered since they had no evidence of renal involvement. The renal tissue obtained was put in 10% formalin. Thin paraffin sections were stained with standard stains including periodic acid Schiff (PAS) and Congo Red. The slides were examined by light microscopy.

RESULTS

The clinical, biochemical and histological data are indicated in Table 2. Of 9 patients with significant proteinuria, 7 were females and 2 males. The proteinuria ranged from 1.9 gm to 14.4 gm(mean 7.3 gm) per 24-hours urine specimen. All patients had other manifestations of the nephrotic syndrome as well. The mean serum protein was 4.4 gm (range 3.2 to 5.4 gm). Two patients had renal failure of which one died in hospital. None of the patients had hypertension. Four female and the 2 male patients had renal biopsy. Two of these were of Amhara, 3 Tigre and 1 of Oromo ethnic group. The incidence of renal amyloidosis was 5.0 percent.

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Table 2

Clinical, biochemical and histological data in nine Ethiopian tuberculosis patients

No.	Age (yrs)	Sex	Duration of tuberculosis before renal biopsy (yrs)	Duration of oedema (weeks	Serum protein (gm)	24-hours urine protein (gm)	Blood urea nitrogen (mg%)	Creatinine (mg%)	Type of tuberculosis	Renal amyloidosis
1	33	M	1	12	3.80	13.70	33.00	0.96	Lymphnode	+
2	35	F	5	24	5.00	1.90	43.00	1.70	Pulmonary	Biopsy not done
3	16	F	1	3	3.20	12.30	15.10	0.71	Disseminated	Biopsy not done
4	30	F	3	12	5.40	6.70	9.20	—	Pulmonary	+
5	45	M	1	8	4.30	1.90	86.00	3.90	Pulmonary	+
6	40	F	<1	2	4.50	3.70	37.00	2.80	Lymphnode	+
7	18	F	1	4	4.60	8.80	9.60	1.60	Peritoneum	+
8	25	F	<1	2	5.00	2.30	18.00	—	Lymphnode	Biopsy not done
9	16	F	2	24	3.90	14.40	4.90	0.70	Lymphnode	+

DISCUSSION.

In East Africa, the earlier reports were on primary renal amyloidosis (4-6). In 1978, various investigators from Egypt, the Sudan and South Africa reported secondary renal amyloidosis in association with schistosomiasis (7-9). However reports on secondary renal amyloidosis due to tuberculosis in Africa appears to be scanty, even though the latter is still prevalent in this part of the world. Of 7 cases reported from South Africa in 1979, 5 were secondary renal amyloidosis cases of which one was due to tuberculosis (10). In Ethiopia, this is the first report on the incidence of renal amyloidosis in tuberculosis patients. Although the study has its own limitations, since the source of the data was from the hospital, it nevertheless gives an idea of the magnitude of renal amyloidosis amongst tuberculosis patients. It is worth noting that the incidence of amyloidosis in this study is much lower when compared with other reports (1,3). The reason for this difference is not obvious. In 1975, it was reported that there was a high incidence (22%) of amyloid related serum protein (Protein ASC) in apparently healthy Ethiopians compared with healthy Norwegians (2.9%) (11). Whether or not such differences explain the obvious variation between the results of this study and those of others is unknown.

During the study period there were a total of 8 renal amyloidosis cases of which 6 were secondary to tuberculosis. Three of these had tuberculous lymphadenitis. Hence, tuberculosis was the main cause of amyloidosis. The cause of amyloidosis in the other 2 cases was not clear.

All the 6 patients came from the countryside where transportation facilities were not easily available. Hence, it was not possible to follow the 5 patients closely to assess the effect of anti-tuberculous therapy on the renal lesion. Two patients were, however, seen at 6 months and 1 year, respectively, after discharge from the hospital and both had still significant proteinuria, but their renal function tests remained normal.

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Triger and Joekes (12) have postulated that in some patients the renal lesion may regress if anti-tuberculous treatment is started promptly. On the other hand, it was recently observed in patients who had been followed-up for 3 years that anti-tuberculous therapy had no effect in the course of renal amyloidosis once the kidney is extensively involved (2). All the 6 patients had extensive amyloidosis (Fig 1) of which one died within a year. The intravenous pyelography of the deceased showed non-functioning kidneys. An autopsy was requested but as usual the relatives were uncooperative.

Fig. 1

Photomicrograph (× 250) of glomeruli showing deposit



...ated complex (9, 10).

What is the source of HIV infection in Ethiopia? Since epidemics of AIDS are claiming thousands of lives in Central and East Africa, it may be speculated that the new and delayed introduction of HIV infection into Ethiopia is part of the trans-continental spread (7). Migration of refugees across the borders, frequent visits to existing harbours by sailors, the fact that Addis Ababa is the seat of many international organizations hosting several international meetings annually and the frequency of prostitution in this capital city all favour HIV introduction and spread.

What could be the most likely mode of transmission among this population? In North America and Western Europe, homosexual promiscuity and parenteral transmission account for the majority of cases while in Africa, heterosexual promiscuity is believed to be the predominant means of transmission (11, 12). Considering the high prevalence of HIV infection among prostitutes (8), promiscuity might be the major mode of transmission in this population. However, the multiple use of inadequately sterilised hypodermics so widely practised in this country needs serious attention. "Medically promiscuous hypodermics" are known to have caused viral infections of epidemic proportions in the past (13, 14) and may be the cause for the high prevalence of hepatitis B virus infection in this country (5). Among the 13 subjects found to have HIV antibodies in their sera, 7 had several injections at different places, often for minor reasons. Until very recently, blood transfusion was carried out without screening. It is likely that at least one of the 3 blood recipients (Code No. 162) acquired HIV infection from multiple, unscreened blood transfusions. At present, with the knowledge of spread of HIV outside Addis Ababa (Bahr Dar, Dese, Mekane Selam (Welo), Aseb, Akaki and Nazareth), it is unethical to limit the screening of blood for transfusion to Addis Ababa alone. Therefore, the current efforts to extend screening facilities to other parts of Ethiopia should be pursued urgently.

In summary, this serological survey suggests the HIV infection was probably introduced to this country by 1984 and that there is a rising trend in the rate and spread of infection. We suggest that the existing health policy for the prevention of HIV infection should be pursued more vigorously than ever at this opportune moment.

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PREVALENCE OF PARALYTIC POLIOMYELITIS IN RURAL AND URBAN POPULATIONS IN ETHIOPIA: REPORT OF A HOUSE-TO-HOUSE SURVEY

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Abstract. A house-to-house survey was carried out to determine the prevalence of poliomyelitis. During the survey 37,219 households were visited and 17,941 children 5–9 years old were found. Of 231 lame children, lameness compatible with paralytic poliomyelitis was found in 131, of these 91% had their condition before the age of 3 years. Nineteen percent needed a stick support for walking while 12% were unable to walk even with support. This problem was more common in rural populations. The prevalence of paralytic poliomyelitis was 7.3/1,000 children 5–9 years old.

In recent years poliomyelitis has been recognized as a major public health problem in developing countries. Recent lameness surveys have shown prevalence rates ranging from 1.0–7.5/1,000 children, higher than initially suspected.[1–4]

Poliomyelitis is presumed to be endemic in Ethiopia, however, no reliable data on the size of the problem exists. A house-to-house survey was carried out to determine the prevalence of the sequelae of poliomyelitis.

MATERIALS AND METHODS

Children aged 5–9 years were surveyed to gain information on the incidence of the disease over the previous 5 years.

In the Gondar region a random selection was not possible; 30 clusters were drawn from communities accessible to health services. The communities chosen represented urban, urban-rural, and rural populations. An urban cluster had a population >2,000 and some piped water, electricity, a clinic, and elementary and high schools. An urban-rural cluster included a town with a population <2,000 and the people living in the surrounding area. A rural cluster is one where the population lived in homesteads in scattered areas. Of the 30 clusters, 10 were urban, 8 were urban-rural, and 12 were rural. A house-to-house survey was done from February to July 1983. The number of children in the 5–9 year age group was determined and information was obtained on any children in that age group with lameness from any cause.

All instances of lameness in 5–9-year-old children were investigated by a pediatrician, an internist, and an experienced health officer. The criteria for inclusion in the category of residual paralysis from poliomyelitis included: asymmetrical muscle weakness, atrophy and flaccid paralysis or paresis, diminished or absent tendon reflexes, normal sensation, and history of nonprogressive lameness following an acute febrile illness.

RESULTS

In the survey of the 30 population clusters 37,219 households were visited and 17,941 children aged 5–9 years were found. Of these children 231 were lame (1.3%). Residual paralysis compatible with poliomyelitis was the most common cause (131) of lameness (Table 1). The second common cause was lathyrism (43), a spastic paraplegia caused by excessive consumption of the beans of *Lathyrus sativus*. Children with this disease were found in 3 clusters near Lake Tana which had been affected by severe flooding resulting in a severe food shortage in 1974. Other causes of lameness were cerebral palsy, trauma of all kinds, and congenital deformities.

Fifty-four percent of the 131 cases of poliomyelitis with residual paralysis was in males. The rate by age showed a stable endemic situation (14.8, 18%) for all the age groups, except for the

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TABLE 1

Causes of lameness in children 5–9 years old in the Gondar region, Ethiopia

Cause	No. cases	Percent
Poliomyelitis	131	56.7
Lathyrism	43	18.6
Cerebral palsy	21	9.1
Trauma, including burns	16	6.9
Congenital deformity	11	4.8
Other	9	3.9
Total	231	100.0

TABLE 2

Age at onset of paralytic poliomyelitis

Age at onset (months)	No. cases	Percent	Cumulative percentage
≤6	22	16.8	16.8
7–11	40	30.5	47.3
12–23	39	29.7	77.1
24–35	18	13.7	90.8
36–47	7	5.3	96.1
48–59	1	0.8	96.9
≥60	4	3.1	100.0
Total	131	100.0	

5–6 year group where the prevalence rate was 34.4%.

Age of onset of poliomyelitis was <2 years in 77% of the children and <3 years in 91%. About 97% of the children had poliomyelitis at <5 years (Table 2).

Degree of disability was assessed by ability to walk with or without support. Sixty-nine percent of the lame children managed to walk without support, 19% required a stick support to walk, and 12% were unable to walk. The most common paralysis was of the left lower limb (45%); the right lower limb (36%) was the second most frequently affected extremity (Table 3).

The prevalence rate was estimated to be 7.3/1,000 for children aged 5–9 years. The incidence rate is estimated to be 1.8/1,000 in the 0–4 year age group. The prevalence rate was 3.5 for urban clusters, 10.5 for urban-rural, and 6.5/1,000 in rural clusters (Table 4).

DISCUSSION

Although our study involved a limited population sample in the Gondar Administrative Region, we believe the results are indicative of the magnitude of the disease throughout Ethiopia. It was assumed that paralytic poliomyelitis was the only cause of nonprogressive residual paralysis marked by asymmetric muscle weakness, atrophy and hypotonia of muscle, diminished deep tendon reflexes, normal sensory examination, and onset following an acute febrile illness. However, such paralysis has been described with Coxsackie and Echo virus infections.[5] Paralytic poliomyelitis was the most common (57%) cause of lameness in the 231 lame children. In India poliomyelitis was found to be responsible for 34% to 70% of lameness.[4, 6]

In our study the disease showed no predilection for males (54%). Similarly, Gharpure et al.[7] found no gender bias, but investigators from India[8–11] have found male preponderance.

The age distribution of residual paralytic poliomyelitis showed a lameness rate of 34.4% in the 5–6 year age group, while rates for the other age groups ranged from 14.8% to 18.5%. The higher rate in the 5–6 year olds might be the result of an isolated epidemic of poliomyelitis that occurred 6 years earlier. Seventy-seven percent of the cases had onset of disease at <2 years of age; in 91% of the cases, the onset was at <3 years of age. These findings reflect those found in other studies.[6, 12–14]

Degree of disability was assessed by the ability to ambulate with or without a mechanical support. Nineteen percent required a stick support to walk and 12% were unable to walk. The result was similar to that found by Basu[6] in India. The degree of disability in different countries was variable.

Estimated prevalence rates of poliomyelitis reported in studies from Ghana, Egypt, and Bangladesh[1–4] ranged from 1.0 to 7.5/1,000 for 5–14-year-old children. Our estimated preva-

TABLE 3

Distribution of residual paralytic poliomyelitis cases according to site of paralysis

Site of paralysis	No. cases	Percent	Cumulative percentage
Left leg	59	45.0	45.0
Right leg	47	35.9	80.9
Both legs	16	12.2	[illegible]
One leg + one arm	6	4.6	[illegible]
One lower leg + trunk	2	1.5	99.2
Both lower + upper limbs	1	0.8	100.0
Total	131	100.0	

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TABLE 4

Prevalence rates of residual paralytic poliomyelitis by degree of urbanization

	Urban	Urban-rural	Rural	Total
No. of clusters	10	8	12	30
No. of children surveyed	3,946	6,497	7,498	17,941
Children with residual paralytic poliomyelitis	14	68	49	131
Prevalence rate per 1,000 children	3.5	10.5	6.5	7.3

lence rate of 7.3/1,000 for the 5–9 year age group was similar to that found in rural Ghana[1,2] but lower than rates from Egypt[3] and rural Bangladesh.[4] The significance of this difference is difficult to assess.

The effect of urbanization on the prevalence rate was assessed. Estimated rates for the urban, urban-rural, and rural areas were 3.5, 10.5, and 6.5/1,000, respectively. Studies in India by Jhala et al.[9] showed prevalence rates for residual poliomyelitis of 4.23 for the urban and 5.78/1,000 for the rural areas. Basu[6] in 1981 reported a prevalence rate in India of 3.7–6.18 for urban and 4.4–8.6/1,000 children aged 5–9 years in rural areas. These data also suggest that poliomyelitis is more of a problem in rural than in urban populations. The high prevalence rate for the urban-rural population in our study may be due to a high population concentration in an extremely unhygienic environment, the absence of piped water, and the lack of health service facilities.

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Altered State of Consciousness in Adult Ethiopians: Analysis of Aetiological Factors

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ABSTRACT

A PROSPECTIVE STUDY to determine the relative incidence of diseases causing altered state of consciousness in patients admitted to the medical wards of the Tikur Anbessa University Teaching Hospital, Addis Ababa, Ethiopia was undertaken. 300 consecutive patients with altered state of consciousness were included in the study. The majority of patients were below 40 years of age. The causes for altered state of consciousness were metabolic in 125 (41.7%), infectious in 101 (33.7%) and neurological diseases in 64 (21.3%) patients. Hepatic encephalopathy, found in 74 patients (24.7%) was by far the commonest medical cause of altered state of consciousness. In 10 patients (3.3%) no definite diagnosis could be reached. 173 (57.7%) patients died. The age and disease patterns were found to be different from those seen in Europe and North America.

INTRODUCTION

ALTERED STATE of consciousness is a medical and surgical emergency which has to be dealt with urgently. Knowledge of the relative incidence of diseases causing this condition in a particular area can be most informative to physicians, whose approach to the management of the condition in patients can be likewise facilitated. To our knowledge there has been only one study[1] which has addressed itself to prognosis in non-traumatic coma in a tropical environment. Our prospective study was undertaken at the Tikur Anbessa University Teaching Hospital, Addis Ababa, to determine the relative incidences of diseases causing altered state of consciousness in patients admitted to the medical wards.

MATERIAL AND METHODS

ALTERED STATE of consciousness is defined as a clinical state manifested by conditions ranging from confusion and disorientation to person, place and time to stupor and deep coma[2].

From March 1984, up to September 1985, 300 consecutive patients that were admitted to the medical wards of the Tikur Anbessa Hospital with a diagnosis of altered state of consciousness, and patients who developed such condition while in the hospital and stayed in the same or worse state for at least 24 hours were included in the study.

According to a preset protocol, history was obtained from the closest relative available and from the patient

Age in Years	Metabolic Diseases		Infectious Diseases		Neurological Diseases		Unknown		Total	
	No. of Patients	No. of Deaths	No. of Patients	No. of Deaths	No. of Patients	No. of Deaths	No. of Patients	No. of Deaths	No. of Patients	No. of Deaths
0 - 9	-	-	-	-	-	-	-	-	-	-
10 - 19	18	6	24	10	1	-	-	-	43	18
20 - 29	20	12	35	20	6	3	2	-	63	35
30 - 39	23	15	21	10	9	5	3	2	56	32
40 - 49	23	10	9	3	13	10	2	1	47	24
50 - 59	22	19	10	8	8	5	1	1	41	33
60 - 69	12	8	1	-	13	10	1	1	27	19
70 - 79	6	4	1	-	11	3	1	1	19	8
80+	1	1	-	-	3	3	-	-	4	4
Total	125 (41.7%)	77 (44.5%)	101 (33.7%)	51 (29.5%)	64 (21.3%)	39 (22.5%)	10 (3.3%)	6 (3.5%)	300 (100%)	173 (100%)

Table I. Altered state of consciousness in 300 Ethiopian medical patients. The age pattern, major groups of diseases and their outcome.

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	No. of Patients	Mortality
Metabolic Diseases	125 (100%)	77(61.6%)
Hepatic Encephalopathy	74 (59.2%)	57
Renal Failure	18 (14.4%)	11
acute	2	1
chronic	16	10
Poisoning	14(11.2%)	4
Organophosphate compounds	7	2
Chlorpromazine	2	1
Phenobarbitone	2	-
Carbonmonoxide	1	-
Unknown	2	1
Diabetic Ketoacidosis	13(10.4%)	4
Others	6(4.8%)	1
Infectious Diseases	101(100%)	51(50.5%)
Relapsing fever	20(19.8%)	12
Cerebral malaria	16(15.8%)	8
Septicemia	16(15.8%)	11
Typhoid fever	14(13.9%)	6
Tuberculous meningitis	11(10.9%)	8
Pyogenic meningitis	8(7.9%)	3
Others	16(15.8%)	3
Neurological Diseases	64(100%)	39(60.9%)
Intracranial bleeding*	24(37.5%)	21
Atherothrombotic stroke	17(26.6%)	9
Cerebral emboli	8(12.5%)	6
Others	15(23.4%)	3

Table II - The different diseases and their outcome.

* The diagnosis of intracranial bleeding include hypertensive intracerebral bleed and subarachnoid hemorrhage.

after he or she got better. Detailed general and neurological examination was performed on every patient. Determinations of hemoglobin, white cell count, sedimentation rate, urinalysis, fasting blood sugar, blood urea nitrogen, serum creatinine, serum transaminase levels, alkaline phosphatase, bilirubin, serum sodium and potassium and examination of the blood film for haemoparasites were done. Lumbar puncture for cerebrospinal fluid analysis was performed in patients with suspected infections of the central nervous system and those with cerebrovascular accidents. A bloody cerebrospinal fluid was taken diagnostic for both intracerebral bleeding secondary to hypertensive cerebrovascular accident as well as subarachnoid hemorrhage from other causes.

Hepatic encephalopathy		Septicemia	
Liver cirrhosis	48	Septic abortion	5
Primary hepatocellular carcinoma	13	Post-delivery	1
Cholangiocarcinoma	1	Malingnancy (Hematological)	3
Acute viral hepatitis (1 pregnant)	10	Diabetes mellitus	2
Chronic active hepatitis	1	Ascending cholengitis	1
Reye's syndrome	1	Acute pancreatitis	1
		Unknown	3
Total	74	Total	16

Table III - Underlying Diseases in hepatic encephalopathy and septicemia

RESULTS

OF THE 300 patients included in the study, there were 186 males and 114 females. 83.3% of patients were below the age of 60 years, 54.0% were below the age of 40 years and 35.5% were below the age of 30 years. 173 patients died (57.7%) (Table 1).

The major groups of diseases encountered were metabolic in 125 (41.7%), infectious in 101 (33.7%), and neurological in 64 (21.3%) patients. No definite diagnosis could be be reached in 10 patients (3.3%). Hepatic encephalopathy was the single most common disease and 59.2% of the metabolic diseases (Table 2). Table 3 shows the underlying diseases in patients with hepatic encephalopathy, and septicemia. The precipitating factors for hepatic encephalopathy were upper gastro-intestinal bleeding, infection, hepatotoxic drugs and for diabetic ketoacidosis mainly infection (Table 4).

Out of 13 patients with diabetic ketoacidosis diabetes mellitus was diagnosed for the first time in 6 patients. The ingestion of poisons or overdose of drugs was intentional in 11 patients and accidental in three patients. Jaundice was present in 14 of 20 and 12 of 16 cases of relapsing fever and cerebral malaria respectively.

The cerebrovascular accidents accounted for 49 of the 64 patients (76.6%) with neurological diseases. History of hypertension was obtained from 14 of 24 and five of 17 patients with intracranial bleeding and thrombotic stroke respectively. In all patients, treatment of the hypertension was irregular and follow-up poor and erratic. Out of eight patients with cerebral emboli, six patients had atrial fibrillation. In three of the six patients, the cause of atrial fibrillation was mitral stenosis secondary to rheumatic heart disease.

Hepatic Encephalopathy	
Upper Gastrointestinal Bleeding	21
Infection	8
Hepatotoxic drugs	3
Undetermined	42
Total	74

Table IV - Precipitating Factors of hepatic encephalopathy.

DISCUSSION

IN A prospective study of non-traumatic coma done in Europe and North America, Bates *et al.*[3] and Levy *et al.*[4] found that diffuse hypoxic ischemia due to cardiac arrest, profound hypotension, and respiratory arrest accounted for the majority of the cause of coma, which is in contrast to our finding where hepatic encephalopathy and infectious diseases were the major aetiologic factors.

The majority of our patients were young reflecting the population structure of our society. This age distribution pattern was also noticed in other similar studies reported from different parts of the country[5-10]. But in the European study[3] the majority of patients were

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between the age of 50–79 years with a mean age of 58 years. Hepatic encephalopathy was the most common single diseases encountered (24.7%). This reflects the common occurrence of liver disease in Ethiopia as shown in previous studies where it accounted for up to 12% of diagnoses of medical admissions to hospitals in Ethiopia[5–9]. This is in contrast to findings in Europe and North America where hepatic encephalopathy was found in 10.7%[3] and 10.2%[4] of patients with altered state of consciousness.

Infectious diseases were the cause in 33.7% of our patients while it was only found in 13.2% and 3.2% patients reported by Bates *et al.*[3] and Levy *et al.*[4] respectively. Jaundice was present in the majority of patients with relapsing fever and cerebral malaria. Thus examination of the blood film for haemoparasites, repeatedly if need be, should be one of the first investigations in the unconscious and jaundiced patients in the African setting. This prevents further delay in diagnoses and management of these curable diseases, which is the major factor for unfavourable outcome[13,14]. As shown in previous studies, the absence of fever does not rule out the presence of these diseases[15].

Organophosphate compounds were the most common poison used. Similar findings were reported from Kenya[11] and Uganda[12]. These compounds are used as pesticides in farms and are also available at low cost in the open markets for use as insecticides at home. Appropriate measures to control the availability of these compounds for use other than the one they are intended for is necessary.

In the six patients with septicemia, and two patients with acute renal failure, septic abortion was the underlying illness. A similar finding was reported previously in patients with acute renal failure[16].

The reasons for inadequate treatment and poor follow-up of patients with hypertension and cerebrovascular accidents are not well studied. From our clinical observation, the lack of adequate facilities for early diagnosis, treatment and follow-up of patients and the lack of aggressive effort by medical practitioners to set up a programme for control of hypertension are the main reasons at this stage. Other contributing factors include the low socio-economic status of patients to afford long term drug therapy, return of patients to their native villages after diagnosis where no further follow-up is possible and their low education status to comprehend the long-term complications of the disease. These problems have also been encountered in other African countries[17,18].

Thus there is a need to intensify our efforts in the early diagnosis of hypertension in the community and inform the public through mass health education programmes the dangers of hypertension and the value of treatment and regular follow-up. Several studies have shown that there is a definite favourable effect of control of hypertension in the prevention of stroke[19–23].

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was part of an epidemiological study of hookworm endemicity in the area. The study area is located at an altitude of 1900m, about 45km west of the city of Gondar in a small town called Mizaba in North-west Ethiopia.

RESULTS

The highest rate of infection was observed in April 1985 and the lowest in February and July of the same year (Figure 1). There are apparently two peaks, although not well defined, per year, one in March-May and the second one in August-October.

Figure 1

The monthly rates of infection of 103 school boys and girls who were examined monthly for 14 consecutive months beginning in August 1984 and ending in September 1985.

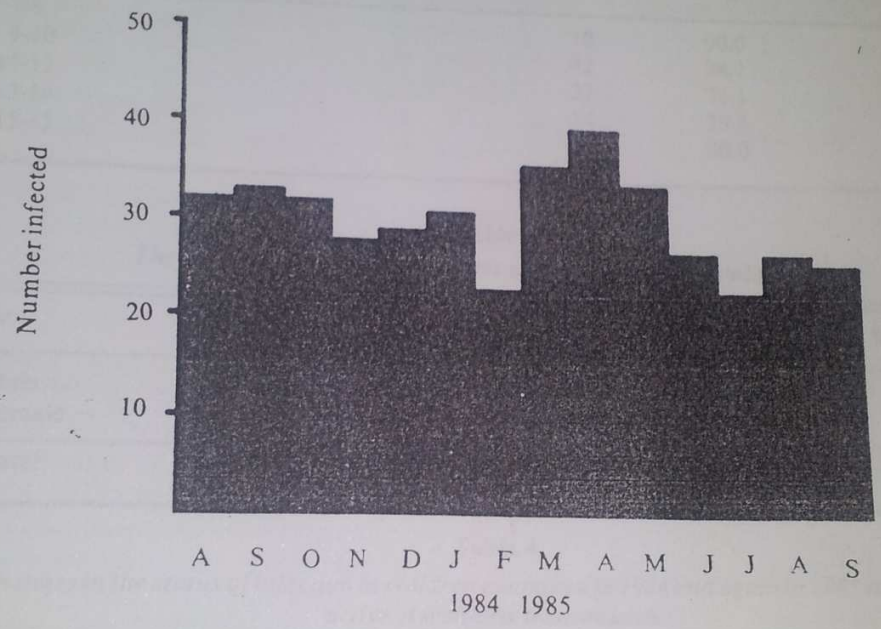


Table 1

Frequency of appearance of eggs in stool of 103 school children who were examined every month for 12 consecutive months (August 1984 to July 1985). Frequency is defined as the number of months in which eggs of "A. lumbricoides" were recovered in the year.

Frequency	*No. of pupils*	% of total
0	17	16.5
1-3	39	37.8
4-6	26	25.2
7-9	14	13.6
10-12	7	6.8

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The frequency of appearance of ova of *A. lumbricoides* in stool during a period of one year varied from 0 to 12 (Table 1). Most stool specimens did not have ova for most of the year (Table 1).

The highest rates of infection as measured by period prevalence were observed in children below 11 years of age (Table 2). The frequency of appearance of eggs appears to be independent of the period prevalence observed in each age group (Table 2).

Table 2

The relationships of age and rates and frequency of infection by "A. lumbricoides". Frequency here denotes the number of times (months) in which eggs were found in stool of any one individual. (Frequency ranges from 0-12). One slide per stool sample per month was examined for consecutive 12 months (August 1984 to July 1985).

Age groups (yrs)	*No. exam.*	*% + ve*	*Frequency*
7-8	10	90.0	3.5
9-10	42	88.1	4.2
11-12	27	74.1	3.7
13-14	14	78.6	3.9
15-18	10	80.0	3.0

Table 3

The relationships of sex and rates of infection by A. lumbricoides

Sex	*No. exam.*	*No. infected*	*% + ve*
Male	30	23	76.7
Female	73	63	86.3
Total	103	86	83.5

Table 4

Changes in the status of infection in children examined in 1984 and again in 1985 in an area of active Ascariasis transmission.

Month	*Age (yrs)*	*No. Exam. (both yrs.)*	*No. +ve 1984**	*Conversion+*	*Reversion*	*No. +ve 1985*
August	7-18	103	32 (29.9)	20 (28.2)	25 (78.1)	27
September	7-18	103	33 (32.0)	13 (18.6)	20 (60.6)	26

*Number of parenthesis are percentages
+Number in parenthis indicated percentage incidence.

There was no significant difference between the rates of infection of males and females (Table 3).

There appears to be a reduction in incidence of infection as measured by the ratio

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DISCUSSION

The overall infection rate by *A. lumbricoides* at any one time is low compared to previous studies (1, 7). A more reliable picture of infection patterns can be obtained by examining more than one slide per specimen per month; this was not possible in the present study.

There are apparently two peaks in the monthly rates of infection, one in March-May and the second in August-October. These peaks may be associated with the rainy seasons in the year. The region normally receives rain twice a year, once during February-April (small rainy season) and the second in June-September (the heavy rainy season). The availability of moisture which is required for the survival of Ascaris ova in soil may have reflected itself in the transmission pattern observed in this study. The infection that occurred during the rains, leaving a couple of weeks for larval development in soil at the beginning of the rains, appears to manifest itself about 8 weeks after the beginning of the rains. About six weeks after infection were required prior to the detection of ova in stool. The results obtained may indicate continuous loss and gain of parasites.

Some pupils were apparently free from infection throughout the year, while most were free for most parts of the year (Table 1). It is likely that low levels of infection may have been maintained throughout the study period and still remaining undetected due to the resultant low level of the number of eggs in stools.

The highest period prevalence is 90%, 7-8 year old group and the lowest 74.1%, 11-12 year old group (Table 2). The frequency of appearance of ova in stool of each age group may indicate an apparently low rate of infection in the community. It must, however, be noted that the number of pupils examined in each age group is small, and comparisons based on such small numbers are not reliable.

It is surprising to note that the frequency of appearance of eggs and the period prevalence do not show any association (Table 2). One would have expected the highest period prevalence to occur in age groups in which the highest frequency of appearance of ova is recorded. One possible explanation for the present observations may be that period prevalence indicated susceptibility to infection, while frequency of appearance of ova indicated resistance to infection.

It is not surprising to note that there is no difference in the period prevalence of infection in males and females, since most studies in Ethiopia have shown similar results (7).

The incidence of infection was declining during the study period (Table 4). In the absence of any known direct man-made intervention that affects the prevalence of the parasite in the community, it is suspected that the reduction may be due to environmental changes. The overall dry conditions of 1985 may have contributed to the apparent reduction in transmission. The reduced moisture level may contribute towards the reduction in transmission, by detrimentally affecting the development of the infective stage.

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A HOUSE-TO-HOUSE SURVEY OF NEONATAL TETANUS IN URBAN AND RURAL AREAS IN THE GONDAR REGION, ETHIOPIA

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Abstract. A house-to-house survey of neonatal tetanus was performed in 30 population clusters in Gondar, Northwestern Ethiopia. At the end of the survey 37,219 households were visited and 2010 live births were recalled. Out of the 2010 live-born children 127 had died. Eighty died during the neonatal period. Nine of the neonatal deaths were due to tetanus, giving a neonatal tetanus mortality rate of 4.5/1000 live births. The problem of neonatal tetanus in developing countries, particularly that of Ethiopia, is discussed.

Key words: Neonatal tetanus; house-to-house survey; Ethiopia

Introduction

Recent community surveys have shown that neonatal tetanus is a serious health problem in developing countries. The high prevalence of this preventable disease is due to lack of education and inadequate antenatal care of the mother and immediate postnatal care for the infant.

In Ethiopia the Expanded Programme on Immunization was started in urban areas in 1980. The antenatal and postnatal care is still rudimentary and inadequate. The mortality and incidence rates of neonatal tetanus are unknown.

In order to save resources and to test the feasibility of a combined survey method, a house-to-house survey in the same population was performed to determine the mortality and the annual incidence rates of neonatal tetanus and the prevalence of the sequelae of poliomyelitis.

Methods

In most fatal cases of neonatal tetanus, the history obtainable from the mother is precise enough for the causes of death to be diagnosed with reasonable accuracy. In a survey performed in Ivory Coast, it was shown that the accuracy of recall deteriorated after seven months [1]. An effective survey may therefore be carried out by a house-to-house enquiry into the fate of all children born over a period of six months. Because children born in the month leading up to the date of the survey were still in their neonatal period (and therefore were still at risk of dying as neonates), they were excluded from the survey and enquiry was made only of those live-births occurring in the six months period which ended one month before the date of the survey.

In the conditions prevailing in Gondar administrative region, northwestern Ethiopia, a truly random selection was not possible. Therefore selection of the 30 population clusters was made from communities

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which are currently accessible to the health services. The communities for the survey have been chosen to represent urban and rural populations as well as high land and low land areas.

In the 30 population clusters selected a house-to-house survey was carried out from February to July 1983. Using pretested survey forms a number of clinical and epidemiological data were collected on 67 live births in each cluster population. During the same household visits, the number of children in the age group of 5 to 9 years was determined. Information was obtained on any children in that age group with lameness from any cause (reported elsewhere). Well-known national and local events as well as religious holidays were used to assist parents in recalling the date of birth, death and onset of the disease. The survey was carried out by 12th grade school leavers who were trained for the purpose and supervised by the investigators. The possible causes of death were determined by the investigators. The criteria for accepting a neonatal tetanus death as due to tetanus were: death occurring between the third and the thirtieth day of life of a child who was breast fed and behaved normally for the first two days after birth, and failure to suck at the onset of illness, followed by trismus, spasm, rigidity and convulsions before death.

Results

At the end of the survey 37,219 households were visited and 2010 live births were recorded. Out of the 2010 live-born children 127 had died. Eighty of the deaths occurred within the neonatal period. The main causes of death were bronchopneumonia, prematurity, tetanus, asphyxia and sepsis. In 20.5% the cause of death could not be ascertained. Nine infants died of neonatal tetanus. Seven out of the nine died within 15 days after birth. Eighty-nine percent of the 127 infants who died were delivered at home. Of these, 104 were delivered by untrained traditional birth attendants (TBA). The umbilical cords were cut in all cases with new blades. The nine neonatal cases were delivered by untrained TBA. Three of them had surgical procedures by a local healer.

Out of the 2006 mothers 452 (22.5%) had two vaccinations with tetanus toxoid. When this was analysed by locality it was found that only 245 (36.6%) of the urban, 133 (22.1%) of the urban-rural, and 74 (10.1%) of the rural mothers were vaccinated. All the mothers of the neonatal tetanus patients were unvaccinated.

The overall annual incidence of neonatal tetanus was 4.5/1000 live births. The incidence for the urban clusters was zero, while that of the urban-rural areas and rural areas were 6.6 and 6.8/1000 live-births respectively. The incidences for the clusters with altitudes below 2000 meters and above 2000 meters were 3.7 and 5.0/1000 live births respectively.

A retrospective study of the paediatric admission records of the Gondar Hospital from January 1977 upto January 1983 showed the average case fatality rate for neonatal tetanus to be 71% and the annual incidence 4.4/1000 paediatric admissions.

Discussion

Neonatal tetanus is a major health problem which is associated with high morbidity and mortality. In Ethiopia the magnitude of the problem has not been defined. The case fatality rate of neonatal tetanus from our hospital admissions was 71% which is comparable to that found by Anu Gupta *et al.* [2] and Seghal *et al.* [3] which ranged between 70-80%. The fatality rate is also high in other parts of the world [4-7].

The mortality rate of neonatal tetanus from our survey was 4.5/1000 livebirths, which we think is a gross underestimination of the real situation. The high rate (89%) of home delivery, the high delivery rate (81.8%) by untrained TBA, the low maternal vaccination rate (22.5%) and the frequent traditional surgical interventions, such as tonsillar scrabbing, circumcision and avulectomy, favour a high neonatal tetanus infection rate. However the reluctance of mothers to give information about dead

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infants and the inability to diagnose 20.5% of the cases might have contributed in reducing the neonatal mortality rate.

The result is, however, similar to that of recent surveys which showed neonatal tetanus mortality rates of less than 5/1000 live births [8]. The mortality rates in Bangladesh, India, Somalia [8] and Pakistan [9] were more than 20/1000 live births.

The survey also showed that neonatal tetanus is more of a problem in rural than in urban areas which is similar to the results of surveys done elsewhere [8-11]. Clusters with altitudes above 2000 meters had a higher neonatal tetanus mortality rate than those below 2000 meters, which is contrary to the findings of Mazzefero *et al.* [12] who reported the highest incidences in subtropical regions, intermediate rates in temperate and the lowest rates in cold regions.

As expected tetanus occurred more frequently among babies delivered at home by untrained TBA than those delivered in hospitals or clinics, which is similar to the findings of Chen [13] in rural Malaysia. The maternal vaccination rate in our study was only 22.5% and the mothers of the nine neonatal tetanus cases were not vaccinated. The value of using trained TBA and maternal immunization with tetanus toxoid in reducing the neonatal tetanus mortality rate was clearly demonstrated by Berggren *et al.* [14] in a rural area of Haiti in 1972. Newell *et al.* [15], in 1966, used toxoid vaccine for the prevention of neonatal tetanus in a double controlled field trial. Not a single case of neonatal tetanus occurred in the babies of mothers given two or three doses of tetanus toxoid.

Neonatal tetanus is a serious public health problem in Ethiopia and it can only be controlled if measures are taken to train TBA and immunize all expectant mothers with two or more doses of tetanus toxoid.

Our study also demonstrated that the combined survey method is a relatively cheap and effective epidemiological tool.

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THE USE OF HAEMOGLOBIN A_1 IN THE EVALUATION OF DIABETIC CONTROL IN ADULT ETHIOPIAN DIABETICS

Mulugetta Mengistu, MD

ABSTRACT. *In 69 non-insulin-dependent (NIDDM) and 54 insulin-dependent (IDDM) consecutive diabetics and 70 healthy controls, all Ethiopians, diabetic control was initially assessed in an Addis Ababa hospital by the traditional method (TM), and later glycosylated haemoglobin (Hb) A_1 was checked, to assess the diabetic control and also to evaluate the TM's usefulness. There were 65 NIDDM patients on oral agents, and 4 on diet control. The majority of the IDDM patients required more than 40 units of Lente insulin. The mean HbA_1 for the IDDM, NIDDM and controls was, respectively, 11.3% ± standard deviation 3.1, 9.6% ± 1.9 SD, and 6.9% ± 1.6 SD. The overall concordance rate between the two methods of assessment was 57%; concordance was better in the IDDM (66.7%) than in the NIDDM (49.3%). Of 74 diabetics judged as poorly controlled by the TM, only 51 (68.9%) had HbA_1 over 10%, and 9 of 17 patients who had good control according to the TM had normal HbA_1, indicating that the TM is not always reliable, and thus confirming other studies' observations. It is suggested that HbA_1 assay should be available at least in major teaching and research centres, where many diabetics are being followed up.*

Although glycosylated haemoglobin has been available for the assessment of diabetic control for over a decade, its clinical application has been limited to specialised laboratory centres until fairly recently. However, with the introduction of the micro-column chromatographic techniques, using kits, the determination of glycosylated haemoglobin has become much simpler for wider clinical use.

There are various types of chromatographically separable minor haemoglobins in the red blood cell haemolysates of normal adults. But the ones used to monitor diabetic control are Hb (haemoglobin) A_1 and HbA_1c (1-3). HbA_1 is composed of HbA_1a, HbA_1b and HbA_1c. Although all the fractions are increased in poorly controlled diabetics (3), HbA_1c accounts for about 70% of the total HbA_1.

Glycosylated haemoglobin is an important tool in assessing the state of diabetic control over the previous several weeks. At the Tikur Anbessa (Black Lion) Hospital Diabetic Clinic, Addis Ababa, we have been relying on the traditional method (TM) (i.e. patient history, and urine and blood glucose measurements, at the time of clinic visits) to evaluate diabetic control. Although the limitations of the TM are well known (4-7), there was formerly no objective way of evaluating its worth in our circumstances. Thus, in this study, HbA_1 was checked in diabetics, firstly to assess the state of diabetic control, and secondly to compare the result with that of the TM in order to evaluate the latter more objectively, and then to find out the extent of

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usefulness under our conditions.

PATIENTS, MATERIALS AND METHODS

Patients. A total of 123 consecutive Ethiopian diabetics was included in the study. The details of the clinical data are given in Table 1. Each patient was examined for evidence of complications, and the fasting blood sugar (FBS) was determined on at least 2 occasions before checking the HbA_1 2 to 3 months later. In addition, the patients were interviewed for symptoms of diabetes, particularly nocturia, thirst and blurred vision, which are better recalled, and so give more reliable information. Urine sugar was checked less frequently.

Of the non-insulin-dependent diabetes mellitus (NIDDM) patients, 65 were on oral agents, and 4 on diet control. A majority of the insulin-dependent diabetes mellitus (IDDM) patients required over 40 units of Lente insulin, taken as single injection; split doses were less frequently accepted. None of the NIDDM or IDDM patients had excessive blood loss, alcoholism, renal failure or haemolytic anaemias. There were 8 NIDDM and 4 IDDM patients who had liver cirrhosis, but without decompensation. The diagnosis of liver cirrhosis was made on the basis of clinical findings and abnormal liver function test results.

The patients were divided into 3 groups according to the degree of diabetic control as judged by the HbA_1 level or by TM: (a) poor control, when the HbA_1 was over 10%, or when the FBS was more than 10mmol/L (> 180mg/dl), nocturia of more than 3 times, presence of blurred vision, and moderate to severe thirst (drinking 3 litres or more daily); (b) fair control, if the HbA_1 was 8.1%-10%, or if the FBS was 7.8 to 10mmol/L (140 to 180mg/dl), nocturia up to twice, and mild thirst (drinking up to 2 litres daily); (c) good control, when the HbA_1 was equal to or less than 8%, or when the FBS was below 7.8mmol/L (< 140mg/dl), nocturia of nil to once, and no thirst.

Other tests performed included urine protein, blood urea nitrogen, liver function tests and creatinine.

Neither patients nor controls were screened for haemoglobinopathies, since the conditions were extremely unlikely to be present.

Controls. Seventy consecutive healthy Ethiopian individuals (38 females and 32 males) with a mean age of 38.4 ± 15.8 years (± standard deviation) participated in the study.

HbA_1 assay. Blood drawn from each person was assayed for HbA_1 on the same day by the microcolumn chromatography technique (Boehringer Mannheim GmbH Laboratories, West Germany). The method used was modified from Schnek and Schroeder (8), and all observations were meticulously carried out in accordance with the manufacturers' directions. Briefly, 0.05ml of whole blood was mixed with 0.2ml of 0.1% borate buffer (eliminator for labile HbA_1) reagent, pH 7.0, and the mixture, shaken thoroughly once or twice during that time, was kept at room temperature for 30 minutes. Then 0.05ml of the haemolysate was applied to a weakly acidic cation-exchange resin in a disposable column. To this, 0.2ml of phosphate buffer, pH about 6.7 (the elution reagent), was added; the eluate was allowed to drain completely, and was then discarded. Another 4ml of the phosphate buffer was added to the column; the eluate, collected over a period of 30 to 40 minutes, was thoroughly mixed, and the absorbance A_1 was measured by the Beckman spectrophotometer (Du-50, USA) within 5 minutes. Finally 4ml of sodium chloride was added to the column, and the eluate was collected in 10 minutes. Fifteen millilitres of redistilled water was added to this eluate, and, after thorough mixing, the absorbance A_2 was measured within 30 minutes. HbA_1 was then calculated, using

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the following formula:

$$\% HbA_1 = \frac{A_1}{A_1 \pm (4.75 \times A_2)} \times 100$$

According to the manufacturers, HbA_1 value of 5%-8% indicates normal metabolism, while a value over 10% indicates poor metabolic adjustment.

The unpaired T-test for independent means with pooled variance was used for statistical analysis. The chi-square test was used to check for differences between proportions.

RESULTS

The mean HbA_1 in the IDDM patientswas 11.3% ± 3.1(± SD), significantly different ($P < 0.001$) from the mean HbA_1 of 9.6% ± 1.9 SD in the NIDDM patients. In the control group, the mean HbA_1 was 6.9% ± 1.6 SD (range 5.6 to 7.9), and this was significantly different ($P < 0.001$) when compared with that of the IDDM and NIDDM. Furthermore, the finding in this group of healthy individuals was similar to that in the Caucasians catered for by the manufacturers of the materials for the assay (5%-8%). The overall concordance rate between the evaluations by the HbA_1 and the TM was 66.7% in the IDDM and 49.3% in the NIDDM patients.

The relations between the TM of evaluation and the HbA_1 level are given in Tables 2 and 3. Among the NIDDM group (Table 2), 26 patients (37.7%) had HbA_1 greater than 10%, and, of these, 19 had poor metabolic control when they were assessed by the TM. Of the 21 NIDDM patients (30.4%) with normal HbA_1, 7 had good metabolic control and 3 poor control, according to the TM. In the IDDM group (Table 3), 36 patients (66.7%) had HbA_1 over 10%, while 12 (22.2%) had normal HbA_1; 32 of the former and 5 of the latter had poor control, as judged by the TM.

Five of the 8 NIDDM and 3 of the 4 IDDM patients who had liver cirrhosis had HbA_1 over 10%.

DISCUSSION

The pathogenesis of the long-term diabetic complications, such as the microvascular disorders, still remains a controversial issue. One of the hypotheses that has been advanced is the presence of poor diabetic control over a long period of time (9). Indeed, there are studies which indicate the usefulness of good metabolic control in the prevention of long-term complications (10,11).

Thus, while good metabolic control is believed to prevent long-term diabetic complications, good control *per se* requires an objective means of long-term assessment. Traditionally, clusters of symptoms and signs, with urine glucose and blood glucose values at the time of each visit, have been and are still being used to assess diabetic control. The inaccuracy of urine glucose in some patients, and the poor specificity of historical data, are well known (4-7); hence these parameters are not wholly dependable. In addition, sporadic FBG determinations, as practised in different hospitals and clinics in Ethiopia as well as in other developing countries, reflect no more than the metabolic state at single points in time, chosen from a frequently changing continuum of blood glucose control; hence these cannot give information about the previous metabolic state. (The gap in time between the FBG tests and the HbA_1 assay was unavoidable.) Certainly, home glucose monitoring is important in properly assessing diabetic control, but the cost is high for use in our circumstances, while spot blood glucose determinations are important for the im-

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TABLE 1. Clinical data of non-insulin-dependent diabetes mellitus and insulin-dependent diabetes mellitus patients

Clinical data	NIDDM[1]	IDDM[2]
Total number	69	54
New patients[3]	23	14
Old patients[4]	46	40
Male	33	27
Female	36	27
Age (years)		
Range	23 - 75	15 - 46
Mean ± standard deviation	47.9 ± 12	28.5 ± 10.9
Complications		
Neuropathy	29	15
Retinopathy	17	17
Nephropathy	9	12
Peripheral vascular disease	3	2
Haemoglobin A_1 (%)		
Range	6.2 - 16.3	7.3 - 20
Mean ± SD	9.6 ± 1.9	11.3 ± 3.1
Fasting blood glucose (mmol/L)		
Range	5.9 - 13.7	9.7 - 16.4
Mean ± SD	11.4 ± 2.1	12.8 ± 2.9

[1]non-insulin-dependent diabetes mellitus; [2]insulin-dependent diabetes mellitus; [3]duration of diabetes less than one year; [4]duration of diabetes more than one year

TABLE 2. Relation between traditional method of evaluation and HbA_1 value in 69 NIDDM patients

HbA_1 value (%)	Traditional method of evaluation			Total
	Good	Fair	Poor	
8	7	11	3	21
8.1 - 10	3	8	11	22
> 10	2	5	19	26
Total	12	24	33	69

TABLE 3. Relation between traditional method of evaluation and HbA_1 value in 54 IDDM patients

HbA_1 value (%)	Traditional method of evaluation			Total
	Good	Fair	Poor	
8	2	5	5	12
8.1 - 10	0	2	4	6
> 10	3	1	32	36
Total	5	8	41	54

mediate management of the diabetic.

In this study, the usefulness of the TM in the evaluation of long-term diabetic control was studied, using HbA_1. The overall concordance rate between the TM and the HbA_1 level was about 57%; concordance rate between the NIDDM and TM versus the IDDM and TM was not different ($\chi^2 = 3.74$, $P > 0.05$) (Tables 2 and 3). It should be noted that this finding was not affected by the inclusion of the 12 patients with liver cirrhosis. Of the total 74 patients (60.2%) who were judged as poorly regulated by the TM, 51 (68.9%) had HbA_1 over 10%; the concordance rate between the two methods was better for the IDDM group than for the NIDDM group (32/41 vs 19/37), the difference being significant ($\chi^2 = 6.12$, $P < 0.025$). Of the total 17 patients who had good control according to the TM, only 9 had normal HbA_1 level. These findings indicate that judgements made by using the TM are not always reliable. The non-specificity and poor sensitivity of the TM in assessing diabetic control has been reported by Nathan *et al.* (12) and Gonen *et al.* (13).

On the other hand, the usefulness of the glycosylated haemoglobin assay in the long-term assessment of diabetic control has been studied by different authors (14-16). Indeed, currently there is no single assessment that is as informative as the glycosylated haemoglobin assay about the long-term metabolic control of the diabetic. The technique is simple, and the cost per test is about 7 Birr (1 US$ = 2.07 Birr). The cost of HbA_1, as it stands, may appear expensive, but, when compared with the costs incurred in making sporadic blood glucose and urine glucose determinations, together with the limitations these tests have (4-7), it may in fact be relatively cheaper. Therefore, for a better long-term assessment of the diabetics, it is suggested that the HbA_1 assay should be available at least in the major teaching and research centres, where the course of diabetes in many patients is being followed up.

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ADDENDUM. Reference 8, above, should read as follows:

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INCIDENCE OF RENAL AMYLOIDOSIS IN ADULT ETHIOPIAN TUBERCULOSIS PATIENTS

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INCIDENCE OF RENAL AMYLOIDOSIS IN ADULT ETHIOPIAN TUBERCULOSIS PATIENTS.
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INCIDENCE OF RENAL AMYLOIDOSIS IN ADULT ETHIOPIAN TUBERCULOSIS PATIENTS.

M. MENGISTU

SUMMARY

In a study of 120 adult Ethiopian tuberculosis patients who were admitted to the Black Lion Teaching Hospital (BLTH) in Addis Ababa, Ethiopia, there were 9 patients who had significant proteinuria. Of these, 6 had renal amyloidosis which was proven by renal biopsy; this makes an incidence of 5%. Two patinets had renal failure of which one died. The difficulties in following patients to assess the effect of anti-tuberculous therapy on the renal lesion is discussed. Renal amyloidosis is almost always fatal and the only way to prevent it is by controlling tuberculosis.

INTRODUCTION.

Secondary amyloidosis has been reported in connection with tuberculosis. In 1974, it was reported that 75% of 200 cases from India, 54% of 37 cases from a Scottish series and about 33% of 22 patients from an American series had secondary amyloïdosis due to tuberculosis (1). In Iran tuberculosis was the main cause of renal amyloidosis (2,3).

In Ethiopia, tuberculosis, in its various forms, is still prevalent; and indeed, it is estimated that 2% of the population or 600,000 people suffer from the disease and of these only very few patients get the proper treatment.

The incidence of renal amyloidosis in tuberculosis patients in Ethiopia is unknown. A study was conducted in 120 patients who were consecutively admitted to the BLTH, in order to find out the incidence of renal amyloidosis. The results of this study are described in this paper.

MATERIALS AND METHODS

Of 120 tuberculosis patients who were admitted to the medical department between April 1980 and December 1981, 67 were females and 53 males. The age ranged from 14 to 70 years (mean 28.2 years). The diagnosis of tuberculosis was

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established by radiology, positive acid fast bacilli in the sputum or visceral fluid, biopsy and a positive Mantoux test. The types of tuberculosis and the distribution by sex are given in Table 1.

Table 1

Type of tuberculosis according to sex and incidence of renal amyloidosis in 120 Ethiopian tuberculosis patients.

Type	Male	Female	Total	Number of Renal amyloidosis	Incidence (%)
Pulmonary tuberculosis	33	37	70	2	1.67
Disseminated tuberculosis	6	14	20	0	0.00
Tuberculous peritonitis	4	10	14	1	0.83
Tuberculous lymphadenitis	5	4	9	3	2.50
Tuberculous spondylitis	4	1	5	0	0.00
Tuberculous pericarditis	1	0	1	0	0.00
Renal tuberculosis	0	1	1	0	0.00
Total	53	67	120	6	5.00

Nine of 120 patients (7.5%) had significant proteinuria in 24 hours urine specimen on different occasions. Renal biopsy was performed in 6 of these patients who consented to the procedure.

In the remaining 111 patients renal biopsy was not considered since they had no evidence of renal involvement. The renal tissue obtained was put in 10% formalin. Thin paraffin sections were stained with standard stains including periodic acid Schiff (PAS) and Congo Red. The slides were examined by light microscopy.

RESULTS

The clinical, biochemical and histological data are indicated in Table 2. Of 9 patients with significant proteinuria, 7 were females and 2 males. The proteinuria ranged from 1.9 gm to 14.4 gm(mean 7.3 gm) per 24-hours urine specimen. All patients had other manifestations of the nephrotic syndrome as well. The mean serum protein was 4.4 gm (range 3.2 to 5.4 gm). Two patients had renal failure of which one died in hospital. None of the patients had hypertension. Four female and the 2 male patients had renal biopsy. Two of these were of Amhara, 3 Tigre and 1 of Oromo ethnic group. The incidence of renal amyloidosis was 5.0 percent.

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Table 2

Clinical, biochemical and histological data in nine Ethiopian tuberculosis patients

No.	Age (yrs)	Sex	Duration of tuberculosis before renal biopsy (yrs)	Duration of oedema (weeks	Serum protein (gm)	24-hours urine protein (gm)	Blood urea nitrogen (mg%)	Creatinine (mg%)	Type of tuberculosis	Renal amyloidosis
1	33	M	1	12	3.80	13.70	33.00	0.96	Lymphnode	+
2	35	F	5	24	5.00	1.90	43.00	1.70	Pulmonary	Biopsy not done
3	16	F	1	3	3.20	12.30	15.10	0.71	Disseminated	Biopsy not done
4	30	F	3	12	5.40	6.70	9.20	—	Pulmonary	+
5	45	M	1	8	4.30	1.90	86.00	3.90	Pulmonary	+
6	40	F	<1	2	4.50	3.70	37.00	2.80	Lymphnode	+
7	18	F	1	4	4.60	8.80	9.60	1.60	Peritoneum	+
8	25	F	<1	2	5.00	2.30	18.00	—	Lymphnode	Biopsy not done
9	16	F	2	24	3.90	14.40	4.90	0.70	Lymphnode	+

DISCUSSION.

In East Africa, the earlier reports were on primary renal amyloidosis (4-6). In 1978, various investigators from Egypt, the Sudan and South Africa reported secondary renal amyloidosis in association with schistosomiasis (7-9). However reports on secondary renal amyloidosis due to tuberculosis in Africa appears to be scanty, even though the latter is still prevalent in this part of the world. Of 7 cases reported from South Africa in 1979, 5 were secondary renal amyloidosis cases of which one was due to tuberculosis (10). In Ethiopia, this is the first report on the incidence of renal amyloidosis in tuberculosis patients. Although the study has its own limitations, since the source of the data was from the hospital, it nevertheless gives an idea of the magnitude of renal amyloidosis amongst tuberculosis patients. It is worth noting that the incidence of amyloidosis in this study is much lower when compared with other reports (1,3). The reason for this difference is not obvious. In 1975, it was reported that there was a high incidence (22%) of amyloid related serum protein (Protein ASC) in apparently healthy Ethiopians compared with healthy Norwegians (2.9%) (11). Whether or not such differences explain the obvious variation between the results of this study and those of others is unknown.

During the study period there were a total of 8 renal amyloidosis cases of which 6 were secondary to tuberculosis. Three of these had tuberculous lymphadenitis. Hence, tuberculosis was the main cause of amyloidosis. The cause of amyloidosis in the other 2 cases was not clear.

All the 6 patients came from the countryside where transportation facilities were not easily available. Hence, it was not possible to follow the 5 patients closely to assess the effect of anti-tuberculous therapy on the renal lesion. Two patients were, however, seen at 6 months and 1 year, respectively, after discharge from the hospital and both had still significant proteinuria, but their renal function tests remained normal.

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Triger and Joekes (12) have postulated that in some patients the renal lesion may regress if anti-tuberculous treatment is started promptly. On the other hand, it was recently observed in patients who had been followed-up for 3 years that anti-tuberculous therapy had no effect in the course of renal amyloidosis once the kidney is extensively involved (2). All the 6 patients had extensive amyloidosis (Fig 1) of which one died within a year. The intravenous pyelography of the deceased showed non-functioning kidneys. An autopsy was requested but as usual the relatives were uncooperative.

Fig. 1

Photomicrograph (× 250) of glomeruli showing deposit



Liver necropsy studies revealed extensive amyloid deposit, thus it is more likely that the patient succumbed from the amyloidosis. Except in few instances, amyloidosis is a progressive disease and is almost always fatal and that renal involvement is associated with the poorest prognosis. Forty-eight such patients were closely followed-up for as long as 14 years and the result showed that the mean survival time was 44 months; only 6 patients lived for 5 years or longer, and renal failure or its complications was the usual cause of death (12). Two of the patients in this study had renal function impairment and one died from renal failure. In conclusion, renal amyloidosis due to tuberculosis is a preventable disease. Preventative medicine is far better economy and hence emphasishas to be placed on preventing tuberculosis.

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RELATION BETWEEN URINE AND BLOOD GLUCOSE IN ADULT ETHIOPIAN DIABETICS[1]

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ABSTRACT. *The relation of urine and blood glucose was studied in 170 diabetics without proteinuria (Group A), and in 56 with proteinuria (Group B), at the Tikur Anbessa Teaching Hospital in Addis Ababa, in 1986. The results showed that 5 of 42 (12%)patients in Group A, and 5 of 15 patients in Group B, had glycosuria when the blood glucose was equal to or less than 180mg/dl; 3 of those from Group A and 2 from group B had 4+ glycosuria. Twenty-two of 128 (17.2%) diabetics in Group A, and 13 of 41 (31.7%) in Group B, had no glycosuria when the blood glucose was greater than 180mg/dl; 14 (11%) of the 22, and 8 (19.5%) of the 13, had blood glucose over 200mg/dl. Furthermore, when clinically important glycosuria and blood glucose were considered, the sensitivity, specificity, accuracy and positive predictive values of the Clinitest method were, respectively, 75%, 82%, 77% and 89% for Group A, and 61.8%, 81.8%, 69.6% and 84% for Group B patients. Thus, the Clinitest is shown to be not totally reliable; hence, in the absence of a better alternative, it should be used cautiously.*

Semiquantitative glucose determination on spot urine specimens has been accepted both by patients and physicians as a means of adjusting the quantity, type and frequency of insulin or oral hypoglycaemic therapy. The basis for this has been the assumption that the urine glucose reflected and correlated well with the ambient blood glucose, the most crucial parameter in the assessment of diabetic control at any given time.

Several commercial products are available both for qualitative and quantitative urine glucose determination. However, the presence of several factors in the urine affects the accuracy and reliability of these products (1-4); hence they are not always dependable. Nevertheless, these products are still used in countries like Ethiopia to assess diabetic control. Better but more expensive alternatives are very rarely used in these countries. Moreover, semiquantitative urine glucose values are frequently used by physicians working in developing countries to adjust the insulin dose for the acutely ill or newly diagnosed diabetics, who are traditionally put on "sliding-scale". In these instances, there have been occasions when the semiquantitative urine glucose test showed only trace or 1+ glycosuria, when

[1] Adapted from a paper presented at the XXIIIrd Annual Medical Conference of the Ethiopian Medical Doctors' Association, May 1987, Addis Ababa.

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the blood glucose was well over 300mg/dl. Such wide discrepancies between the blood and urine sugar values are sources of confusion, and often result in improper management of the diabetes.

There are very few studies which indicate the limited value of urine glucose determination in the assessment of diabetic control in hospital patients (5,6). Except for the study by Morris *et al.* (7), there are no similar studies on ambulatory diabetics, the group which heavily depends on urine glucose determination to control their diabetes. This study was made in 1986 to compare the urine and blood glucose values, to find out the extent of reliability of the urine glucose in the assessment of diabetic control.

PATIENTS AND METHODS

A total of 226 consecutive diabetics, diagnosed and classified according to World Health Organization criteria (8), and attending the Diabetic Clinic at the Tikur Anbessa Teaching Hospital in Addis Ababa, was included in the study. All pregnant diabetics were excluded. There were 102 males and 124 females, none with clinical evidence of bladder dysfunction. Of the total, 108 were insulin-dependent (IDDM) and 118 non-insulin-dependent diabetics (NIDDM). The mean age was 40.3 ± 14.3 years (± standard deviation), and all age-groups (14 to 61 years) were represented.

There were 170 patients without proteinuria (Group A), and 56 with persistent proteinuria (Group B) but without renal failure.

History of drug intake, other than for diabetes, was recorded, and all the biochemical tests were performed at the clinic itself. About 79% of the tests were done within 3 hours after a meal, and, in the remaining 21%, the tests were made in the fasting state.

Capillary blood glucose was determined, about 20 to 30 minutes before the second-voided urine collection, with Dextrostix and a glucometer (Ames Division, Miles Laboratories, Elkhart, Indiana, USA), which was calibrated with chips. Aliquots of second-voided urine were collected 30 minutes after the first voiding, and were tested for glucose by the Clinitest (Ames Division, Miles Laboratories, England) method. In both determinations, all obeservations were meticulously carried out in accordance with manufacturers' directions.

The capillary blood and urine glucose were determined by two separate persons throughout the study; neither person was aware of the results of the other. For the purpose of this study, and also in view of the therapeutic implications in our circumstances, glycosuria was considered as clinically important when there was 750mg/dl (2+) and above. Similarly, the blood glucose level was considered clinically important when it was 200mg/dl and above.

RESULTS

None of the patients took any drug or other compounds which are known to interfere with the Clinitest method.

Table 1 shows the urine and capillary blood glucose values in Group A diabetics. Of the 42 diabetics with blood glucose equal to or less than 180mg/dl, 5 (11.9%) had important glycosuria (2 with 3+; 3 with 4+ glycosuria). Of 128 patients who had blood glucose of more than 180mg/dl, 22 (17.2%) had no glycosuria, of whom 14 (10.9%) had blood glucose over 200mg/dl. When clinically important glycosuria and blood glucose alone were considered, the sensitivity, specificity, accuracy and positive predictive values of the Clinitest method were 75%, 82%, 77% and 89%, respectively (Table 2). Thus, a good number of our patients were shown to have misleading urine glucose results, for reasons that were unclear, or possibly because of differences

TABLE 1
Capillary blood glucose versus urine glucose in diabetics without proteinuria (Group A)

Capillary blood glucose (mg/dl)	Clinitest Negative	Positive	Total
⩽ 180	36	6	42
181 - 299	20	40	60
⩾ 300	2	66	68
Total	58	112	170

TABLE 2
Urine glucose by Clinitest in relation to the blood glucose value in Group A diabetics

Semiquantitative urine glucose (mg/dl)	Blood glucose (mg/dl) ⩾ 200	⩽ 199	Total
⩾ 750	TP[1] 86	FP[2] 10	96
< 750	FN[3] 28	TN[4] 46	74
	Total 114	56	170

[1]TP : true positive; [2]FP : false positive; [3]FN : false negative; [4]TN : true negative

TABLE 3
Capillary blood glucose versus urine glucose in diabetics with persistent proteinuria but without renal failure (Group B)

Capillary blood glucose (mg/dl)	Clinitest Negative	Positive	Total
⩽ 180	10	5	15
181 - 299	11	13	24
⩾ 300	2	15	17
Total	23	33	56

TABLE 4
Urine glucose by Clinitest in relation to the blood glucose value in Group B diabetics

Semiquantitative urine glucose (mg/dl)	Blood glucose (mg/dl) ⩾ 200	⩽ 199	Total
⩾ 750	TP[1] 21	FP[2] 4	25
< 750	FN[3] 13	TN[4] 18	31
	Total 34	22	56

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in the renal threshold values. Certainly, these patients would suffer from the consequences of inappropriate management of their diabetes if urine glucose test alone was used either to initiate or adjust therapy.

The capillary blood and urine glucose results for Group B diabetics are given in Table 3. Of the 15 patients with blood glucose equal to or less than 180mg/dl, 5 had glycosuria; 2 of the latter had 4+ glycosuria. Of the 41 patients who had blood glucose greater than 180mg/dl, 13 (31.7%) had no glycosuria, and 8 of these 13 had blood glucose over 200mg/dl. The sensitivity, specificity, accuracy and positive predictive values of the Clinitest method, when clinically important glycosuria and blood glucose were considered, were 61.8%, 81.8%, 69.6% and 84%, respectively (Table 4). This again indicates the unreliability of the Clinitest method in a good proportion of the patients with proteinuria.

DISCUSSION

The major drawback of the various commercial products for urine glucose determination, including the Clinitest method itself, is the lack of absolute dependability (Tables3 and 4). When present in the urine, various drugs such as Vitamin C, and metabolites such as gentisic acid, interfere with the test, and may result in inaccurate values. None of the patients in this study had taken any of these drugs, yet quite a number had a disproportionately important or unimportant glycosuria when it was compared with the ambient blood glucose levels. Hence, there must be some other explanation for the discrepancy. One possible reason could be the state of renal threshold for glucose in these patients. Indeed, there are various studies to indicate that age affects the renal threshold, which is higher in the elderly than in the young (9). In this study, 27 of the 116 (23.3%) diabetics in Group A who were less than 50 years old had clinically unimportant (16.4%) or important (6.9%) glycosuria. By the definition stated under Patients and Methods, we found that 12 (22.2%) of the 54 diabetics, belonging to the same group but 50 years of age and over, had glycosuria which was clinically unimportant in 10 (18.5%) and important in 2 (3.7%) patients. Among the 56 diabetics in Group B, 34 were below the age of 50 years, and, of these, 11 (32.3%) had glycosuria which was either unimportant (23.5%) or important (8.8%); and of 22 diabetics in the same group but aged 50 years and above, 7 (31.8%) had glycosuria which was important in only one, and unimportant in 6 (27.3%) patients. These results are in keeping with those in other studies (4). Thus, although the younger diabetics appear to have a relatively lower threshold for glucose when compared with the older diabetics, no definite conclusion could be drawn, since the numbers were not comparable. Nevertheless, a point worth stressing is that these patients could be treated inappropriately on the basis of the urine sugar values, and they might subsequently run into the danger of acute complications, such as hypoglycaemia, which may be fatal. Indeed, we might consider checking the renal threshold at diagnosis, and use that value for interpreting subsequent urine sugars, but the test is impractical for routine use. A simpler and more reliable alternative is to use Chemistrip bG (e.g. Haemoglukotest: Boehringer, Mannheim, West Germany) for blood glucose determination, but the cost is quite high (about US $ 0.23 per strip) for wide use in our present circumstances. Nonetheless Chemistrip is cheaper than Dextrostix (Ames, U.K.; about US $ 0.27 per strip), and the cost could be cut by half if either is used economically. We realise, however, that, especially in rural hospitals, a physician has very few resources at his or her disposal.

Because of the lack of better alternatives, many of our patients who attend the weekly

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Diabetic Clinic in Addis Ababa still use the much cheaper Clinitest (about US $ 0.07 per tablet) for assessing control of their diabetes, while a few others use it to alter their intake of medication. In this study, 30% of the patients were using the Clinitest, of whom about a third, mainly NIDDM patients, used the test for adjusting the dose of their medication. Moreover, the "sliding-scale" mode of therapy, using urine sugar values, is a common practice in many of our hospitals. This method of therapy is used in many instances, but more commonly in newly diagnosed but uncomplicated IDDM patients, or in those who have just come out of ketoacidosis but have not yet started their regular daily dose of insulin. The results of this study indicate that the Clinitest method is not totally reliable for use in "sliding-scale" therapy, and it certainly cannot offer a more accurate result than the result it is designed for.

Thus, on the basis of our findings, the following suggestions are made for physicians practising in Ethiopia and other similar countries, if facilities are available:

(a) When the "sliding-scale" mode of therapy is necessary, we strongly recommend that Chemistrip bG, rather than Clinitest, should be used economically.

(b) Newly diagnosed IDDM cases, without acute complications but admitted for initiation of treatment, should be directly started on intermediate-acting insulin at a dose of 0.6 to 0.8 unit per kilogram body weight, after taking precautions necessary to prevent hypoglycaemia - thus circumventing the usual practice of putting such patients on "sliding-scale" first, and later switching them to their daily doses. The initial dose of insulin may then be adjusted every 3 to 4 days according to the blood glucose result. We should mention here that, in a well-organised Diabetic Clinic, the insulin therapy for uncomplicated IDDM patients is initiated on an ambulatory basis, after proper education. This is obviously much cheaper and more meaningful in terms of primary health care.

(c) Ambulatory diabetics who check their urine glucose should be advised to see their physicians when their urine glucose values are either clinically important or unimportant, instead of making their own decisions about treatment.

(d) Blood glucose should be periodically determined to confirm judgements made on diabetic control using the urine glucose values.

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The authors wish to thank all those physicians, nurses and technicians who were directly or indirectly involved in the care of the patients. We also thank Dr Hagos Beyene for valuable suggestions, Sister Yeshareg Lungi for assistance, and W/o Fantaye Takele for typing the manuscript.

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Clinical experience with ^{99m}Tc-MAG3, mercaptoacetyltriglycine, and a comparison with ^{99m}Tc-DTPA

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Abstract. The preparation, application and clinical usage of ^{99m}Tc-mercaptoacetyltriglycine, MAG3, a tubular secreted compound, is described in the first 225 patients in a phase III study. Image quality, relative renal function, and renal transit times were compared with a 4 fold greater administered activity of ^{99m}Tc-DTPA in 11 patients. Correlation coefficients of 0.94 for relative function, 0.83 for parenchymal transit time index and 0.82 for whole kidney transit time index were found. Frusemide responses were similar. ^{99m}Tc-MAG3 is an efficacious radiopharmaceutical for routine renal radionuclide studies, giving excellent image quality in patients with hypertension, poor renal function, obstructive nephropathy or a renal transplant.

Key words: ^{99m}Tc-MAG3 – ^{99m}Tc-DTPA

nce its introduction into clinical use in 1970 (Hauser et al. 1970), technetium labelled diethylenetriamine penta-acetic acid (^{99m}Tc-DTPA) has played an unchallenged role as the ain radiopharmaceutical for detecting functional abnormalities in the urinary tract in routine clinical use.

^{99m}Tc-DTPA is cleared by glomerular filtration and provides an excellent alternative to iodine labelled orthoiodohippurate, OIH, because of its physical properties and reduced radiation exposure (Taylor et al. 1980; Barbour et al. 1976). Disadvantages, however, stem from the fact that its low extraction efficiency (20%) gives rise to a proportionately low target to background ratio, a fact that should be taken into account when interpreting results in cases of reduced renal function. A high extraction efficiency, up to 87% (Britton and Brown 1971), can be achieved with orthoiodohippurate, OIH, labelled with ^{131}I or ^{123}I, but the disadvantages of the former include a high radiation dose, especially in the presence of outflow obstruction (Elliott and Britton 1978) and poor spatial resolution and sensitivity of images, while the higher cost and reduced availability of the latter precludes its use as a routine renal imaging agent.

Recently, a new and promising series of technetium complexes were synthesized as potential replacements of OIH in kidney function studies (Davison et al. 1981). The new chelating agents were based on an amide nitrogen and thiolate sulphur donor groups.

A preliminary member of the series, ^{99m}Tc-N, N'-bis (mercaptoacetyl) ethylenediamine (^{99m}Tc-DADS) showed rapid extraction and clearance by the kidney but was inferior to OIH as regards to its biological properties (Fritzberg et al. 1981; Fritzberg et al. 1982; Klingensmith et al. 1982, 1983, 1984).

Efforts to avoid sterioisomer formation resulted in the development of a new (N3-S) ligand, ^{99m}Tc-mercaptoacetylglycylglycylglycine (^{99m}Tc-MAG3) which was shown to be a potential replacement of OIH in animals (Fritzberg et al. 1986). Preliminary studies with volunteers (Taylor et al. 1986) and patients (Taylor et al. 1987; Jafri et al. 1988) has shown ^{99m}Tc-MAG3 to be a single radiochemical agent with fast renal excretion.

As outlined in recent work from this department (Jafri et al. 1988), phase I and II studies were done to compare the simultaneous clearance of ^{99m}Tc-MAG3 and ^{131}I-OIH and to compare renal handling of ^{99m}Tc-MAG3 with ^{123}I-OIH. In this work (phase III), a clinical evaluation of ^{99m}Tc-MAG3 involving 225 patients has been undertaken. In a sub group, the results obtained in 11 patients with ^{99m}Tc-MAG3 have been compared with those obtained within 4 weeks with ^{99m}Tc-DTPA. This work is undertaken to evaluate whether ^{99m}Tc-MAG3 meets the requirements of the ultimate renal radiopharmaceutical which should be safe, cheap, readily available, easy to prepare and clinically useful.

Materials and methods

A total of 225 patients referred to the Nuclear Medicine Department for routine radionuclide renography were selected for this study (males 135, females 90 mean age: 47 years range 9 to 75 years). The majority of patients came from either the hypertension clinic or the Urology Department at St. Bartholomew's Hospital, London. The causes for referral were hypertension (94), assessment of a renal transplant (42), possible urinary tract obstruction (75) and (14) for various other reasons. Table 1, 33 of these studies were follow-up tests in the same set of patients.

The studies with MAG3, being approved by the City and Hackney District Ethical Committee for routine use, were carried out with a thorough explanation given before each routine procedure and most patients were willing to try a new imaging agent in preference to the existing one.

...requests to: A. Al-Nahhas

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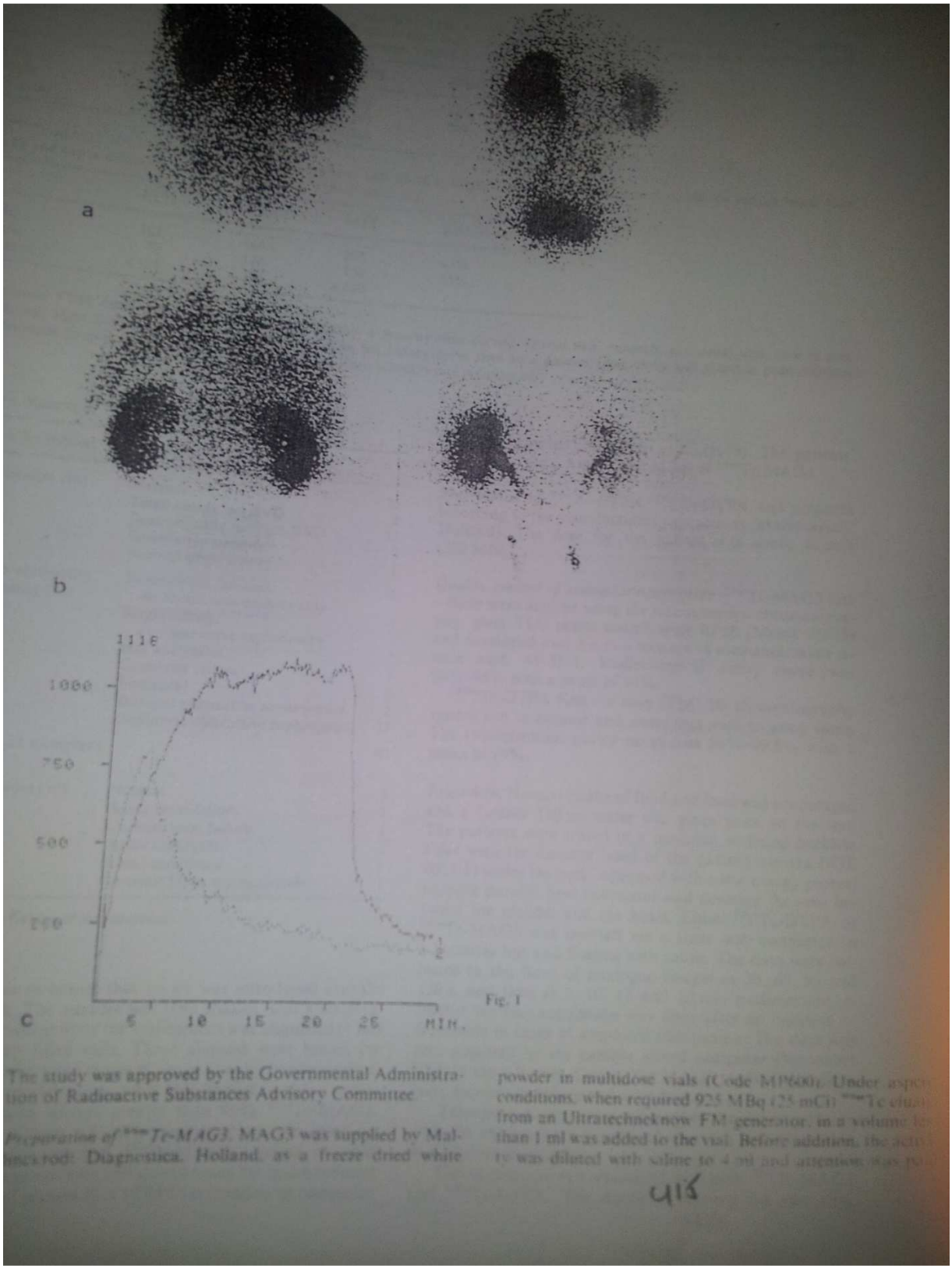


Fig. 1

The study was approved by the Governmental Administration of Radioactive Substances Advisory Committee.

Preparation of ^{99m}Tc-MAG3. MAG3 was supplied by Mallinckrodt Diagnostica, Holland, as a freeze dried white powder in multidose vials (Code MP600). Under aseptic conditions, when required 925 MBq (25 mCi) ^{99m}Tc eluate from an Ultratechnekow FM generator, in a volume less than 1 ml was added to the vial. Before addition, the activity was diluted with saline to 4 ml and attention was to

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ig. 1a–c. JH 56-year-old male with renal colic and a radiolucent renal stone in the left ureter. Renal radionuclide study. a ^{99m}Tc-DTPA 00 MBq Posterior abdominal views. Left 60–90 s, Right 15 min. High background is seen on the 1st image and a dilated left pelvis nd upper ureter is seen in the left kidney on the 15 min image. Transit times in s.

	PTTI	WKTTI	MTT	Relative function
eft	198	294	278	46%
ight	63	86	193	54%
ormal	<156	<170	<240	

^{99m}Tc-MAG3 100 MBq Posterior abdominal views. Left 60–90 s, Right 15 min. Lower background is seen on the 1st image than 1a and better definition on the 15-min image. Transit times in s.

	PTTI	WKTTI	MTT	Relative function
eft	182	544	282	45%
ight	70	120	150	55%
ormal	<156	<170	<240	

bnormal PTTI demonstrates obstructive nephropathy. c Activity time curves: vertical axis, counts/s, horizontal axis, time in min. normal right kidney curve is seen (*light dots*). The left kidney curve rises to a plateau (*dark dots*) and shows a good response frusemide in spite of renal colic and an obstructing stone clinically and radiologically

able 1. Results of ^{99m}Tc-MAG3 studies in 225 patients

eason for request	Diagnosis	
pertension (94)	Normal	75
	Small kidney, no RVD	5
	Symmetrically function RVD	12
	Renal artey stenosis	2
	Normal single kidney	1
ssible obstructive phropathy (75)	Symmetrical function, no obstructive nephropathy	15
	Single kidney, no obstructive nephropathy	2
	Not analysable	2
	Computer failure	1
	Equivocal	2
	Bilateral obstructive nephropathy	2
	Unilateral obstructive nephropathy	15
sess renal transplant		42
scellaneous (14)	Normal	3
	Acute renal failure	3
	Chronic renal failure	3
	Acute aneurysm	3
	Renal carcinoma	1
	Systemic lupus erythematosis	1

RVD Renovascular disorder

technique to ensure that no air was introduced into the paration. The mixture was then shaken, and after mea- ing the total activity the vial content was aliquoted (1 ml) nitrogen filled vials. These aliquots were boiled for min, as and when required, up to four h after reconstitu- n. These modifications have been shown to give a radio- mical purity always greater than 90% ^{99m}Tc-MAG3. n in an aliquot 4 h after reconstitution. An injection accidentally unboiled ^{99m}Tc-MAG3 resulted in good lity analogue images and transit times but much reduced ctive renal plasma flow (ERPF) estimation as compared with the expected value Jafri et al. (1988). The patients' dose was about 2.5 mCi (92.5 MBq) of ^{99m}Tc-MAG3.

Preparation of ^{99m}Tc-DTPA. ^{99m}Tc-DTPA was prepared according to the manufacturers instructions (Mallinckrodt, Holland). The dose for the patient was about 10 mCi (370 MBq).

Quality control of radiopharmaceuticals. ^{99m}Tc-MAG3 kits – these were assayed using the recommended chromatography, glass TLC plates coated with RP18 (Merck 15683) and developed over 3 h in a mixture of methanol:saline:acetic acid, 45:55:1. Radiochemical purity range was 90%–96% with a mean of 94%.

^{99m}Tc-DTPA Kits – a twin ITLC-SG chromatography system run in acetone and water was used to assay these. The radiochemical purity range was 98%–99.8% with a mean of 99%.

Procedure. Normal intake of fluid and food was encouraged and a further 180 ml water was given prior to the test. The patients were seated in a modified reclining backless chair with the detector head of the gamma camera (IGE 400AT) under the back, equipped with a low energy general purpose parallel hole collimator and covering the area between the bladder and the heart. Either ^{99m}Tc-DTPA or ^{99m}Tc-MAG3 was injected via a three way connector to a butterfly line and flushed with saline. The data were collected in the form of analogue images at 30, 60, 90 and 120 s, and then at 5, 10, 15 and 20 min postinjection. A further ten min acquisition was done after an injection of frusemide in cases of suspected obstruction. The data was also acquired by the camera linked computer (Nodecrest V76) in ten s frames. During the MAG3 studies, vital signs were monitored before and after injection.

Transplant studies were acquired in the supine position with the camera head positioned over the transplant area and bladder anteriorly.

Eleven patients were examined with both ^{99m}Tc-MAG3 and ^{99m}Tc-DTPA. The duration between the two tests

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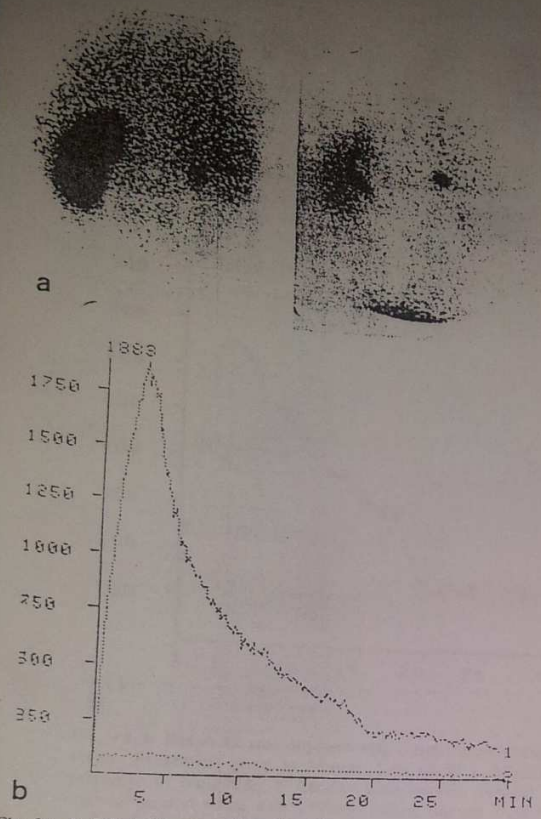


Fig. 3a, b. DB A 20-year-old male with asymptomatic proteinuria was shown to have a right hydronephrosis on intravenous urography. Renal radionuclide study. a ^{99m}Tc-MAG3 100 MBq Posterior abdominal views. Frusemide given at 18 min. Left 90–120 s, Middle 15 min. Right 30 min. A small right kidney with a response to frusemide is seen into a dilated ureter displaced laterally. b Activity time curves: vertical axis, counts/s; horizontal axis, time in min. The left kidney curve is normal (*dark dots*). The right kidney curve is a low plateau. Transit times

	PTTI	WKTTI	MTT	Relative function
Left	48	83	148	95%
Right	22	188	82	5%
Normal	<156	<170	<240	

Conclusion: Poorly functioning right kidney without obstructive nephropathy

kidney transit time (WKTT) were corrected for this obligatory Min. TT leading to parenchymal transit time index (PTTI) and whole kidney transit time index (WKTTI) respectively (Britton et al. 1980). Normal ranges are:

PTTI – 10–156 s
MPTT – 100–240 s
WKTTI – 20–170 s

The data sampling rate of 10 s is such that the very short time for, and the slight difference in timing between, the filtration of ^{99m}Tc-DTPA into and the secretion of ^{99m}Tc-MAG3 into the proximal tubular lumen is totally lost. Thus the transit times of these two compounds along the nephron are expected to be similar. In interpreting the response to frusemide, the persistence of a rise of the activity time curve was taken to indicate obstructive uropathy while a rapid fall indicated the absence of such obstruction. When renal function is reduced, a normal response is that rate of fall appropriate to the previous rate of rise of the renal activity time curve (Britton et al. 1987).

2. Hypertension cases. Applying the same analytic procedure, the presence of renovascular disorder likely to be due to renal artery stenosis as a cause of hypertension was concluded if the relevant kidney appeared smaller in size, showed reduced relative function less than 40% of total and a delay of more than 60 s in MPTT compared with the normal kidney. In kidneys with symmetrical uptake and

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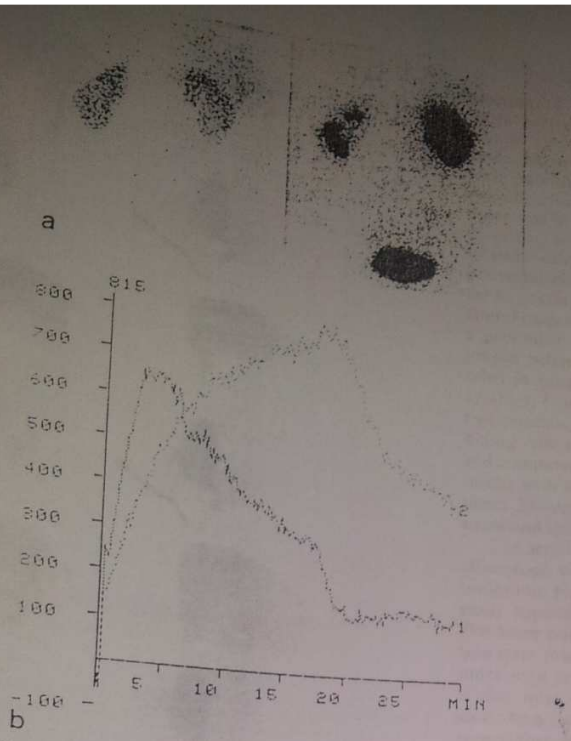


Fig. 4a, b. RH A 49-year-old man with a right ureteric calculus. Renal radionuclide study: a ^{99m}Tc-MAG3 100 MBq posterior abdominal views. Frusemide given at 18 min. Left 60–90 s. Middle 15 min. Right 25 min. Right kidney has a dilated pelvis with a moderate response to frusemide. b Activity time curves: vertical axis, counts s; horizontal axis, time in min. The left kidney curve shows a normal second phase and a slower falling uneven third phase (*dark dots*). The right kidney curve shows a slow rise until the response to frusemide causes a fall. Transit times

	PTTI	WKTTI	MTT	Relative function
Left	61	124	161	63%
Right	126	545	246	37%
Normal	<156	<170	<240	

Conclusion: no evidence of obstructive nephropathy

a prolonged MPTT (over 240 s), renovascular disorder likely to be due to small vessel disease or as a consequence of severe hypertension was discovered. In all cases of renovascular disorder, pelvic transit time is normally less than 240 s.

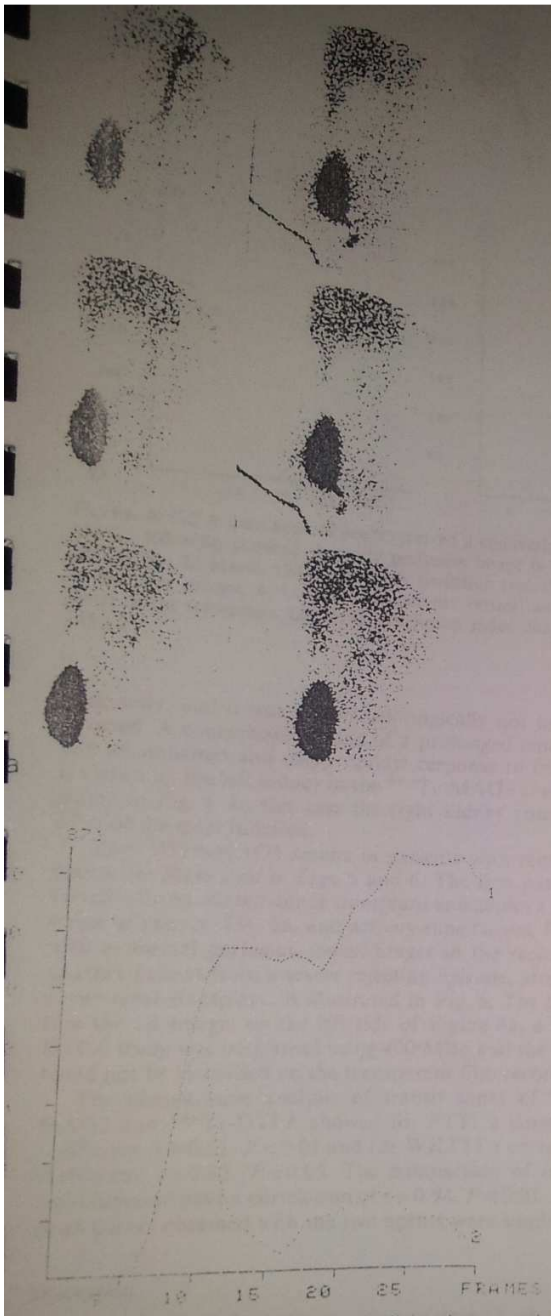
3. Transplant cases. The concept of perfusion index (PI) was adopted (Hilson et al. 1978). Acute tubular necrosis was suggested by the absence of calyceal activity usually with good early perfusion, and a reduced PI improving with time from operation. A rise in PI together with a reduction of a previously satisfactory early perfusion of the transplant usually indicated deterioration due to a rejection episode.

Data interpretation. Besides the computer analysed data, the analogue images were considered visually, to determine the size, shape and perfusion of both kidneys, the presence of pelvi-calyceal retention, and its response to frusemide. The physicist undertaking the transit time analysis was unaware of the clinical condition of the patient, and since the results were numerical, no bias was introduced.

Results

The reasons for requesting the renal radionuclide study and the consequent diagnoses in the 225 patients are summarised in Table 1. Only 2 patients with renal artery stenosis confirmed radiologically were found in the 94 hypertensives

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a, b. N-M A 19-year-old woman received a living donor renal plant. a Renal radionuclide study one day later with ^{99m}Tc-3 100 MBq Anterior abdominal views. Left hand images 30 s, Middle 30–60 s, Bottom 60–90 s. Right hand images 90–120 s, Middle 4.5–5 min, Top 9.5–10 min. Conclusion: mal renal transplant study with good early perfusion and r and urinary catheter activity at 5 min. b Activity time vertical axis, counts/s; horizontal axis, time in min. 1 Renal lant; 2 Iliac artery distal to the transplant. Perfusion index Conclusion: Normal perfusion

whereas 12 with symmetrical function and a prolonged mean parenchymal disorder characteristic of small vessel disease due to glomerulonephritis or as a consequence of severe hypertension were found. These frequencies accord with published data (Page and McCubbin 1968). In the possible obstructive nephropathy group (75), the usual request was in a patient with either pain thought to be renal in origin, or dilated renal outflow tract or the presence of stone disease on intravenous urography or ultrasound, or combinations of these. Some requests were for postsurgical or postlithotripsy follow up (Bomanji et al. 1987). Unilateral obstructive nephropathy meeting the criteria of both a prolonged parenchymal transit time index with a prolonged pelvic transit time and subsequently confirmed by other investigations, surgery and follow up was present in 15 (Figs. 1 and 4) and bilateral in a further 5 patients. In two patients with less than 4% of total function in one kidney, the transit time analysis could not be performed and computer failure lost the data in one patient. Equivocal results with borderline PTTI values were noted in two patients. Frusemide responses were uninterpretable in six patients and misleading in two.

The serial studies of renal transplants were particularly efficaceous with ^{99m}Tc-MAG3. In this situation the high resolution, high uptake, low background pictures were generally superior to previous experience with ^{99m}Tc-DTPA. The same criteria for acute tubular necrosis and for rejection were found to apply and similar changes in perfusion index with recovery and with rejection were noted. There is also none of the slight hepatic uptake in the field of view. As a result of this excellent initial experience all renal transplants are now being monitored using ^{99m}Tc-MAG3. Figs. 5 and 6. In the miscellaneous group, the visualisation of the kidneys in acute or in chronic renal failure were better than with ^{99m}Tc-DTPA used previously.

A more detailed comparison was performed in 11 patients. The images obtained with ^{99m}Tc-MAG3 in these patients were without exception of better quality and provided improved detail of the kidneys with a higher target to background ratio as compared to ^{99m}Tc-DTPA studies done with four times the administered activity. Some clinical examples are illustrated in Figs. 1 to 6.

A comparison of ^{99m}Tc-DTPA and ^{99m}Tc-MAG3 is made in a 56-year-old man with renal colic due to a radiolucent ureteric stone, Fig. 1. Note the much better definition of renal and calyceal detail and the lower tissue background when using MAG3 at one quarter of the administered activity, Fig. 1b, compared with Fig. 1a. Both these studies show a prolonged parenchymal transit time index, indicating obstructive nephropathy and yet there is a normal response to frusemide, Fig. 1c. Ureteric obstruction was confirmed radiologically and lead to operative intervention. A false frusemide response may be seen in the presence of obstructive nephropathy when renal function is very good (Britton et al. 1987).

A 59-year-old female had a left hydronephrosis with very poor function, 6% of the total, as shown by ^{99m}Tc-MAG3, Fig. 2. PTTI shows left obstructive nephropathy and there is no response to frusemide, Fig. 2b, but at this level of function this lack of response may occur due to an inability to induce a diuresis. A further illustration of this is given by the results of a ^{99m}Tc-MAG3 study shown in Fig. 3. A normal PTTI is seen in the right kidney which contributes 5% of total function. Visual response [illegible]

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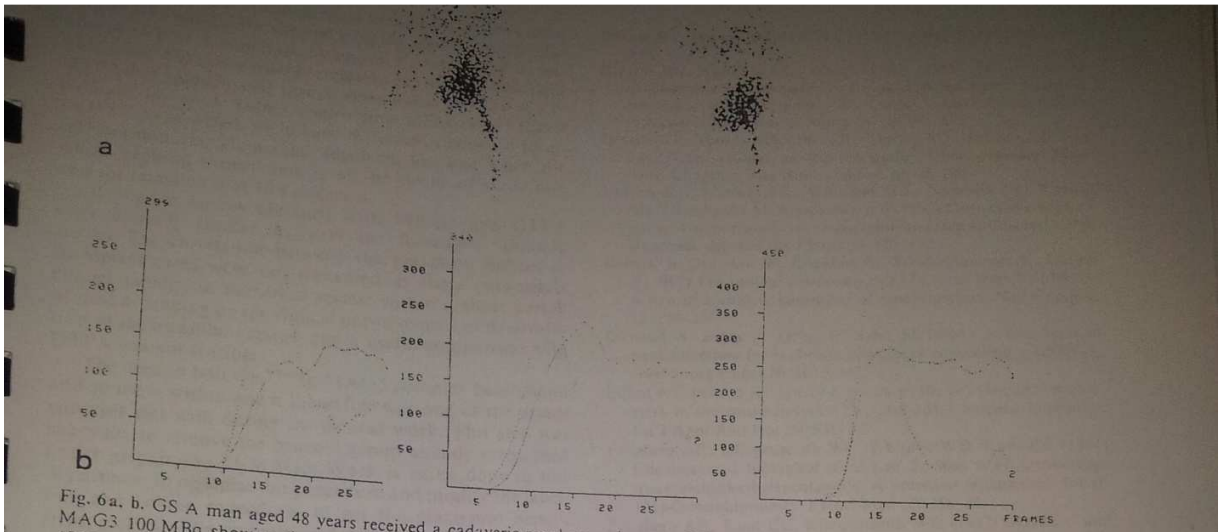


Fig. 6a, b. GS A man aged 48 years received a cadaveric renal transplant on 19 February 1987. Renal radionuclide studies with ^{99m}Tc-MAG3 100 MBq showing the early perfusion image 0–30 s on an anterior abdominal view. a Left 6 March 1987, Middle 10 March 1987, Right 20 March 1987. Poor early perfusion typical of rejection is seen on the first image with subsequent recovery demonstrated in the later images. b Activity time curves: vertical axis, counts/s; horizontal axis, time in min. 1 Renal transplant; 2 iliac artery distal to the transplant. Left 6.3.87 Perfusion index 263±24; Middle 10.3.87 Perfusion index 213±16; Right 20.3.87 Perfusion index 145±9

mide only, and it was shown radiologically not to be obstructed. A concordant finding of a prolonged renal PTTI and an impaired and inappropriate response to frusemide is shown by the left kidney in the ^{99m}Tc-MAG3 study illustrated in Fig. 4. In this case the right kidney contributed 37% of the total function.

Two ^{99m}Tc-MAG3 results in patients with renal transplants are illustrated in Figs. 5 and 6. The first patient received a living related donor transplant and shows a normal series of images, Fig. 5a, and activity time curves, Fig. 5b, with a normal perfusion index. Stages in the recovery of another patient from a severe rejection episode, after a cadaver renal transplant, is illustrated in Fig. 6. The day before the 1st image, on the left side of Figure 6a, a ^{99m}Tc-DTPA study was performed using 400 MBq and the kidney could not be visualised on the transparent film record.

The comparative analysis of transit times of ^{99m}Tc-MAG3 and ^{99m}Tc-DTPA showed for PTTI a correlation coefficient, $r=0.83$, $P<0.05$ and for WKTTI a correlation coefficient, $r=0.82$, $P<0.05$. The comparison of relative renal function gave a correlation of $r=0.94$, $P<0.01$. Renogram curves obtained with the two agents were similar.

Discussion

In a previous study from this department (Jafri et al. 1988), phase I and II studies were done to compare the simultaneous clearance of a new renal radiopharmaceutical, mercaptoacetyltriglycine (MAG3) labelled with ^{99m}Tc with that of ^{131}I labelled orthiodohippurate (OIH) and to compare the renal handling of ^{99m}Tc-MAG3 with that of ^{123}I-OIH in serial studies.

The purpose of this study (phase III) was to evaluate the clinical usefulness and robustness of ^{99m}Tc-MAG3 in routine practice and to make a comparison with technetium labelled diethylenetriamine penta-acetic acid ^{99m}Tc-DTPA.

The study involved a total of 225 patients with a wide range of renal function impairment, and the results of 11 patients were compared with those obtained, within 4 weeks, with ^{99m}Tc-DTPA, given 4 times the activity of that used for ^{99m}Tc-MAG3. Visual analysis and interpretation of analogue images obtained with ^{99m}Tc-MAG3 were clearly superior to those obtained with ^{99m}Tc-DTPA with higher target to background ratio, particularly in cases where the renal function was so depressed as to render DTPA images difficult to evaluate.

The extraction efficiency of MAG3 was determined recently in rats (Fritzberg et al. 1986) and was found to be about 85% compared to 69% for ^{131}I-OIH, and as MAG3 was predominantly protein bound at 77% compared to 33% for OIH, the corrected tubular cell extraction was found to be 75% for MAG3 and 43% for OIH. Protein binding, however, showed different values in different studies. A value of 88% was found in volunteers (Taylor et al. 1986) and 91% in patients (Bubeck et al. 1987), while our measurements produced a value of 78%. These differences may simply reflect different techniques used, and further evaluation of this point is clearly needed.

A good DTPA substitute should be able to assess accurately the percentage contribution by each kidney to the

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total renal function. A comparison of such values obtained with MAG3 and DTPA showed a highly significant correlation of $r = 0.94$. Comparative computer analysis for transit time values showed a good correlation between MAG3 and DTPA for parenchymal transit time index (PTTI) of $r = 0.83$ and for whole kidney transit time index (WKTTI) of $r = 0.82$. As expected, slight time differences between tubular secretion and glomerular filtration are lost when the whole nephron transit time is of the order of three min and the sampling is at 10 s intervals.

Renogram curves obtained with MAG3 and DTPA were basically similar, as were the frusemide response curves. The correlation between the perfusion indices in transplant cases were not measured as these parameters change rapidly, in numerical terms, within a short period of time depending on the clinical improvement or deterioration of the transplant status, and a useful comparison with DTPA was not feasible.

The need to boil the ^{99m}Tc-MAG3 complex beforehand and to use it within one h thereafter was one of the disadvantages met with during the clinical work. This step was necessary to remove the benzoyl group already mentioned under preparation of MAG3. Work is being done in this department to optimise this procedure and modify the labelling and boiling procedures to get the maximum benefit from each kit. The preliminary findings show that the boiling step can be separated by as much as four h from the time of addition of ^{99m}Tc to the MAG3 without increase in the lipophilic liver secreted components particularly when the radiopharmaceutical is kept cold. At each of these preparative steps, one may divide the kit into pairs of doses to give finally four doses arranged at times convenient for the patient studies during a morning or afternoon session. Another minor disadvantage was a 4% hepatobiliary excretion of MAG3 which did not interfere with data processing or interpretation and was shown to be unrelated to the state of kidney function. No untoward changes in vital signs were noted after the MAG3 injection. No side effects were observed and there were no unexpected haematological or biochemical findings.

We conclude that ^{99m}Tc-MAG3 is an excellent renal radiopharmaceutical in routine use. It has some advantages over ^{99m}Tc-DTPA with comparable relative function and transit time studies and it is particularly suitable for the evaluation of renal transplants.

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IDIOPATHIC ULCERATIVE COLITIS AMONG ETHIOPIAN PATIENTS WITH CHRONIC DIARRHOEA

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ABSTRACT. *Using both exclusion and inclusion criteria, a search for idiopathic ulcerative colitis was made among patients who presented with chronic diarrhoea over a period of 3 years. Five of 19 patients with chronic diarrhoea were clinically, histologically and radiologically compatible with idiopathic ulcerative colitis. Though rare, idiopathic ulcerative colitis does exist among this population and, therefore, should be looked for in patients presenting with chronic diarrhoea.*

INTRODUCTION

Idiopathic ulcerative colitis is defined as a chronic disease of unknown aetiology characterized by inflammation of the mucosa and submucosa of the rectum and colon (1).

The disease was first recognized as a separate entity around 1875. This disease is relatively common in Northern Europe and North America with an estimated incidence and prevalence of 2-7 and 40-100 cases per 100,000 population, respectively (1). Ulcerative colitis was not recognized in the tropics until Chuttani and colleagues (2) called attention to the existence of the disease in India in 1967. While the disease has a relatively higher incidence in industrialized western countries, over the northern half of Europe, North America, Australia and New Zealand, cases have been reported from other countries of the world such as South and Central America, the Middle East, Africa, India and Japan (3,4).

In Africa, the disease is rare. Billinghurst (5) reported three cases of idiopathic ulcerative colitis in 1964. During the same year Pillay (6) reported 4 cases of ulcerative colitis from Durban, South Africa. In 1966, Billinghurst (7) gave a detailed account of 4 cases of ulcerative colitis diagnosed at Mulago Hospital in Uganda. More case reports appeared in East Africa, from Dar es Salaam and Nairobi in 1971 and 1972, respectively (8,9). Powel and Wilmot (10), in 1966, and Sobel and Schamroth (11), in 1970, reported cases of ulcerative colitis among Blacks in South Africa. In Africa, south of the Sahara, Segal et al (12) estimated that 18 cases were reported up to 1975. Recently, Aubry and co-workers (13) stated that 46 cases of ulcerative colitis have been reported up to 1982.

However, to the best of our knowledge, there has been no case report of ulcerative colitis from this country and, therefore, we considered it appropriate to search for cases of ulcerative colitis among patients with chronic diarrhoea, studied during the last 3 years, 1985-1988.

MATERIALS AND METHODS

Diagnostic methods: Chronic diarrhoea is defined as bloody and mucoid diarrhoea which has lasted for more than 6 months,

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with the aetiology not identified on simple stool tests for ova and parasites and cultures of stool for common organisms (e.g. *Salmonella* and *Shigella*). Cases of malabsorption syndrome, chronic diarrhoea due to diabetic automatic neuropathy and vagotomy were exluded in this study. Villous adenoma and carcinoma of the colon and rectum were also exluded. Therefore, patients who presented with chronic diarrhoea with blood and mucus in their stools, who had repeated negative stool tests for ova and parasites, who have received antibiotics and antiamoebic chemotherapy and who, upon failing to respond to such treatment modalities, were considered for further evaluation. These patients were investigated with physical examination, stool tests for ova and parasites, liver function tests and, in some cases, total serum protein and electrophoresis, stool culture for enteropathogens and *Entamoeba histolytica (E. histolytica)*. Barium enema using double-contrast method, barium meal with follow-through, chest X-ray, sigmoidoscopic and colonoscopic visualization were carried out.

RESULTS

Using the criteria and investigative methods outlined under material and methods, 19 cases of chronic diarrhoea were classified as follows: 5 idiopathic ulcerative colitis, 5 non-specific colitis, 2 amoebic colitis and 2 cases of colitis due to *Schistosoma mansoni*. The remaining 5 cases had either normal mucosa or could not be diagnosed by any criteria.

A brief summary of the clinical picture of each case of idiopathic ulcerative colitis is presented.

Case 1. A 26-year-old male health assistant was referred from Dessie Hospital in 1980. He had chronic diarrhoea of 10 months' duration. The patient had episodic bloody and mucoid diarrhoea with tenesmus and cramping abdominal pain. He was treated with antibiotics and antiamoebic medications without any finding on stool examinations. He had no relief from such therapy and was referred for further investigation.

Physical examination of the patient revealed no positive findings and laboratory investigations revealed no parasites in a number of stool specimens.

Using a rigid sigmoidoscope, the mucosa of the rectum and sigmoid colon showed diffuse inflammation. Multiple biopsies taken from the rectum and sigmoid for histological examination revealed purulent slough. He was referred to a military hospital where fibreoptic colonoscope was available. The entire mucosa from the rectum to the caecum was viewed. Again multiple biopsies were obtained from all parts of the colon and the rectum, the histology of which revealed inflammatory changes with crypt abscesses.

On clinical and histological grounds, a diagnosis of idiopathic ulcerative colitis was made. However, as his symptoms were mild he was followed as an outpatient with symptomatic management.

In 1986, the patient came with severe and acute attack of bloody diarrhoea, cramping abdominal pain with tenesmus, fever, weight loss and dehydration. He lost significant amount of blood per rectum and required blood transfusions. Repeated stool tests and stool culture for enteric organisms were negative. He was admitted to the hospital and was treated with oral and parenteral steroids. The patient improved after about 3-4 weeks of steroid therapy which was gradually tapered. He was advised to continue with a maintainance dose of sulfasalazine. The steroid treatment caused hyperglycaemia and diabetes mellitus which disappeared after it was discontinued. Sigmoidoscopic examination after the acute phase of his illness revealed acutely inflammed rectal and sigmoid mucosa with friability and granularity.

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The histology report indicated few inflammatory cells in the mucosa but no typical crypt abscess. A barium enema performed after the symptoms subsided showed typical radiographic appearances of ulcerative colitis (Fig. 1). The patient was followed regularly after discharge for over a year. He was doing very well except when he discontinued sulfasalazine which was not available in Ethiopia.

Case 2. A 23-year-old single woman presented with complaints of bloody diarrhoea of one year duration. This patient was healthy until the death of her mother at which time she started to have diarrhoea intermittently. She was seen and treated symptomatically for diarrhoea which was bloody and mucoid with a frequency of 4-5 times during the day and night. She also had cramps and tenesmus. She lost weight and developed easy fatiguability. She was admitted on two occasions and received antiamoebic treatment and also underwent haemorrhoidectomy in another hospital. Finally she came to Tikur Anbessa Hospital. At this point the patient had lost 10 kg. of body weight.

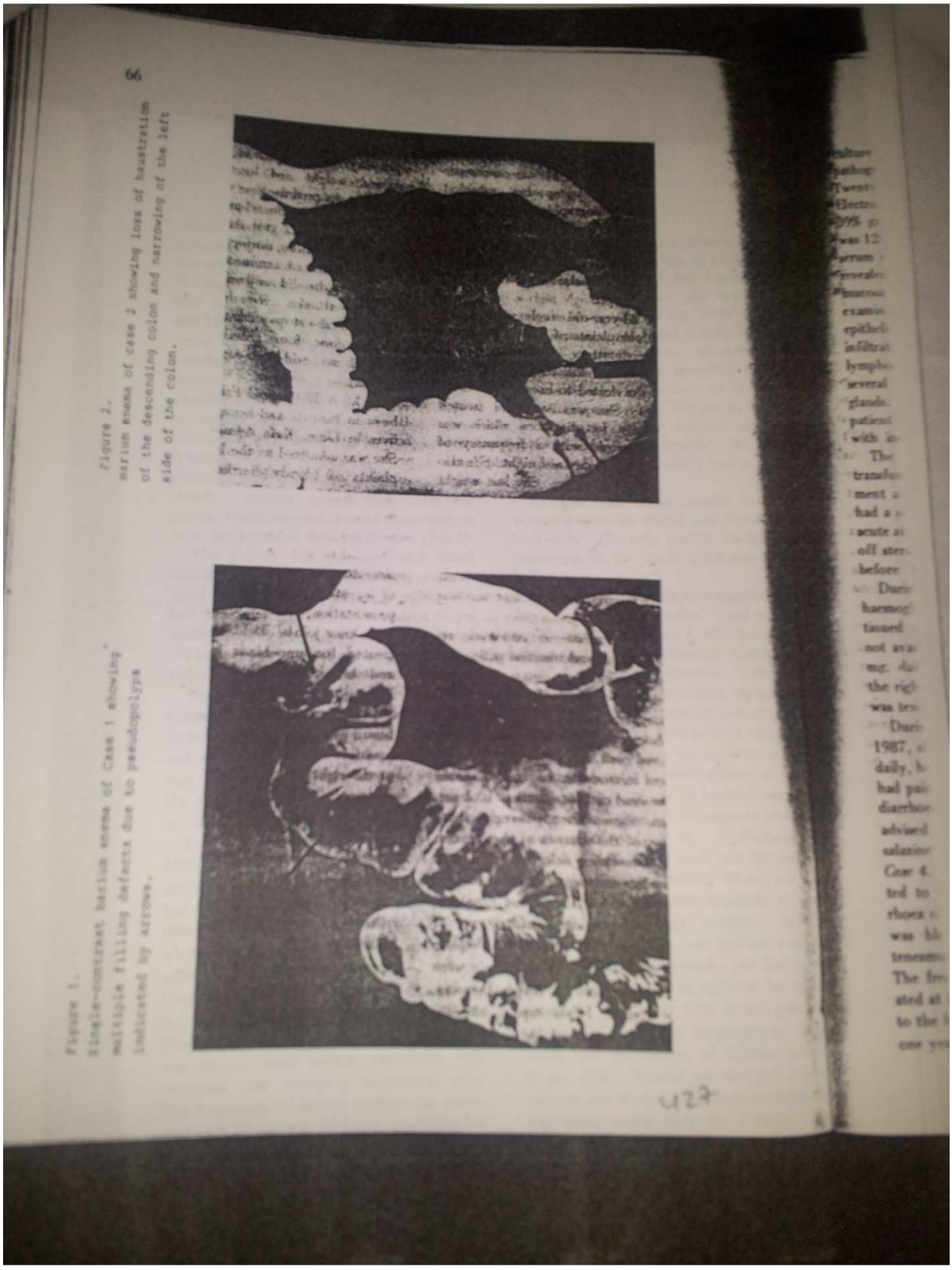
Physical examination on admission revealed conjunctival and mucosal pallor and a soft systolic ejection murmur over the precordium.

Laboratory investigations were all normal except for haemoglobin which was 10 gm/dl. Peripheral red cell morphology was hypochromic and microcytic. Lactose tolerance test was abnormal and fecal fat was 10.4 gm. per 24 hours. Sigmoidoscopy revealed acute inflammation of the mucosa of the rectum, sigmoid and descending colon and there was purulent exudate covering the mucosa which was friable. Histology indicated considerable inflammation with infiltration of lamina propria with cells rich in eosinophils and plasma cells. The mucosal glands were normal and there were no crypt abscesses, parasites or cysts. Two repeat biopsies over the last 3 years revealed nonspecific colitis. The patient was given blood transfusion, antibiotics and prednisolone 40 mg. per day. She improved dramatically. She gained weight and her symptoms disappeared. As prednisolone was tapered, sulfasalazine was introduced and finally, she was on sulfasalazine 2 gms daily. She has had 4 acute recurrences during the last 3 years. Steroids induced remissions during two attacks and she did well with sulfasalazine in between attacks. She develops symptoms whenever she stops sulfasalazine. A barium enema done four years after her illness showed no evidence of ulcerative colitis (Fig. 2).

Case 3. A 50-year-old Ethiopian housewife, born in Nairobi and brought up there, now lives in Limu, Kafa Administrative Region. She was admitted to the hospital with complaints of bloody diarrhoea and cramping abdominal pain of 3 years' duration. The diarrhoea was episodic. She had 3-4 bowel motions daily during periods of her illness. She had no tenesmus or fever. She lost considerable weight and had occasional vomiting of ingested food. A few days prior to her presentation, she developed arthralgia in both knee joints. Before admission, she was treated for amoebiasis in different clinics and hospitals. Physical examination on admission showed a chronically sick-looking woman but in no apparent distress. The blood pressure was 110/70 mmHg. in supine position. She had a scaly lesion on the scalp at the right temporal and parietal area. She had pale conjuctivae and buccal mucosa. The abdomen was diffusely tender all over and there was no ascites or hepatosplenomegaly. The rest of the examination was normal.

After admission to the hospital, the condition of the patient became critical. Her diarrhoea increased and vomiting was frequent. She became hypotensive. At admission, her haemoglobin was 8.3 gm/dl and serum albumin 4.8 gms %. Repeated stool tests were negative for ova and parasites

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Figure 1.
Single-contrast barium enema of Case 1 showing multiple filling defects due to pseudopolyps indicated by arrows.

Figure 2.
Barium enema of case 2 showing loss of haustration of the descending colon and narrowing of the left side of the colon.

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culture and stool did not grow entero pathogens (*Salmonella* and *Shigella*). Twenty-four hours faecal fat was normal Electrophoresis showed 28.5% albumin and 39% gamma globulin. The serum sodium was 120 mEq/L, potassium 3.06 mEq/L and serum calcium 5.5 mEq/L. Sigmoidoscopy revealed an inflammed granular and friable mucosa. Biopsy was taken and histological examination showed partially ulcerated epithelium, increased vascularity with heavy infiltration of mucosa and submucosa with lymphocytes and plasma cells. There were several crypt abscesses in the epithelial glands. Barium enema done after the patient's improvement showed pseudopolyps with incompetent ileo-caecal valve (Fig 3).

The patient was managed with blood transfusion, fluid and electolyte replacement and parenteral and oral steroids. She had a smooth induction of remission of her acute attack of ulcerative colitis, was weaned off steroid and maintained on sulfasalazine before her discharge from the hospital.

During her first follow-up, she had a haemoglobin of 15 gm/dl. She discontinued sulfasalazine because the drug was not available. She was on prednisolone 10 mg. daily. She developed knee stiffness; the right knee joint had effusion. The liver was tender and palpable on deep inspiration.

During her last follow-up in September of 1987, she was still on prednisolone 10 mg. daily, her joint swelling had subsided but she had pain in the right knee joint. She had no diarrhoea. She had Cushingoid face. She was advised to stop steroid and to start sulfasalazine which was then available.

Case 4. A 35-year-old housewife was admitted to the hospital with a history of diarrhoea of 14 months' duration. The diarrhoea was bloody with mucus, associated with tenesmus and cramping abdominal pain. The frequency of bowel motion was estimated at 8-10 times in 24 hours, confining her to the house. During her illness for the last one year, she was treated for amoebiasis in a number of clinics, but her symptoms did not improve. She lost 19 kgs. in 14 months. She was asthmatic and had hypertension for the last 2-3 years. She was taking hydrochlorothiazide 25 mg. daily for her hypertension and Franol tablets, a combination of theophylline, ephedrine and phenobarbital, for her bronchial asthma. She had no family history of bronchial asthma or hypertension. The patient lived in Addis Ababa with her husband and four children who were all healthy. She stated that her marital relationship was a happy one.

Physical examination revealed an obese woman despite her weight loss. She did not look sick. The only positive finding was tenderness in the lower quadrants of the abdomen.

Examination of stools were negative three times for ova and parasites. Stool cultures for enteropathogens and *E. histolytica* were also negative. Sigmoidoscopic examination revealed diffusely inflammed, friable and granular mucosa of the rectum, sigmoid and descending colon. Histology indicated purulent inflammation with at least one crypt abscess. There were no parasites or ova.

Barium enema showed evidence of ulcerative colitis, with loss of haustral markings and pseudopolyps of the sigmoid and descending colon (Fig. 4). A diagnosis of ulcerative colitis was made and the patient was started on prednisolone 40 mg. per day per os. Ten days after initiation of prednisolone therapy, her condition became worse; the diarrhoea was profuse and the patient became hypotensive and had to be on parenteral fluids to maintain her blood pressure. Stool test done at this point revealed *E. histolytica* trophozoites, 8 per silide and trophozites of *Ciardia lamblia*, 5 per slide. Steroid was stopped and the patient was treated with metronidazole 750 mg. three times daily for 7 days. Subsequent stool tests were negative while the patient was still having diarrhoea. She was

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started again on prednisolone and this was continued until the patient was on sulfasalazine. She was discharged on sulfasalazine and followed at short intervals. The patient has no diarrhoea as long as she continues to take sulfasalazine.

Case 5. A 45-year-old male nurse was referred from the Gondar College of Medical Science with complaints of diarrhoea of 8 years' duration. Diarrhoea started 8 years ago when the patient was on duty in northern Ethiopia on temporary assingment. The diarrhoea was intermittent and light at the onset with long periods of remissions. It gradually became worse and, during the last 8 months, the diarrhoea persisted and increased in frequency, from 4-5 to 10 times in 24 hours. The nature of the stool also changed from watery to bloody at times. He had boring abdominal pain in the lower quadrants and the pain was worse after meals. He lost 10 kg. of body weight over the last 8 months. He has no family history of similar illness. He received antibiotics and chemotherapy which did not help at all. He was treated with trimethoprim and sulfamethoxazole (Bactrim) and metronidazole (Mezil). Sigmoidoscopy done in Gondar revealed normal mucosa up to 25 cm. from the anal orifice. Biopsy taken from levels of 10, 15, and 25 cms. showed "chronic destructive proctitis with evidence of scars". He was referred to Tikur Anbessa Hospital for further management. A repeat endoscopic examination showed an erythematous mucosa with patchy petechiae, granularity and a few diverticulae on the sigmoid area. Histology revealed a severe, chronic, purulent inflammation of the lamina propria with crypt abscesses. It also showed loss of surface glands without ulceration. Barium enema showed signs compatible with ulcerative colitis. Stool test revealed *Strongyloides* larvae. The patient was treated with thiabendazole for his strongloidiasis but the diarrhoea did not improve. On clinical, radiographic and histologic grounds, a diagnosis of ulcerative colitis was made and the patient was started on prednisolone 40 mg. per day to induce remission. He was then weaned off steroids and given sulfasalazine 500 mg t.i.d. for indefinite period of time. The patient did so well that he was given appointment to come after 6 months for evaluation of his long term response to this therapy. He was not seen since.

DISCUSSION

This study indicates that idiopathic ulcerative colitis exists in Ethiopia but uncommonly, as reported in some other African countries (11-13). Awori and associates (9) used the criterion of diarrhoea of six months' duration in their study of causes of chronic diarrhoea in Kenya and uncovered the first four cases of ulcerative colitis. However, they did not exclude cases of malabsorption and malignancies of the colon and rectum, nor did they limit their study to patients with bloody and mucoid stools. Our criteria are very rigid and, in retrospect, they may be considered valid for use when one has to search for idiopathic ulcerative colitis in a setting where infectious diarrhoea is so common and overwhelming. Amoebic diarrhoea can recur and may simulate idiopathic ulcerative colitis. Powel and Wilmot (10) described an entity called "Ulcerative post-dysenteric colitis" which is believed to be due to a non-specific chronic colitis that occurred after the specific infection had died out. They described such complication following severe attacks of amoebic colitis in 20 out of 33 patients. Their patients continued to have dysentry for as long as 9 months. Although this entity is no longer mentioned in textbooks of medicine, its response to steroid should not be misinterpreted as idiopathic colitis. The sigmoidoscopic and histological findings of acute amoebic colitis may, at times, appear identical with idiopathic ulcerative colitis

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Figure 3. Double-contrast barium enema of Case 3 showing colonic wall contour irregularity of the pseudopolypoid descending colon with mucosal swelling.

Figure 4. Doble-contrast barium enema of Case 4 showing absence of haustrae of sigma and part of descending colon with filling defects shown by arrows. This case had a widening of soft tissue space between the sacrum and posterior wall of the rectum on lateral radiographs.

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(10, 14).

Schistosoma mansoni infection is widely prevalent in this country. It can cause recurrent chronic diarrhoea and the ova may be missed in stool tests unless special concentration methods are used. One of the differential diagnoses of ulcerative colitis in this country, therefore, is *Schistosoma mansoni* infection. Repeated stool tests, using Ritchie's modified concentration method, and rectal biopsies will eventually reveal the diagnosis. Although pulmonary, peritoneal and lymphatic tuberculosis is rampant in Ethiopia, enteric tuberculosis is exceptionally uncommon (15), (Personal Communication Prof. Landells). Of infectious causes that can cause chronic diarrhoea, *Yersinia enterocolitica* should also be considered. However, we have no facility to culture this organism at the moment. Both the sigmoidoscopic appearance and histological findings of *Yersinia enterocolitica* infection of the colon may present a picture similar to idiopathic ulcerative colitis (16). Crohn's colitis or ileitis is extremely rare in this part of the world. Only one authenticated case has been reported recently (17) and a few cases have been diagnosed by the surgeons in Tikur Anbessa Hospital (Personal communication; Orvar Johnson). In all cases, the presenting signs and symptoms were those of intestinal obstruction and/or appendicitis.

The age of onset of the disease, in the 5 cases, is between 23 and 47. Except case 3, all were between 20 and 40 years at the onset of the illness, similar to observations made elsewhere (18,19). The duration of symptoms ranged between 10 months and 8 years. This is because recognition of this disease has been delayed by the lack of experience in making the diagnosis in a setting where specific colitis predominates. Interestingly, all of our patients are from middle class urban population. Only one case (Case 3) came from the rural area, and she too was born and grew up in Nairobi, Kenya. Dietary changes and urbanization are believed, by some, to play a role in the predisposition to the acquisition of idiopathic ulcerative colitis (4,20). The peasants constitute the majority in this country and the absence of idiopathic ulcerative colitis in this population is of interest. Of course, the utilization of medical services is one factor that should be taken into account before making a conclusion. Two of the patients with idiopathic ulcerative colitis had significant emotional stress before the onset of their disease. But the question of ulcerative colitis being a psychosomatic disease due to life stress has been challenged and recent studies by Feldman and associates and Monk and colleagues (21, 22) have refuted the previously held views that were based on earlier studies.

These cases can be classified into mild and moderate forms of ulcerative colitis with a chronic course. One case had one severe attack in 6 years and another had two moderate attacks in 2 years. Case 3 had arthritis with effusion and this is the only case that had extracolonic complication.

Microscopically, the lesions we observed are compatible with idiopathic ulcerative colitis. The microscopic lesions have the same characteristics in all cases. Crypt abscesses are one of the hallmarks of active idiopathic ulcerative colitis, however, crypt abscesses are not the sine qua non of idiopathic ulcerative colitis. These lesions have been seen in bacillary and amoebic colitis. Four of our cases had crypt absecesses. Aubry and associates (13) found only two cases with crypt absecesses in a series of 14 cases of idiopathic ulcerative colitis. Some of our patients showed typical radiological changes of idiopathic ulcerative colitis while others had normal barium enemas. During the early stage of the disease, the barium enema findings are known to be normal (16).

In conclusion, we would like to recom-

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mend that all patients with long standing dysentery be investigated thoroughly, not only for infectious causes and malignancies, but also for idiopathic inflammatory bowel diseases. All patients suspected to have idiopathic ulcerative colitis should be given antiamoebic medication empirically before they are put on steroids as some cases of idiopathic ulcerative colitis may co-exist with amoebic dysentry (7,23). This is a safe policy in all tropical countries where amoebic colitis is very common.

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VIRAL INFECTIONS AND BELL'S PALSY:

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Summary

Antibody titers for cytomegalo virus (CMV), coxsackie B virus (Cox B), herpes simplex virus (HSV), varicella zoster virus (VZV) and Epstein Barr virus (EBV) in sampled "acute" and "convalescent" sera from 167 Ethiopian patients with Bell's palsy did not differ significantly from age and sex matched controls. However, two of the 167 patients were found to be seropositive for human immunodeficiency virus (HIV) by western lot test and none in the 100 controls. The possible actiological relationship of HIV to Bell's palsy in the present situation of increasing incidence of the infection is discussed.

Resume

Le taux d'anticorps dirigés contre le cytomegalo virus (CMV), le virus coxsakies B (Cox B), le virus herpetique (HSV), le virus de la varicelle (VZV) et le virus d'Epstein Barr (EBV) ont été dosés à la phase aigue et la phase de convalescence chez 167 patients Ethiopiens qui présentaient une paralysie faciale: ces taux ne différaient pas significativement en ce qui concerne l'âge et le sexe des témoins. Cependant, 2 des 167 patients présentaient une séropositivité en Western Blot pour le virus du SIDA (HIV), mais aucun parmi les 100 témoins. Il existe une relation étiologique possible entre le paralysie faciale et les rétrovirus HIV favorisée par l'incidence accrue actuelle de cette infection.

KEY WORDS: BELL'S PALSY-VIRUS INFECTION

Introduction

Many factors have been considered in actiopathogenesis of the common neurological disorder of non-traumatic idiopathic facial paralysis (Bell's palsy). Vascular insufficiency[1,2] and preceding viral infec- tions[2,4,5,6,7] have been proposed as possible mechanisms for the sudden loss of facial nerve function. The viral connection has particularly received a lot of attention in the literature.

In a previous study we have reported on the clinical features of 167 Ethiopian patients with Bell's palsy[8]. This is a follow up study to examine the possible relationship to viral infections and the development of idiopathic facial paralysis in the same patients.

Patients, Materials and Methods

During the years 1983-85, over a 15-month period, 167 consecutive Ethiopians with Bell's palsy were studied in our Neurology Unit at the Tikur Anbessa Teaching Hospital in Addis Ababa. These patients underwent complete clinical and laboratory evaluations and they were followed up for an average of 10 months.

"Acute" sera were drawn from each patient at the onset of the facial paralysis and subsequent "convalescent" sera were collected 3 to 4 weeks later. The samples were stored at 20°C and were later sent to the Laboratory for Microbiology of the Ulleval Hospital in Oslo, Norway for virological investigations.

A sample of 20 patients and 29 controls was drawn at random, from the total number. They were tested for evidence of recent infection with cytomegalo virus (CMV), coxsackie B virus (Cox B), varicella zoster virus (VZV) and herpes simplex virus (HZV). Matched acute and convalscent sera were tested by standard complement fixation test (CFT). A four fold rise in specific antibody titre (two steps) was considered diagnostic for recent infection. The possibility of CMV infection was also explored by an IgM specific ELISA test.

Eight patients were tested for evidence of recent Epstein Barr virus (EBV) infection by MONOSPOT test for hetrophilic antibodies. All sera from patients and controls were tested for the presence of antibodies to human immunodeficiency virus (HIV). Sera were first screened with Organon ELISA. Sera found initially positive in this test (41 individuals), were further tested in the Welcome inhibition assay. If they were found consistently positive for antibodies, the result was finally confirmed in Western Blot.

Results

(Table 1) shows the age distribution of the patients with Bell's palsy compared to the general national population.

Table 1

AGE DISTRIBUTION OF 167 PATIENTS WITH BELL'S PALSY

Age Group (Years)	Number	Percent	Percent of General Ethiopian Population *
0-10	16 (1)	9.60	33.90
11-20	42 (8)	25.10	21.60
21-30	40 (8)	24.00	13.70
31-40	28 (2)	16.70	11.10
41-50	16 (1)	9.60	8.10
51-60	14 (0)	8.40	5.30
61-70	10 (0)	6.00	3.50
70+	1 (0)	0.60	2.80
Total	167 (20)	100.00	100.00

The figures in parentheses represent patients for whom viral serological tests were performed.

*Source: Central Statistical Office, Addis Ababa, 1984.

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It also indicates those cases whose sera were tested for viral antibodies.

The data of virological investigations (Table 1) do not indicate that any of the viral agents tested for were common causes of infections preceding Bell's palsy in this material. Of special interest is the finding that two of the patients and none of the controls were positive for HIV antibodies.

Three subjects in the control group (Table 2) had significantly high titers of antibodies to several viral antigens. In the absence of EBV infection, this probably may be due to non-specific hypergammaglobulinemia, although this aspect was not specifically looked into.

Table 2

VIRAL ANTIBODIES IN PATIENTS WITH BELL'S PALSY AND THEIR AGE AND SEX MATCHED CONTROLS

Viral	Control			Bell's		
Antigen	Total	Neg.	Pos.	Total	Neg.	Pos.
CMV	29	24	5(17.2%)	20	17	2(10%)
COX B	29	29	0	20	19	1(5%)
HSV	29	28	1(3.4%)	20	20	0
VZV	29	29	0	20	18	2(5%)
EBV	—	—	—	80	80	0
HIV	100	100	0	167	167	2(0.10%)

CMV = cytomegalovirus

COX B = coxsackie B virus

HSV = herpes simplex virus

VZV = varicella zoster virus

EBV = Epstein B virus

HIV = human immune-deficiency virus

The high number of initial positive results in screening sera with Organon ELISA test for HIV antibodies was probably also a result of general stickiness of sera due to hypergammaglobulinemia or immune complexes or crossreactivity to other antigens[9]. Welcome inhibition test seems to overcome this problem, as only two were found positive with this test; the same two that proved positive in Western Blot.

Discussion

As reported in an earlier study (8), among 167 patients with Bell's palsy, 26% recounted a history of preceding infections in the form of 'cold', sore throat, ear ache and gastrointestinal disturbances. These findings suggested direct or indirect relationships between Bell's palsy and viral infection.

The studies by Pietersen and Cant (5) and Berg et. al. (4) have convincingly shown that there is a serological evidence to herpes zoster infection in those patients who have developed Bell's palsy in association with herpes zoster oticus. However, in both studies sera from patients with idiopathic facial paralysis were generally negative for other viruses including influenza, adenovirus, herpes simplex, enterovirus, mumps, measles, cytomegalovirus and Epstein Barr virus.

On the other hand, Djupesland et. al. (3), on the basis of their findings of acute phase reaction and increased serum immunoglobulins in the majority of their patients, proposed that an active or recent infection (probably viral) had preceded or coincided with Bell's palsy. Similarly, Aviel et. al.[10] have suggested that their findings of increased serum interferon (IFN) and antiviral state (AVS) of blood cells in patients with Bell's palsy was indicative of an acute viral infection, although none of their patients had increased antibody titers to herpes simplex and varicella-zoster viruses.

Our findings revealed no clustering of recent infections with CMV, HSV, or Cox B in patients compared to controls. From the figures observed in the test sample, it can be concluded that an increase in sample size would very unlikely change the conclusion. Two cases of recent HZV infection were noticed among 20 patients; none among 29 patients in the control group. An increase in sample size might have very well confirmed earlier findings in this regard. Nevertheless, HZV infection could only be the cause of Bell's palsy in a few patients. Mononucleosis, reported in some studies (6) to be associated with Bell's palsy, was not found in this study. 50% of the patients, screened in the monospot test for hetrophilic antibodies, were all negative.

Koroczyn et. al.[11] studied 150 cases of Bell's palsy, exeluding those with herpes zoster oticus. They found no increase of complement fixing antibodies to a number of ciruses similar to the ones we studied.

More recently, Johnson et. al.[12] have found that the frequency of sera positive for CMV, HSV-1 and VZV in patients and controls did not differ significantly. Although there have been a number of studies on the role of viral infection in the non-traumatic idiopathic facial paralysis, on the balance, there is no convincing laboratory support of a viral etiology.

However, it is interesting to observe that the two HIV seropositive cases that we discovered were from among the patients with Bell's palsy and none from the control group lending to the suspicion that this finding may be significant. Unfortunately, as the test for the HIV serology was performed two years after the sera were collected, we could not report on the fate of the seropositive individuals with Bell's palsy whom we were unable to trace back. Was the finding coincidental? Or, could the neurological disorder be the initial clinical manifestion of an HIV infection? Occasionally, mononeuropathy multiplex has been reported in HIV infections[13]. We have recently seen a patient with confirmed HIV infection who developed a transient and mild Bell's palsy. Our findings raise the question of HIV etiology in Bell's palsy. Under the present situation of an increasing incidence of HIV infection, this neurological disorder deserves much more attention in the future.

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CHAPTER 5. MEDICAL ASPECTS, DIAGNOSIS AND CHEMOTHERAPY IN SCHISTOSOMIASIS.

Daniel Fekade, Tilahun Wolde Michael and Ahmed Ali.

INTRODUCTION

Schistosomiasis in man is an infection with worms of one or more of the species of *Schistosoma*, usually *S. haematobium*, *S. mansoni* or *S. japonicum* and to a lesser extent *S. intercalatum* and *S. mekongi*. In Ethiopia only *S. mansoni* and *S. haematobium* are reported. Schistosomiasis is a disease of wide spectrum of clinical manifestations where ill health may be a product of sequel rather than of an immediate infection and the picture could be modified by concomitant conditions such as other parasitic infections and malnutrition. Symptoms of schistosomiasis show great variation. Few patients might give history of schistosomal dermatitis. Although the majority might obviously be exposed to contaminated water, only very few know where or when they were exposed.

There are several parasitologic and epidemiologic surveys of schistosomiasis in Ethiopia, but very little has been written on the morbidity of schistosomiasis, both in the community and individual patients; although Hiatt (1976) and Hiatt and Mehari Gebre-Medhin (1977) reported on the morbidity of *S. mansoni* in three Ethiopian highland villages. In spite of such few reports on the morbidity from schistosomiasis the disease is being recognized as an important public health problem with serious consequences to agricultural development in the country (Aklilu Lemma, 1969).

PATHOGENESIS AND PATHOLOGY

The first stage in the pathogenesis of schistosomiasis occurs when the cercariae penetrate the skin, during which time they elicit a local hypersensitivity reaction. Affected persons develop general ill-health, with low grade fever and eosinophilia, urticarial rash, the so called "swimmer's itch". This is usually seen in non-immune individuals and can also be caused by non-human schistosomes which are unable to develop to the adult stage in man. It is a self-limiting illness and resolves spontaneously and is unusual in residents of endemic areas.

The next important pathogenic stage is at the beginning of oviposition and migration of the eggs through the tissues to the lumens of the intestine or bladder. Patients are acutely ill with fever, arthralgias and myalgias. An acute "serum-sickness" like illness called "katayama fever" occurs, particularly in non-immune persons infected with *Schistosoma japonicum*.

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Since as much as 40-80% of the eggs laid are retained in the tissues; it is the retained eggs and their products that are responsible for most of the morbidity from schistosomiasis.

Both cellular and humoral immunity play roles in the pathogenesis of schistosomiasis. The schistosome antigen that elicits intense cellular and variable antibody response is now known to be a soluble egg antigen (Warren, 1978; Nash et al., 1982; Lehman, 1978). Monocytes and neutrophils accumulate around the eggs trapped in the tissues. Later multinucleated giant cells form the typical granuloma around the egg. This initial granuloma formation is gradually attenuated, so that later deposition of fibrous tissue is dominant and it is this that causes the chronic sequele of schistososmiasis. Thus in schistosomiasis the main pathogenic changes are results of the host's immune response to the soluble egg antigen and not from the activity of the parasite per se. The adult worms, on the other hand, are able to escape host defense mechanisms by acquiring "host antigens" on their surface. Though granuloma formation around the eggs is able to contain the egg in the tissues, the role of cellular and humoral immunity in prevention or amelioration of reinfection is not well established. Circumstantial evidence for some protective immunity is inferred from the fact that egg excretion reaches a plateau after the second decade of life in endemic areas.

Through anatomic connection between mesenteric, vesical and lumbar venous plexuses or during migration through the lungs, adult schistosomes may be found in unusual sites. The lungs and the central nervous system are the most common sites of ectopic infections.

Several community based clinical studies have shown that both morbidity and the late sequele of hepatosplenic and urinary schistosomiasis are directly related to intensity of infection (Cook et al., 1974; Lehman et al., 1976; Cline et al., 1977; Salih et al., 1979; Lehman et al., 1973). In endemic areas only a few heavily infected individuals develop the late sequele of schistosomiasis.

CLINICAL FEATURES

Intestinal Schistosomiasis

The initial and early manifestations are that of a diarrhoeal illness with or without blood and mucus in the stool. There may be associated abdominal cramp, tenesmus, flatulence, anorexia and general ill-health. These symptoms by themselves are nonspecific and subside simultaneously after a variable period. These symptoms can occur intermittently with symptom free individuals. In non-immune individuals and with infection by *S. japonicum* an acute serum sickness like "katayama fever" could occur.

Depending on worm burden, that is intensity of infection, a small proportion of infected individuals develop a chronic hepatosplenic disease. The

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characteristic lesion is deposition of dense fibrous tissue around the hepatic lobules with the preservation of the overall hepatic architecture. This is known as "pipe-stem" fibrosis or Symmer's cirrhosis. This results in a presinusoidal obstruction to hepatic portal circulation and leads to portal hypertension. The consequences of portal hypertension, ascites, congestive splenomegaly and of portosytemic collateral ciculation with oesophageal varices, are seen in long standing cases. Death is usually due to exosanguinative bleeding from oesophageal or gastric varices. These patients rarely develop hepatic encephalopathy (Salih et al., 1979).

In some patients localized granulomas occur in the colon, abdominal cavity and the genitalia in women-"bilharziomos" (Smith et al., 1977a) which may simulate various neoplasms. Two such cases are reported in Ethiopian patients (Roberts, 1984; Frost, 1979). These presentations should be kept in mind by physicians practicing in endemic areas , who might otherwise do unnecessary surgery. In chronic hepatosplenic schistosomiasis an immune complex glomerulonephritis with demonstration of schistosome antigens by immunoflourescence has been described, but this rarely leads to renal failure (Andrade et al., 1971 ; Hashino-Shinuz et al., 1976).

Urinary Schistosomiasis

The adult worms of *S. haematobium* usually reside in the vesical plexus in the submucosa of the bladder and the eggs are released into the bladder. The brunt of the injury is born by the lower urinary tract. Initial symptoms are dysuria, suprapubic pain and haematuria. There is ulceration of the bladder mucosa with bleeding and in later stages formation of polyps and diverticula in the bladder (Smith et al., 1977b; 1977c). In some cases the eggs may be calcified in the bladder wall. If the uretric orifices and the lower ureters are diseased, an obstructive uropathy with hydroureter and hydronephrosis develops (Lehman et al., 1973; Smith et al., 1977c; 1977d; Young et al., 1973). The obstructive uropathy causes tubular dysfunction with loss of urinary concentrating and acidifying mechanisms (Lehman, 1970). However many of the early lesions which did not have time to develop uretric fibrosis particularly in the young subjects are reversible with appropriate medical treatment (Farid et al., 1967; 1976). Loss of muscular contractility leads to retention of residual urine with subsequent infection that may possibly develop chronic pyelonephritis. The association of chronic salmonella urinary infections and urinary schistosomiasis has been observed in several studies (Farid et al., 1979; Higashi et al., 1975). Another well recognized complication of urinary schistosomiasis in an immune complex glomerulonephritis with various degrees of haematuria and proteinuria. The association between urinary schistosomiasis and bladder cancer has been documented in several studies (Dimette et al., 1956; El Boulkany et al., 1972).

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Other Sites of Schistosome Infection: (Ectopic Schistosomiasis)

Schistosomal Cor Pulmunale

When schistosomula pass through the pulmonary circulation and through portosystemic anastosmoses they may be trapped in the lungs where they develop to adult worms. When ova are deposited, small granulomas are formed; later adjacent pulmonary vessels are occluded and fibrous tissue forms in the smallest pulmonary arteries which leads to pulmonary hypertension. This in long standing cases causes pulmonary heart diseases (Andrade and Andrade, 1970).

Schistosomiasis of the Central Nervous System

Schistosomiasis of the central nervous system may manifest as schistosomal granulomas in the brain or spinal cord. The eggs reach the central nervious system through anatomic connection between vertebral plexuses and vesical and mesentric veins. These, typically present with space occupying lesions in the central nervous system and may be confused with various tumors. Another mode of involvement of the central nervious system is an acute or subacute encephalopathy that is thought to be due to hypersensitivity reaction to schistosome eggs (Gelfand, 1973; Ghaly and El-Banhawy, 1973). This may also be seen in "katayama fever".

DIAGNOSTIC AND SCREENING METHODS IN SCHISTOSOMIASIS

The standard methods in use for diagnosis of human schistosomiasis may be generally divided into three: (1) Parasitological, (2) Sero-Immunological and (3) Clinical.

Parasitological Methods:

Detection of the characteristic eggs of the schistosome species under the microscope is a fairly reliable and simple means of diagnosis. A number of specific egg detection methods for both intestinal and urinary schistosomiasis are available.

Microscopic Egg Detection Methods for Intestinal Schistosomiasis:

Direct Smear Method: Observations of the characteristic egg in the faecal film prepared in normal saline, lugols iodine or 1% iodine in potassium iodide is a quick and specific diagnostic means. However, failure to detect eggs from the preparation does not rule out infection, for in light infections eggs could be scanty and irregularly excreted.

Sedimentation Methods: The principle is that when faeces are well mixed with water or saline the eggs settle more slowly than the faecal matter and so concentrate on or near the surface from which samples can be pipetted for examination. About one hour may be needed to allow complete sedimentation,

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and this long time requirement is considered as one of the draw-backs of this method. There are a number of concentration methods used to demonstrate the eggs of schistosomes using centrifugation, salt precipitation, Ritchie's method, the Army Medical Services III Method (AMS.III) the Merthiolate Iodine Formaldeyde Concentration Method (MIFC); of these Ritchie's Formol Ether Concentration Method is widely used because of its rapidity and very high sensitivity.

Kato-Thick Smear Method: The celophane thick smear method is also effective and sensitive and advantageous in epidemiological surveys. It can also be used to quantify intensity of infection.

Microscopic Egg Detection Methods for Urinary Schistosomiasis

Urine Sedimentation: The terminally spined eggs of *S. haematobium* could be observed from the urine sediment of a reatively heavily infected individual. The method is not very sensitive and may fail to demonstrate eggs in case of light infections.

Centrifugation: The principle being similar to sedimentation, but is rapid, simple and more sensitive.

Filteration Method: Filteration of urine through filter paper demonstrates ova of *S. haematobium*. However, the staining requirement is one of its drawbacks. Filteration of urine through a nucleopore filter 13mm in diameter and 8u pore size could serve for an immediate microscopical detection without staining. The latest rapid filteration technique in use is that with re-usable Nytrel filters of 12mm diameter and 20u in pore size.

Miracidial Hatching Test: The method helps in the detection of hatched miracidia of the intestinal and urinary forms of schistosomes. It is also used to measure therapeutic efficiency after treatment with schistosomicidal drugs.

SERO IMMUNOLOGICAL DIAGNOSIS:

Immunological Methods: Immunological tests have their limitations in the diagnosis of schistosomiasis because of lack of specificity. They are mostly used for seroepidemiological population surveys.

The Intradermal Tests: The intradermal or skin test is based on the appearance of a wheal and flare type of reaction to the introduction of a very small quantity of bilharzial antigen into the skin of an infected individual. The test however is non-specific.

Serological Tests: There are a number of serologic tests developed for the diagnosis of schistosomiasis. However because of lack of "specific" parasite antigen, they are not very specific for the diagnosis of schistosomiasis. The

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commonly used tests include complement fixation test, slide floculation test, flourescent antibody test, circumoval precipitation test, immunodifusion test.

Enzyme Linked Immunosorbent Assay (ELISA): This method is widely used for epidemiological work of large numbers of specimen both for *S. mansoni* and *S. haematobium* screening. An ELISA test with sensitivity of 87% has been developed for seroepidemiologic survey in Ethiopia (Sioum Taticheff and Melamed, 1983).

CLINICAL DIAGNOSIS:

Clinical Diagnosis of Intestinal Schistosomiasis

Sigmoidoscopy and Rectal Snip: Lesions caused by schistosomiasis may be demonstrated by sigmoidoscopy. The parasite may be demonstrated by histologic examination of the rectal mucosa.

Biochemical Methods: Although this method also is not specific, changes may be detected in the liver function. Hypergammaglobulinemia, elevation of bromsulphalein retention test and an elevated serum bilirubin level may occur. Barium swallow and oesophagoscopy may demonstrate the presence of oesophageal varices.

Ultrasound of the liver and spleen have also been used to monitor response to therapy in chronic hepatosplenic schistosomiasis.

CLINICAL DIAGNOSIS OF URINARY SCHISTOSOMIASIS

Liver Biopsy: This is of value in chronic hepatosplenic schistosomiasis. Histologic examination may reveal the characteristic "pipe-stem" fibrosis (Symmer's cirrhosis).

Cytoscopy: Varying degrees of fibrosis or calcification of the urinary bladder may be observed through the cystoscope. Histologic examination of the bladder mucosa may reveal the characteristic eggs.

Radiological Method: This method of investigation is of value in assessing organic structural changes in individual cases. Plain film of the abdomen may demonstrate calcification of the urinary bladder. Intravenous pyelography may demonstrate hydroureters and hydronephrosis. Ultrasound of the kidneys and ureters are also used to asses structural changes in the urinary tract.

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MANAGEMENT OF SCHISTOSOMIASIS:

General Management:

Management of the late sequelae of Schistosomiasis: The development of safe and effective antischistosomal drugs has enabled the majority of patients, with uncomplicated schistosomal infections, to be treated on outpatient and rural dispenseries basis. However, cases of *S. mansoni* and *S. haematobium* with severe complications, such as portal hypertension with collateral circulation, ascites and obstructive uropathy with renal insufficiency, should still be treated in hospitals. The general medical management of such patients is as important as specific chemotherapy.

Ascites are treated with bed rest, salt restriction and gentle diuresis. Bleeding oesophageal varices are potentially fatal and should be treated agressively with blood transfusions and measures to stop bleeding by tamponade and pharmacologic means. Injection of sclerosing agents around the varices through fibreoptic endoscopy has added new dimensions in the management of chronic hepatosplenic schistosomiasis with portosystemic collaterals. Some patients may benefit from surgical procedures aimed at decreasing portal venous pressure.

Although many of the early structural lesions in urinary schistosomiasis are reversible by chemotherapy alone (Farid et al., 1967; 1976), in the later stages, when the structural and functional abnormalities are permanent, careful medical and surgical management is very useful. Close attention to fluid, mineral and protein metabolism is essential in subjects with renal insufficiency. Reconstruction surgery on the urinary tract may be necessary to alter anatomic abnormalities that resulted from fibrotic changes.

Clinical, parasitological, clinico-pathologic measurements, radiology and endoscopy are useful in assessing the effectiveness of chemotherapy and overall patient care.

Specific management

Chemotherapy: Development of antischistosomal drugs has not been very dynamic for some time. However, the advent of newer chemotherapeutic agents, viz. oxamniquine, metrifonate and praziquantel, has revolutionized chemotherapy in the managememnt of schistososmiasis. Although the move is towards the use of newer chemotherapeutic agents which are relatively safe and easy to administer, older chemotherapeutic agents, especially niridazole and hycanthone are also used clinically under medical supervision. Chemotherapy, besides relieving the symptoms of schistosomal infection and the reversal of acute or subacute pathological conditions, is known to play an essential role in the control of schistosomiasis by eliminating the excretion of eggs. The following criteria have been recommended by World Health Organization (1983) for selecting

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appropriate drugs for schistosomiasis control programmes: (1) their low cost (2) being well tolerated (3) administration without medical supervision (4) high and prolonged therapeutic index (5) chemical stability without special storage conditions and (6) non-interaction with other drugs, foodstuffs, alcohol and tobacco.

Antimonial compounds

- antimony sodium tartarate
- sodium antimonial gluconate
- stibocaptate antimony sodium dimercaptosuccinate, (Astibs Roche)

Antimony drugs fell far short of satisfaction, because of their toxic effect and because therapeutic courses require prolonged intravenous or intramuscular administrations.

Side effects:

- prominent gastro-intestinal symptoms, including anorexia nausea,vomiting,etc.
- liver function test may show changes indicative of hepatocellular disturbance,
- complaints of general weakness, arthralgia and myalgia,
- various types of skin rash, some even very severe,
- substernal discomfort or pain and electrocardiographic changes which are indicative of cardiac toxicity, etc.

Non-Antimonal Compounds

a) **Lucanthone hydrochloride** (Nilodon, Milarcia, D.Bayer)

- A fairly high cure rate is expected in *S. haematobium* infections,
- owing to the advent of new schistosomicides, the high frequency of side effects and relatively low therapeutic effect, its use for short term curative courses had diminished.

Dose: Total dose of 60 t0 75 mg/kg of body weight for 3 to 6 days is recommended to minimize side effects.

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Side Effects:

- Short term course produce side effects in a high proportion of treated patients,
- gastric intestinal symptoms are frequent and often lead to failure to complete the course,
- anorexia, nausea, vomiting which can be severe and distressing, loose stools or diarrhoea sometimes accompanied by intestinal colic may be encountered,
- vertigo, insomnia, occasionally states of mental confusion, excitement or mania can occur,
- urine becomes yellow during treatment and yellow non-icteric staining of the palms and soles disappearing after completion of the courses, may be seen,
- tolerance to lucanthone was found to vary apparently.

b) **Hycanthone** (Etrenol, Stirling-Wintrop)

- is a hydromenthyl derivative of lucanthone produced by bacterial decomposition
- its schistosomicidal activity was found to be greater than lucanthone and it had outstanding advantages since it was given in a single intramuscular injection.
- It is effective against *S. haematobium* and *S. mansoni*.

Dose: The usual dose is 3.0mg of base per kg.body weight given in a single intramuscular injection.

Side Effects:

- Vomiting, a common complaint, minimal and transient electrocardiographic changes,
- pain at the site of injection, sometimes leading to abscess,
- in certain instances, post treatment jaundice and a transient rise in serum transaminase levels,
- rarely, hepatic necrosis leading to death,
- medical supervision is very important if hycanthone is used for an extended period.

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c) Niridazole (Nitrothiozolylimidazolidinone), Ambilhar (CIBA).

- Effective schistosomicide against the three common schistosomes of man.

Dose: Total dose may be given as 25mg/kg/day (divided in three doses) 5-10 days.

Side Effects:

- tolerance is generally good,
- anorexia, nausea, vomiting, abdominal pain, diarrhoea, headache and vertigo have been noted,
- skin rashes occasionally seen,
- increased heart rate and minor electrocardiographic changes,
- rarely involvement of the central nervous system leading to hyperexcitability, mania, depression, insomnia, epileptiform attacks have been described.

Contra-indications:

- patients with previous history of mental disease or any form of epilepsy,
- poor liver function
- severe heart disease
- poor general condition,
- pregnancy in the first four months on general grounds.

Latest drugs:

The recent development of safe and effective oral drugs has awakened general interest among those concerned with schistosomiasis control. The current antischistosomal drugs viz. metrifonate, oxamniquine and praziquantel are known to eliminate and cure infection in a high proportion of infected population and reduce intensity of infection in those persons who remained infected (WHO, 1983). These drugs can be administered orally without immediate need for medical supervision.

Metrifonate:

Metrifonate is an organophosphorous compound used as a pesticide since 1952. In 1962 this compound was dicovered to have specific activity against *S. haematobium*. Metrifonate is transformed in the mammalian host to dichlorovos by a non-enzymatic process. Dichlorovos has specific anticholinesterase activity.

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Neither the basis for the lack of activity against *S. mansoni* nor the mode of action against *S. haematobium* is known (WHO, 1983).

Dose: the standard drug regimen is 7.5-10mg/kg of body weight given in three doses at two week intervals.

Side Effects: It is remarkable that in spite of decreases in plasma and erythrocytic cholinesterase after treatment with metrifonate, the clinical manifestations are insignificant or non-existent (Davis and Baily, 1969). The level of plasma cholinestrase returns to normal within two weeks, but the level of erythrocytic cholinesterase takes longer time to return to normal. The side effects are mainly gastor-intestinal, including nausea, vomiting, colic muscular weakness, sweating, fainting and rarely diarrhoea. Atropine sulphate (1mg every 6 hours) may be used to treat severe side effects.

Contra-indications: Agricultural workers who are exposed to organophosphorous compounds should not be treated with metrifonate. Treatment with metrifonate during pregnancy is also not recommended for general purposes.

Oxamniquine:

Oxamniquine (UK 4271; Vansil in Africa and the United Sates; Mansil in Brazil), prepared by Pfizer, Ltd., Kent, is a hydroxylated metabolite of the schistosomicide desoxymansil in a culture of *Aspergillus sclerotinum*. Oxamniquine (Vansil) has a generic name of 6-hydroxmethyl-2 isopropylaminomethyl 1,2,3,4 tetrahydroquincline.

Oxamniquine has therapeutic activity against *S. mansoni* and is well tolerated although the susceptibility of various geographic strains of this species to the drug varies widely (Siongok et al., 1976, Ongom et al., 1975; Pitchford and Lewis, 1978; Eyakuze et al., 1979; Omer, 1978). The optimal dose of this drug is also established for the Ethiopian strain of *S. mansoni* and the drug is found to be well tolerated in adults and children (Teklemariam Ayele, 1984) .

Dose: a single oral dose of 15mg/kg body weight for "sensitive" strains; 15mg/kg two doses 12 hours apart for "intermediate" is the recommended course for the different strains. The short duration of treatment, low toxicity, high reduction in egg out put and high cure rate of Oxamniquine has made it very suitable for individual treatment as well as schistosomiasis mansoni control programmes in a study area in Ethiopia (Teklemariam Ayele, 1984). According to this study, optimal clinical cures were achieved with a total dose of 40mg/kg of body weight in divided doses and a total dose of 30mg/kg of body weight is recommended for targeted mass treatment.

Side effects: The only significant side effect noted is dizziness.

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Praziquantel (Biltricide, Bayer)

Praziquantel is a heterocyclic pyrazino-isoquinoline compound that does not resemble previous antischistosomal drugs. It has a wide spectrum of action against the different species of schistosomes. It is effective against *S. haematobium, S. mansoni, S. japonicum, S. mekongi* and *S. intercalatum*. It is also effective against most other trematodes, cestodes and salmonellosis encountered with *S. mansoni* infections. The mode of action is considered to be on the tegument of the adult worm.

Dose: Praziquantel is taken orally in single or divided doses. For *S. mansoni* and *S. haematobium* infections 40mg/kg in a single dose is recommended. The same dose is found effective against combined *S. mansoni /S. haematobium* infections. For *S. japonicum* infection, 60mg/kg in divided doses is recommended.

Side Effects: Infrequent nausea, vomiting and mild to moderate epigastric discomfort or pain occurred within 8 hours after treatment. However, more recent studies (Polderman et al., 1984) showed the prevalence of more intense side effects including the production of bloody diarrhoea which correlates with intensity of infection as side effects of praziquantel.

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LIGHT AND ELECTRON MICROSCOPIC CHANGES IN SURAL NERVES IN ETHIOPIAN DIABETICS

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ABSTRACT. *The light and electron microscopic morphological changes in sural nerve biopsies from 32 Ethiopian diabetics and 4 malnourished non-diabetic subjects were studied in order to determine the role of malnutrition in the development of diabetic neuropathy. The most prominent finding in diabetics with clinical neuropathy was reduction in the density of myelinated axons of all diameters especially the large ones. Affected nerves showed abundant intraneural collagen, and evidence of nerve regeneration in some cases. Demyelination, though present, was less marked. Changes in the vasa nervorum were seen in only one case. The morphological changes correlated with the duration and severity of the diabetes and with nerve conduction velocity. No changes were seen in malnourished non-diabetics and diabetics without clinical neuropathy, thus suggesting that malnutrition by itself does not contribute significantly to the development of diabetic neuropathy. Axonal degeneration appears to be the predominant feature in diabetic neuropathy.*

INTRODUCTION

Some studies have shown that the pattern and characteristics of the chronic complications of diabetes in Africans are different from those in Caucasians. For instance, diabetic retinopathy is relatively uncommon while neuropathy is more common in Africans than Caucasians (1-5).

It has been suggested that nutritional deficiencies may predispose the African to an earlier development of diabetic neuropathy (6). However, there have been very few studies that have looked into this problem in detail. In this study the neurological morphologic changes in Ethiopian diabetics were studied in comparison to those in malnourished non-diabetic subjects, in order to detect the role of malnutrition in the development of diabetic neuropathy.

PATIENTS AND METHODS

The study involved 32 Ethiopian diabetics, and 4 non-diabetic malnourished patients with loss of subcutaneous fat and muscle atrophy who visited to Tikur Anbessa Hospital for non-neurological problems. The diabetics were consecutive referrals from the polyclinics but diabetics and non-diabetics with evidence of neuropathy of other causes like excessive alcohol intake were excluded from the study.

Detailed medical histories were obtained from each patient, who also underwent general and neurological examinations. Laboratory investigations included routine

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haemogram, blood chemistry, VDRL and chest roentgenogram.

The majority of the diabetics had irregular follow-up and unsatisfactory metabolic control. Ten patients were treated with oral hypoglycaemic agents, and the rest were on insulin. There appeared to be no difference in severity or occurrence of neuropathy between these two groups. Those with symptomatic neuropathy had been diabetics for more than 5 years. The majority of these patients were of relatively poor nutritional status.

The diabetic patients were clinically classified into two groups in accordance with the criteria of Chopra *et al.* (7): (a) Diabetics without neuropathy were patients with normal peripheral pulses, who had no symptoms or signs of neuropathy; (b) Diabetics with neuropathy were patients who had symptoms and at least two objective neurological signs of neuropathy, such as reduced or absent tendon reflexes, sensory loss and motor weakness and wasting.

Nerve conduction studies were performed on the median, ulnar, peroneal, posterior tibial and sural nerves. Details of this method have been described in a previous paper (4).

After obtaining informed consent, fascicular sural nerve biopsies were taken from all the patients following the procedure described by Dyck and Lofgren (8). The patients tolerated the procedure well, and no ill effects or symptomatic sensory deficits were observed.

The nerve biopsies thus obtained were divided into two groups. The first set was fixed in formol saline and embedded in paraffin wax. Transverse sections (5μm) were cut and stained by standard laboratory methods, viz. haematoxylin and eosin, haematoxylin Van Gieson, Luxol fast blue/cresyl violet (for myelin). Palmgren's silver impregnation technique (for axons), and mycobacterial stains. The second set was fixed in 4% glutaraldehyde solution for 24 hours and processed through a standard cycle, including osmium tetroxide, to araldite. Sections were stained with lead citrate and uranyl acetate. Microscopy was performed using a Phillips 201 electron microscope.

RESULTS

As shown in Table 1 there were 4 subjects (aged 23 to 42 years) with severe malnutrition. The others were diabetics without neuropathy (9 patients, aged 17 to 70 years) and with neuropathy (23 patients, aged 14 to 60 years).

The commonest symptoms of neuropathy were numbness, tingling, burning sensation, and pain in the distal legs. One patient (Case no.5) had cranial nerve mononeuritides, involving the oculomotor and facial nerves separately at different times.

Neurological abnormalities included diminished pain, touch and vibration sensations in the distal legs, and also the hands (in the severely affected). The ankle jerk varied from diminished to absent in 14 of 22 (55%) of the diabetics with symptomatic neuropathy. In 6 patients, there were signs of upper limb involvement, with sensory symptoms in the hands and diminished to absent biceps jerks. Autonomic neuropathy expressed in postural hypotension, impotence and incontinence of urine was found in four patients (Cases no. 5,7,14,18).

Nerve conduction velocities were slowed in the lower limbs in 3 of the 9 without neuropathy and in 15 of the 23 diabetics with neuropathy. In 9 of the 23 diabetics with neuropathy, the nerve conduction velocities were within the normal limits.

Light and electron microscopic examinations did not reveal any abnormalities in the axon or myelin structures in the malnourished controls. Only 3 of the 9 diabetics without neuropathy showed mild reduction of myelinated fibers and evidence of demyelination in the sural nerve biopsies.

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TABLE 1. Malnourished and diabetics : Clinical, electrophysiological, and sural nerve biopsy morphological summaries.

Group	Case no.	Age, sex	Neuropathy	Nerve conduction velocity	Loss of myelinated fibers	Demyelination	Intraneural collagen	Vasa nervorum
Malnourished	4	27M	-	N	-	-	-	-
	16	23M	-	N	-	-	-	-
	23	42M	-	N	-	-	-	-
	24	25M	-	N	-	-	-	-
Diabetics without neuropathy	2	20M	+	SL	+	+	-	-
	8	35M	-	N	-	-	-	-
	9	25M	-	N	-	-	-	-
	10	44M	-	SL	++	-	+	-
	11	47M	-	N	-	-	-	-
	32	21F	-	N	-	-	-	-
	13	67F	-	N	-	-	-	-
	12	70M	-	SL	+	+	+	-
	25	17M	-	N	-	-	-	-
Diabetics with neuropathy	1	58M	+++	SG	++	+	++	-
	3	45M	++	SG	+	+++	++	-
	5	23F	++	N	-	-	-	-
	6	17M	++	SL	++	+	+	+
	14	40M	+++	SG	++	-	++	-
	7	37M	+++	SG	+++	+++	++	-
	15	21F	+	N	++	-	+	-
	17	54M	+	N	+	-	+	-
	18	55F	+++	SL	++	+	+	-
	19	20F	++	SG	++	-	+	-
	20	17F	+	SG	++	+	-	-
	21	18F	+	N	+	-	+	-
	22	45F	++	SL	-	-	-	-
	24	14M	+	N	-	-	-	-
	26	52F	++	SL	-	-	-	-
	27	25M	+	N	-	-	-	-
	28	35F	+	N	-	-	-	-
	29	45F	++	N	++	-	+	-
	30	48M	++	SL	++	+	+	-
	31	50F	+++	SG	+++	+	+	-
	33	60M	++	SG	++	+	+	-
	34	55F	++	N	+	+	+	-
	35	45M	++	SG	++	+	++	-

Nerve conduction velocity : N= Normal SL = slowed in legs SG = generalized slowing

Symptomatic neuropathy, Axonal loss, Demyelination, Increased collagen: + = slight, ++ = moderate, +++ = severe, - = nil

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The sural nerves of 17 of the 23 diabetics with neuropathy demonstrated a variety of morphological changes, including reduction in the density of myelinated fibers of different calibers, in particular in the large-diameter axis cylinders (Figure 1). There were unmyelinated fibers in groups, indicative of remyelination in 4 sural nerves (Figure 2). Active degeneration of axons was not seen in any of the nerve biopsies. Varying degrees of demyelination were observed in 10 of the 23 patients with neuropathy. However, the myelin changes were not as significant as the reduction in the density of myelinated axons.

An impressive increase of intraneural collagen, particularly in those nerves worst affected by axonal loss, was encountered in 16 of the 23 sural nerves from diabetics with neuropathy (Figure 2). Abnormalities of the vasa nervorum were not observed except in one patient (Case no.6), where, on electron microscopy, the vessel wall was shown to be slightly thickened.

In 4 sural nerves, Pi granules, lipid vacuoles and unidentified inclusion bodies were found in the Schwann cells. In one case (no.29), an increase in the number of Schwann cell nuclei was the only abnormality observed. There were 6 cases with clinical neuropathy but normal sural nerves histologically. However, the degree of morphological changes observed in the diabetic sural nerves closely correlated with the duration and severity of the diabetes, as well as with the abnormalities of the nerve conduction velocities.

DISCUSSION

Over the years, different views have developed about the pathogenesis of diabetic neuropathy and the major morphological changes seen in nerve biopsies. Whether the initial lesion of the neuropathy is axonal degeneration or segmental demyelination is still unresolved. Earlier studies (9,10) suggested that widespread demyelination was the most prominent abnormality in diabetic neuropathy. But subsequently, a number of workers (11-14) demonstrated frequent degeneration of myelinated and unmyelinated fibers of all diameters in sural nerve biopsies. Segmental demyelination was observed to a lesser extent.

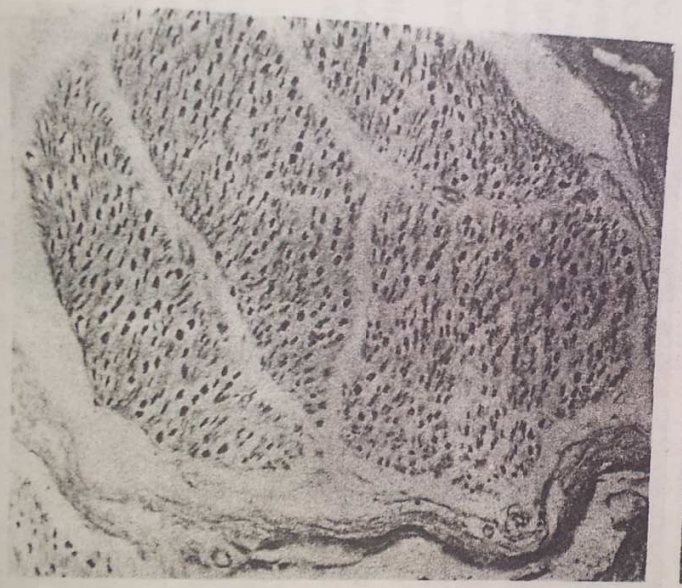
For reasons not yet elucidated, neuropathic complications are more common in African than in Caucasian diabetics (3-5). Besides poor metabolic control, other factors such as nutritional deficiencies have been incriminated (6). However, very few studies have been undertaken to test this hypothesis. Our study on a limited number of malnourished subjects did not reveal any morphological abnormality in sural nerve biopsies. In fact, there were also severely malnourished diabetics from rural areas in this study (Cases no.8,25) without symptoms or histopathologic evidence of neuropathy. Further, some studies have also shown that no beneficial therapeutic effects have been achieved from treatment of diabetic neuropathy with high doses of vitamins (15).

Although Osuntokun (16) described segmental demyelination in 4 nerve biopsies from Nigerian diabetics, we are not aware of other similar histological studies of nerves in African diabetics. Our study reveals that loss of myelinated fibers, particularly those of large diameter, was the most prominent abnormality in the sural nerves of Ethiopian diabetics with neuropathy. Demyelination, though present, was not very significant. We cannot however, comment in detail, upon the state of segmental demyelination, as the specimens were not examined in teased fiber preparation.

In the majority of cases, the degree of morphological change could be correlated with the clinical severity of diabetes, as judged by blood glucose values or the slowing of the nerve conduction velocities, similar to the findings of Behse *et al.* (13). The myelin and axonal morphological

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FIGURE 1. Transverse section through sural nerve fascicles (Palmgren x 100).



Left (Case no.24) : No evidence of axonal loss, sheath normal.



Right (Case no.7) : Marked axonal loss, fine axons distributed sparsely throughout.

FIGURE 2. Electron photomicrographs of diabetic nerves.

Left (Case # 14), Unmyelinated axons are abundant and associated with Schwann cell processes which surround or lie alongside the axons. Dense collagen lies between the axonal group. No myelinated axons (x 12,500).

Right (Case # 31): No myelinated axons. Many unmyelinated axons surrounded by Schwann cell processes. Densely set bundles of collagen (x 12,500).

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changes we observed in the sural nerves of our diabetics with neuropathy were similar to those recorded by Yagihashi and Matsunaga (12).

Structural abnormalities of the vasa nervorum were encountered in only one subject among the diabetics we studied. This concurs with the observation of other workers on non-African diabetics (2,5). However, there are many studies on non-African diabetics that have reported significant angiopathic changes in the nerves of neuropathic patients (12,13,17,18). What we found to be a conspicuous abnormality (but very little commented upon in the literature), was the proliferation of intrafascicular collagen in nerves with loss of fibers.

Considering the marked loss of myelinated fibers in conjunction with the much less prominent demyelination, it is tempting to suggest that these pathologies run independent courses, and that axonal degeneration is the main morphological and probably the primary degenerative change in the diabetic neuropathy of our patients who had generally long standing and often poorly controlled disease. Our diabetic neuropathy is not influenced by malnutrition.

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THE ROLE OF MILK AND LACTOSE INTOLERANCE IN ETHIOPIAN PATIENTS WITH NON–ULCER DYSPEPSIA: A CASE CONTROL STUDY

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ABSTRACT. *Milk intolerance, lactose intolerance and non-ulcer dyspepsia are common among Ethiopians. This study, therefore, was designed to find out if milk intolerance associated with lactase deficiency account for non-ulcer dyspepsia. Ninety-eight patients with non-ulcer dyspepsia and 95 controls were examined and interviewed for demographic data and milk drinking habits. Then each had a lactose tolerance test (LTT), stool examination for pH, ova and parasites. The demographic characteristics and the number of milk drinkers were comparable in the 2 groups. However, milk intolerance and lactose intolerance were significantly higher among the patients with non-ulcer dyspepsia than among the control group ($p < 0.01$, $p < 0.05$ respectively). The combination of milk intolerance, lactose intolerance and LTT was also significantly different ($p < 0.01$). The mean stool pH was markedly reduced after lactose ingestion and there were more ova and parasites in the stools of the control group. These observations suggest that milk intolerance and/or lactose intolerance account significantly for the symptoms of the patients with non-ulcer dyspepsia. However, since lactose intolerance and abnormal LTT are very common among adult Ethiopians symptoms related to the drinking of milk should be interpreted with caution vis-a-vis the results of the lactose loading test.*

A significant number of adults who are not of northern European origin are known to have lactase deficiency, the incidence varying according to race (1-5). Such subjects experience abdominal distention, borborygmi, pain or diarrhoea following ingestion of products containing milk or lactose. These signs and symptoms are a result of the osmotic effect of the unhydrolyzed disaccharide, lactose in this case, within the intestinal lumen, producing fluid retention. Also, when this sugar reaches the lumen of the colon, it is available for bacterial fermentation resulting in a large amount of lactic acid and short chain fatty acids some of which are directly irritant to the colonic mucosa (6). Lactase deficiency is demonstrated indirectly by a diminished rise in blood glucose after ingestion of lactose or directly by the measurement of lactase activity in the intestinal mucosal biopsy specimens.

Non-ulcer dyspepsia or recurrent abdominal complaints are common among Ethiopians. Thorough investigation using conventional methods and facilities often fail to reveal a recognizable cause. A controlled study has shown that Ethiopian patients with non-ulcer dyspepsia and asymptomatic controls are equally exposed to intragastric irritants and that the prevalence of histological gastritis is the same

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in the 2 groups (7). Thus, the cause(s) of abdominal complaints in this group of Ethiopians remain(s) unknown. However, patients presenting with dyspepsia in out-patient health services often complain of milk intolerance and are unable to relieve their symptoms with milk. Furthermore, previous studies have shown that milk and lactose intolerance are common among Ethiopian children and adults (8,9). This study, therefore, is designed to find out if milk intolerance associated with lactase deficiency account for non-ulcer dyspepsia among Ethiopian patients.

SUBJECTS AND METHODS

Patients with non-ulcer dyspepsia: There were 98 patients with non-ulcer dyspepsia. They were seen and investigated as ambulatory patients in Tikur Anbessa Hospital. Fifty-two of these were men and 46 women. The mean age for both sexes was 30 years and the range 17-65 years (see Figure 1). The demographic characteristics of this group are shown in Table 1.

Controls: Sixty men and 35 women with a mean age of 30 years were recruited from the ambulatory service of Tikur Anbessa Hospital to serve as controls (see Figure 1). The demographic characteristics of this group is also shown in Table 1.

Selection criteria: *Patients with non-ulcer dyspepsia:* Non-ulcer dyspepsia was defined as abdominal pain of recurrent nature, lasting for several months or years, often felt soon after and aggravated by meals and with other causes of dyspepsia excluded by appropriate diagnostic means. Those with episode(s) of diarrhoea within 4 weeks prior to the lactose tolerance test, those taking laxative regularly and those who were known to have diabetes mellitus or serious systemic disease were excluded from the study.

Controls: These were ambulatory patients with minor complaints but without any abdominal symptoms. They also fulfiled the above exclusion criteria.

Patients with non-ulcer dyspepsia and controls were consecutively studied after informed consent.

Lactose tolerance test: After an overnight fast (from 8:00 pm until 8:00 am), baseline glucose was dtermined from capillary blood using a glucometer TM Reflectance Photometer/Dextrostix (R) Reagent strip system (Ames Division, Miles Laboratories, Inc., Elkhart, Indiana 46515, U.S.A.). Then the subject was given 50 grams of lactose powder dissolved in 250 cc of water to drink. Capillary blood glucose was determined at 15, 30, 60, 90 and 120 minutes after ingestion of lactose. Stool pH was determined before and 2 hours after lactose ingestion by using the Improved Color Chart strips of pH paper (Mialo Essential Laboratory, Brooklyn, N.Y., U.S.A.). Signs and symptoms experienced by every subject for 8 hours following lactose ingestion were carefully documented. An abnormal lactose tolerance test or a flat curve is defined as a peak rise in blood glucose concentration of less than 20mg per 100ml after ingestion of 50 grams of lactose. Subjects who experienced gas (abnormal distension, borborygmi, increased burping or more flatus than usual), cramps (periodic sharp abdominal pain) and/or diarrhoea (looser than usual stool) within 8 hours following ingestion of 50 grams of lactose are said to have lactose intolerance. Each subject was instructed to inform the physician at the next clinic visit (within 2-7 days) if he/she experienced the above signs and symptoms. Those signs and symptoms occurring during the 2 hours following ingestion of lactose were recorded immediately in the protocol.

Stool for ova and parasites: Ova and parasites were looked for in a direct smear of stool which was not older than 4 hours. Stool examination was conducted by a senior laboratory technician.

Data collection: Demographic data (geo-

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graphic origin, ethnicity, occupation, marital status and religions), milk drinking habits (amount, symptoms following milk ingestion, why milk drinking was stopped, family history of milk intolerance) and symptoms associated with ingestion of glucose or other sweets were documented according to a prospectively prepared questionnaire. Subjects with signs and symptoms similar to those with lactose intolerance, following milk ingestion are said to have milk intolerance.

Statistical analysis: The chi-square test was used to test for statistical significance.

RESULTS

Demographic data: The demographic characteristics of the patients with non-ulcer dyspepsia and controls are relatively comparable. The majority in each group are within the age range of 20-40 years (Figure 1 and Table 1).

Milk ingestion and milk intolerance: The amount of milk ingested by patients with non-ulcer dyspepsia and controls varied between occasional and 4 glasses averaging about one glass (containing approximately 250 cc of milk) per day. The number of patients and controls drinking milk is comparable ($p > 0.5$). On the other hand, as shown in Table 2, there is a significant difference in milk intolerance between the two groups ($p < 0.01$). It is further noted that 15 patients with non ulcer dyspepsia and 7 controls have already stopped drinking milk because of intolerance. A family history of milk intolerance revealed no difference between the patients with non-ulcer dyspepsia and the controls ($p > 0.5$).

Lactose tolerance test and lactose intolerance: Lactose intolerance was significantly higher among the patients with non-ulcer dyspepsia than among the control group ($p < 0.05$). The lactose tolerance test results revealed comparable flat curves ($p > 0.5$) and normal curves ($p < 0.5$) in the patients with non-ulcer dyspepsia and in the controls (Table 3). Similarly, there was no difference in normal curves with symptoms ($p > 0.3$) and in normal curves without symptoms ($p > 0.3$) in both groups. On the other hand, flat curves with symptoms ($p < 0.01$) and flat curves without symptoms ($p < 0.01$) were significantly different between the patients with non-ulcer dyspepsia and the control group.

Stool pH: The mean stool pH and standard deviation before and after the lactose tolerance tests in 94 patients with non-ulcer dyspepsia and in 92 controls were 6.26 ± 0.83 (before), 5.98 ± 0.98 (after) and 6.71 ± 0.85 (before), 6.17 ± 1.13 (after), respectively (Table 3). There is a significant reduction in the mean pH of the stool after lactose ingestion in each group. This is in keeping with the high prevalence of lactose intolerance and abnormal lactose test or flat curve results.

Correlation between milk intolerance, lactose intolerance and lactose tolerance test: The relationship between milk intolerance, lactose intolerance and abnormal lactose tolerance test (flat curves) within each of the study group is shown in Figure 2. The combination of milk intolerance, lactose intolerance and abnormal lactose tolerance test (46/82 or 56% in the patients and 20/80 or 25% in the controls) is significantly different in the 2 groups ($p < 0.01$). It is also noted that 7 of the patients with non-ulcer dyspepsia and 5 of the controls experienced milk intolerance but had no symptoms after lactose ingestion and the lactose tolerance test was normal. Also among milk drinkers, there were 1 patient and 3 controls who had flat curves but were tolerant to lactose. Conversely, there were 2 patients and 2 controls among the milk drinkers with lactose intolerance but with normal lactose tolerance test.

Ova and parasites in stool: Nineteen of 90 (21%) patients with non-ulcer dyspepsia

FIGURE 1. Age and sex distribution of patients and controls

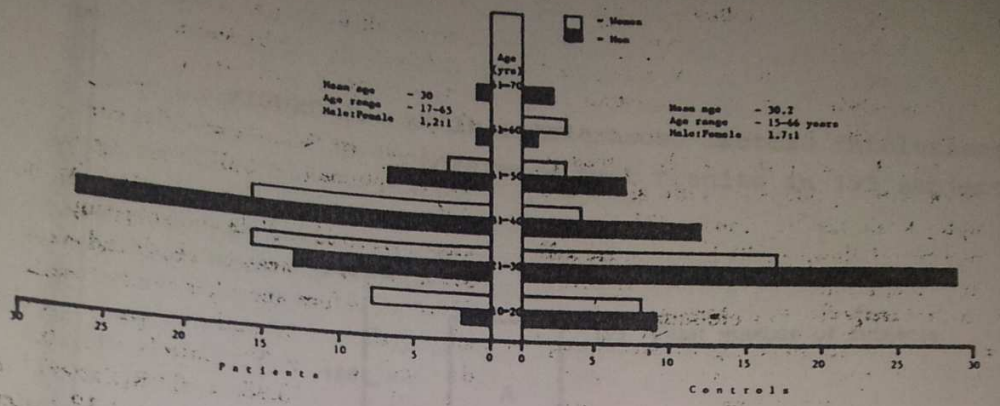
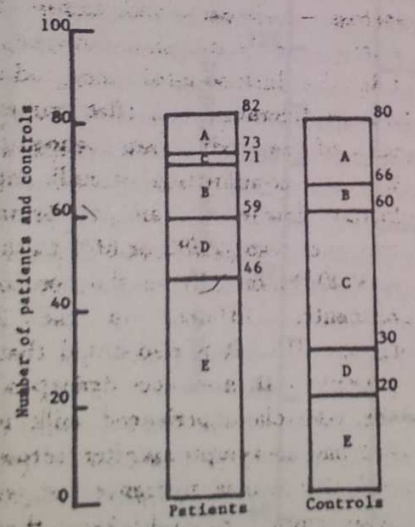


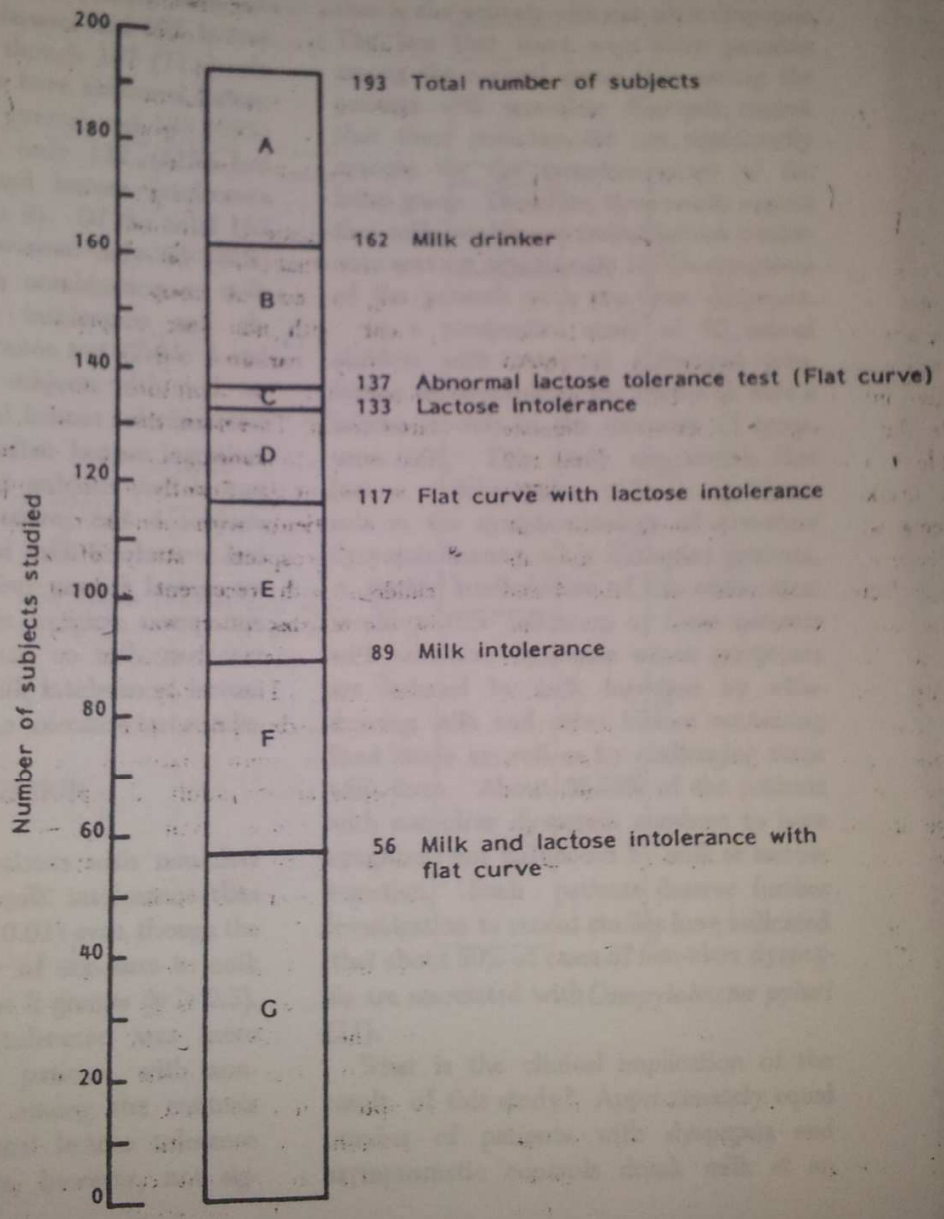
FIGURE 2. Correlation between milk tolerance, lactose intolerance and abnormal lactose tolerance test



A = Milk drinkers
B = Abnormal lactose tolerance test (flat curve)
C = Lactose intolerance
D = Milk intolerance
E = Milk and lactose intolerance with flat curve

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FIGURE 3. Milk intolerance, lactose intolerance and lactose tolerance test results in 193 subjects



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and 31 of 91 (34%) controls were found to have parasites ($p < 0.05$). These included *Ascaris lumbricoides*, strongyloides larvae, *Trichuris trichiura* hookworm, *taenia* species, *Giardia lamblia* trophozoites and *Entamoeba histolytica* trophozoites and cysts.

Overall prevalence of milk intolerance, lactose intolerance and lactose tolerance test results: When all 193 subjects (patients and controls) are considered, 162 (89%) are milk drinkers. Of these, 55% experienced milk intolerance and 69% lactose intolerance. Even though 137 (71%) subjects were noted to have abnormal lactose tolerance test (flat curves) and 133 (69%) lactose intolerance, only 117 (61%) had both flat curves and lactose intolerance (Table 4 and Figure 3). Of the total 162 milk drinkers, there were only 56 (35%) subjects who had a combination of milk intolerance, lactose intolerance and abnormal lactose tolerance test (Table 4 and Figure 3). Twelve subjects with milk intolerance had normal lactose tolerance test and no symptoms after lactose ingestion. Four milk intolerant subjects had lactose tolerance but flat curves and 4 subjects who also experienced milk intolerance had lactose intolerance but normal lactose tolerance test. Age, sex, religion, occupation and ethnic origin had no influence over the prevalence of milk intolerance, lactose intolerance and lactose tolerance test results.

DISCUSSION

There were more patients with non-ulcer dyspepsia who had milk intolerance than normal controls ($p < 0.01$) even though the degree and frequency of exposure to milk was comparable in the 2 groups ($p > 0.5$). Similarly, lactose intolerance was more common among the patients with non-ulcer dyspepsia than among the controls ($p < 0.05$). Abnormal lactose tolerance test (flat curve) was, however, not significantly different between the 2 groups ($p > 0.5$). On the other hand, the combination of milk intolerance, lactose intolerance and abnormal lactose tolerance test (flat curve) is significantly higher in the non-ulcer dyspepsia group than in the control group ($p < 0.01$). There was no difference in the family history of milk intolerance between the 2 groups ($p > 0.05$). Furthermore, intestinal parasites in the stool were more prevalent in the control group than in the patients with non-ulcer dyspepsia. The fact that there were more parasites among the control group than among the patients with non-ulcer dyspepsia suggest that these parasites did not significantly account for the symptomatology of the latter group. Therefore, these results suggest that milk intolerance and/or lactose intolerance account significantly for the symptoms of the patients with non-ulcer dyspepsia.

In a prospective study of 80 school children with recurrent abdominal pain, lactose malabsorption was shown to have a substantial role in the causation of symptoms (10). This study also reveals that lactose malabsorption plays a significant role in the symptomatology of non-ulcer dyspepsia among adult Ethiopian patients. A further confirmation of this observation would require follow-up of those patients with non-ulcer dyspepsia whose symptoms are induced by milk ingestion by withdrawing milk and other lactose containing food items as well as by challenging them with these. About 25-30% of the patients with non-ulcer dyspepsia continue to have symptoms not influenced by milk or lactose ingestion. Such patients deserve further investigation as recent studies have indicated that about 50% of cases of non-ulcer dyspepsia are associated with *Campylobacter pylori* (11).

What is the clinical implication of the result of this study? Approximately equal number of patients with dyspepsia and asymptomatic controls drank milk at an

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TABLE 1. Demographic characteristics of patients with non-ulcer dyspepsia and asymptomatic controls

Demographic characteristics	Patients	Controls
Total number	98	95
Mean age	30.0	30.2
Age range (years)	17-65	15-66
Male-to-female ratio	1.2:1	1.7:1
Geographic origin (%)		
Addis Ababa and vicinity	81.2	81.7
Other administrative regions	18.8	18.3
Occupation (%)		
Civil servants	47.8	27.8
Professionals	22.8	14.4
Students	7.6	20.0
Farmers	1.1	15.6
Merchants	9.8	6.7
Unemployed	6.5	2.2
Others	4.4	13.3
Marital status (%)		
Married	54.4	56.7
Single	45.6	43.3
Religion (%)		
Christian	93.0	86.0
Moslem	7.0	14.0
Ethnic origin (%)		
Amhara	57.0	49.0
Oromo	11.6	21.6
Tigrai	24.4	10.2
Gurage	4.7	18.2
Others	2.3	1.1

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TABLE 2. Milk ingestion and milk intolerance

Milk ingestion ± symptoms	Patients	Control	Difference*
Milk drinkers	82/91(90%)	80/91(88%)	P > 0.5
Non-milk drinkers	9	7	
No information	7	4	
Symptomatic after milk intake	59/82(72%)	30/80(38%)	P < 0.01
Asymptomatic after milk intake	23/82(28%)	50/80(63%)	P < 0.02
Family history of milk intolerance	9/84(11%)	9/70(13%)	P > 0.5

* Chi-square test

TABLE 3. Lactose tolerance test results and lactose intolerance

Types of tests	Patients	Control	Difference[1]
Abnormal lactose tolerance test (Flat curve)	71/98(72%)	66/95(70%)	P > 0.5
Normal lactose tolerance test (Normal curve)	27/98(28%)	29/95(30%)	P > 0.5
Flat curve with symptoms	67/71(94%)	50/66(76%)	P < 0.01
Flat curve without symptoms	4/71(6%)	16/66(24%)	P < 0.01
Normal curve with symptoms	7/27(26%)	11/29(38%)	P > 0.3
Normal curve without symptoms	20/27(74%)	18/29(62%)	P > 0.3
Lactose intolerance	73/98(75%)	60/95(63%)	P > 0.05
Stool mean pH and S.D.[2] before LTT[3]	6.36±0.83	6.71±0.85	-
Stool mean pH and S.D. after LTT	5.98±0.98	6.17±1.13	-

1. Chi-square test
2. Standard deviation
3. Lactose tolerance test

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TABLE 4. Overall prevalence of milk intolerance, lactose intolerance and lactose tolerance test results

Subject, symptoms & tests	Results (percentage)
Total number of cases studied	193
Milk drinkers	162/182 (89)
Symptoms after drinking milk	84/162 (52)
Asymptomatic after drinking milk	73/162 (45)
Family history of milk intolerance	18/154 (12)
Lactose intolerance	113/193 (59)
Abnormal lactose tolerance test (flat curve)	137/193 (71)
Flat curve with lactose intolerance	117/193 (61)
Flat curve without lactose intolerance	20/193 (10)
Normal curve with symptoms	18/193 (9)
Normal curve without symptoms	38/193 (20)
Milk and lactose intolerance + flat curve/milk drinkers	56/162 (35)

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average of one glass per day. Some subjects from each group developed symptoms. More individuals with non-ulcer dyspepsia experienced symptoms of milk intolerance. Furthermore, lactose intolerance and abnormal lactose tolerance tests were significantly more common than milk intolerance in each group, an observation also noted by others (12, 13). This difference is most probably due to the amount of lactose ingested for the lactose tolerance test i.e. 50 grams of lactose which is equivalent to 1.1 littres or approximately 4 glasses of milk (14). In reality the majority of Ethiopians will not consume so much milk at once or per day mainly because of cost and inavailablility. Yet, in a country where avoidance of animal proteins is common due to religious fasting and poverty, the nutritional value of milk should be empasized whenever feasible. Therefore, it would be unrealistic to uniformly recommend avoidance of milk and milk products when patients are found to have non-ulcer dyspepsia. This is in keeping with the suggestions made by the Protein Advisory Group of the United Nations System statement, the Food and Nutrition Board of the National Research Council of the National Academy of Sciences, and the American Academy of Paediatrics (12, 15-17). On the other hand, reasonable advice to the patient with non-ulcer dyspepsia and milk intolerance would be: (a) To abstain from milk and milk products and observe whether symptoms disappear. Following relief of the dyspeptic symptoms, the patients may try to take smaller amounts of milk and milk products either directly or mixed with other food and drink (18). The outcome of such a trial should lead the patient to make a lasting decision. (b) To take as much yogurt as he/she desires because the intestinal absorption of lactose is enhanced by the release of lactase from the bacteria present in yogurt (19).

A total of 12 patients with non-ulcer dyspepsia and controls experiencing milk intolerance had normal lactose tolerance test and no symptoms after lactose ingestion. These subjects may have milk intolerance unrelated to lactase deficiency and may also be due to other factors such as "milk allergy" (6) or the effects of other unhydrolyzed disaccharides within the intestinal lumen (20). Four milk intolerant patients and controls had lactose tolerance but flat curves. Such observations have led to the suggestion that the lactose tolerance test is a poor predictor of actual intolerance to milk (12). Also, 4 patients and controls who experienced milk intolerance had lactose intolerance but normal lactose tolerance test. Because of these variable results, only 56 (35%) of the 162 milk drinkers had the combination of milk and lactose intolerance as well as abnormal lactose tolerance test (flat curves). Like several other studies (12,13,15-17), this study reveals that lactose intolerance and abnormal lactose tolerance test (flat curves) are very common among adults who are not of northern European origin. Therefore, symptoms related to the drinking of milk should be interpreted cautiously vis-a-vis the lactose loading test.

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DO HOSPITAL PERSONNEL IN HYPERENDEMIC AREAS REQUIRE IMMUNIZATION AGAINST HEPATITIS B VIRUS (HBV) INFECTION? IS VERTICAL TRANSMISSION OF HBV INFECTION COMMON IN THIS GROUP?

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ABSTRACT. *Medical personnel working in contact with blood and blood-contaminated body fluids are often considered to be a high-risk group for hepatitis B virus (HBV) infection and, as a result, it is recommended that they should be vaccinated against this infection. To find out if this is necessary in a country hyperendemic for HBV infection and to see if parents transmit the infection to their offspring, a total of 336 volunteer hospital employees, and 103 children of 47 of them, were tested for HBsAg, anti-HBc, anti-HBs, HBeAg and anti-HBe using the radioimmunoassay technique. Of these, 242 (72%) were found to have evidence of past or present HBV infection and only 94 (28%) had no such evidence. The infection prevalence in the 47 parents was 68% comparable to that of the total sample. Only 9 of their 103 children were positive for HBV markers. All tested parents of these positive children were either negative for all markers or positive for anti-HBs. The HBV infection prevalence among this hospital population is not different from that of the general Ethiopian population, and vertical transmission appears unlikely in this group. Therefore, mass vaccination of hospital staff in hyperendemic areas is unnecessary.*

Medical personnel working in hospitals and potentially exposed to blood and blood-contaminated body fluids and hypodermic needles are considered as a high-risk group for hepatitis B virus (HBV) infection (1-6). Vaccination against hepatitis B virus infection for such high-risk populations has been recommended in North America and Europe (7-9).

In a population survey and in a study of volunteer blood donors in Ethiopia, the HBsAg carrier rate was 11-12% and the overall hepatitis B virus infection rate was 76-79% (10,11). Also, chronic liver disease and primary hepatocellular carcinoma, in association with HBsAg carrier state and macronodular cirrhosis, are very common in Ethiopia (12-14).

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Is there a need to vaccinate health personnel in this country against HBV? This study is carried out to answer this question and to find out if this group is responsible for vertical transmission of HBV to their offspring.

SUBJECTS AND METHODS

A total of 336 employees of a teaching hospital in Addis Ababa volunteered to participate in this study. Of these, 152 were men and 184 women (male-to-female-ratio of 1 : 1.2). The mean age was 33.9 years and the range was 21-53 years. Doctors, nurses, health assistants and laboratory technicians accounted for 87% of the total sample. The remaining low risk group, handling blood and blood-products and/or using hypodermic needles inside and outside the hospital, include anaesthetists, X-ray technicians, pharmacists, physiotherapists and others (morticians, porters, cleaners, etc.) (Table 1). One hundred and three children between 2 and 14 years of age and belonging to 47 of the above volunteer employees were also tested.

Eight to ten cc of blood was drawn from each volunteer and centrifuged to separate the serum. All sera from parents and offspring were stored at -20°C until they were shipped by air in ice to the Virology Department of Malmo General Hospital, Malmo, Sweden, for the determination of HBsAg, anti-HBs, HBeAg and anti-HBe by commercial radioimmunoassay kits (Abbott Laboratories, Stockholm, Sweden). As each serum sample was coded, the technician in Sweden was blinded in terms of professional groups, parents and offspring.

The chi-square test, without Yate's continuity correction, was used for statistical evaluation.

RESULTS

Serological studies for HBV markers revealed 19 subjects positive for HBsAg, 13 for anti-HBc alone and 210 for anti-HBs. Of those positive for HBsAg and anti-HBc, only one had HBeAg and 17 had anti-HBe. Thus, the HBsAg carrier state' was 6% and the total infection prevalence was 242 (72%). Ninety-four (28%) were negative for all markers.

Comparison of HBV infection among the 4 groups of professionals at highest risk showed a trend for HBV marker prevalence to decline as follows: health assistants > laboratory technicians > nurses > physicians (Table 2). This small difference may be due to the duration of service of each category of health personnel. However, there is no statistically significant difference between marker prevalence of any 2 groups.

Of the 103 children from 47 families, 9 (8.7%) were found to have HBV markers (1 HBsAg and 8 anti-HBs). Table 3 shows the relationships between HBV markers of parents and positive children. Hepatitis B virus carrier state was absent among those parents. Three of these parents were negative for all markers while 6 had anti-HBs in their sera.

The 47 parents (39 mothers and 8 fathers) who brought their children for HBV marker determination, had an overall HBS infection prevalence of 68% (3 HBsAg, 4 anti-HBc and 25 anti-HBs). When this infection prevalence is compared to that of the general hospital population (72%), there is no statistically significant difference ($p > 0.05$). The prevalence of HBV markers in the 103 children tested (8.7%) is comparable to that (9.6%) of 385 hospital staff children of the same age group (unpublished data) ($p > 0.05$).

DISCUSSION

The 6% HBsAg carrier state is lower than the 11-12% prevalence noted in previous population surveys (10,11). This may be partly due to a predominantly female population. (The male-to-female ratio of the

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TABLE 1. Types of high-risk hospital population

Professionals	Male	Female	Total	Duration of service (yrs.)	
				Mean	Range
Physicians	51	10	61	7.6	2-24
Nurses	17	100	117	11.4	2-29
Health Assistants	23	44	67	17.2	2-30
Laboratory Technicians	32	15	47	14.3	2-26
Anaesthesiologists	5	2	7	-	-
X-ray technicians	9	3	12	-	-
Physiotherapists	3	3	6	-	-
Pharmacists	2	0	2	-	-
Others	10	7	17	-	-
Total	152	184	336	-	-

TABLE 2. Hepatitis B virus markers according to type of profession

Professionals	Total number	HBsAg	Anti-HBc only	Anti-HBs	No marker	Overall infection (percent)
Physicians	61	4	3	34	20	41 (67%)
Nurses	117	4	6	72	35	82 (70%)
Health assistants	67	2	1	51	13	54 (81%)
Laboratory Technicians	47	4	2	30	11	36 (77%)
X-ray technicians	12	0	0	7	5	7
Anaesthetists	7	2	1	2	2	5
Pharmacists	2	0	0	2	0	2
Physiotherapists	6	2	0	4	0	6
Others	17	1	0	8	8	9
Total	336	19	13	210	94	242

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TABLE 3. Relationship of hepatitis B markers between parents and their positive offspring

Code No. of offspring	Parent		Offspring		HBV marker	
	Profession	Age	Sex	Age(yrs.)	Parent	Offspring
59-B	Nurse	36	F	10	None	Anti-HBs
33-B	Nurse	35	M	14	None	Anti-HBs
104-A	Nurse	36	M	8	Anti-HBs	Anti-HBs
52-A*	Nurse	34	M	14	Anti-HBs	Anti-HBs
6-B*	Nurse	34	M	9	Anti-HBs	Anti-HBs
80-B	Nurse	31	M	7	Anti-HBs	HBsAg
98-B	Nurse	38	M	12	Anti-HBs	Anti-HBs
27-A	Technician**	36	F	4	None	Anti-HBs
371-A	Physician**	35	M	12	Anti-HBs	Anti-HBc+ Anti-HBs

*Same mother **Males

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HBsAg carrier state shown in a previous study was 2 : 1) (10). Also, some of the anti-HBc positive cases may have high titres of the IgM type indicative of continued HBV replication as HBsAg. Overall, the prevalence of HBV infection among this group of hospital workers was not significantly different from those of the general population (10,11). Also, the data shows no increased prevalence of infection in any one group within this hospital setting. In a hyperendemic area like Ethiopia, screening health workers to detect only 28% non-immune subjects for prophylactic vaccination against hepatitis B virus infection is economically unrealistic. On the other hand, it is logical and economical for Ethiopia to concentrate on mass vaccination of babies at birth as part of the national vaccination programme.

Since the children are over 2 years of age, their anti-HBs antibodies cannot be from the mothers. If infection was acquired from the mothers by vertical transmission, it is most unlikely that these children had converted from HBsAg to anti-HBs at such an early age (15). Ethiopian HBsAg carrier mothers at the time of delivery have anti-HBe, a situation not commonly in favour of vertical transmission (16). Furthermore, it has been shown that Ethiopian children acquire HBV infection early in life but with hepatitis B marker prevalence increasing gradually through age groups without a tendency to a plateau (11). Therefore, it is likely that these children belonging to professionals working in hospital acquired their HBV infection by means of horizontal transmission.

In summary, the prevalence of HBV infection among hospital staff working close to patients is not different from that of the general population and, therefore, prophylactic vaccination is unnecessary and uneconomical. Also, vertical transmission appears unlikely in this group of hospital personnel.

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VIRAL INFECTIONS AND BELL'S PALSY:

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Summary

Antibody titers for cytomegalo virus (CMV), coxsackie B virus (Cox B), herpes simplex virus (HSV), varicella zoster virus (VZV) and Epstein Barr virus (EBV) in sampled "acute" and "convalescent" sera from 167 Ethiopian patients with Bell's palsy did not differ significantly from age and sex matched controls. However, two of the 167 patients were found to be seropositive for human immunodeficiency virus (HIV) by western lot test and none in the 100 controls. The possible aetiological relationship of HIV to Bell's palsy in the present situation of increasing incidence of the infection is discussed.

Resume

Le taux d'anticorps dirigés contre le cytomegalo virus (CMV), le virus coxsakies B (Cox B), le virus herpetique (HSV), le virus de la varicelle (VZV) et le virus d'Epstein Barr (EBV) ont été dosés à la phase aiguë et la phase de convalescence chez 167 patients Ethiopiens qui présentaient une paralysie faciale: ces taux ne différaient pas significativement en ce qui concerne l'âge et le sexe des témoins. Cependant, 2 des 167 patients présentaient une séropositivité en Western Blot pour le virus du SIDA (HIV), mais aucun parmi les 100 témoins. Il existe une relation étiologique possible entre le paralysie faciale et les rétrovirus HIV favorisée par l'incidence accrue actuelle de cette infection.

KEY WORDS: BELL'S PALSY-VIRUS INFECTION

Introduction

Many factors have been considered in aetiopathogenesis of the common neurological disorder of non-traumatic idiopathic facial paralysis (Bell's palsy). Vascular insufficiency[1,2] and preceding viral infec- tions[2,4,5,6,7] have been proposed as possible mechanisms for the sudden loss of facial nerve function. The viral connection has particularly received a lot of attention in the literature.

In a previous study we have reported on the clinical features of 167 Ethiopian patients with Bell's palsy[8]. This is a follow up study to examine the possible relationship to viral infections and the development of idiopathic facial paralysis in the same patients.

Patients, Materials and Methods

During the years 1983-85, over a 15-month period, 167 consecutive Ethiopians with Bell's palsy were studied in our Neurology Unit at the Tikur Anbessa Teaching Hospital in Addis Ababa. These patients underwent complete clinical and laboratory evaluations and they were followed up for an average of 10 months.

"Acute" sera were drawn from each patient at the onset of the facial paralysis and subsequent "convalescent" sera were collected 3 to 4 weeks later. The samples were stored at 20°C and were later sent to the Laboratory for Microbiology of the Ulleval Hospital in Oslo, Norway for virological investigations.

A sample of 20 patients and 29 controls was drawn at random, from the total number. They were tested for evidence of recent infection with cytomegalo virus (CMV), coxsackie B virus (Cox B), varicella zoster virus (VZV) and herpes simplex virus (HZV). Matched acute and convalscent sera were tested by standard complement fixation test (CFT). A four fold rise in specific antibody titre (two steps) was considered diagnostic for recent infection. The possibility of CMV infection was also explored by an IgM specific ELISA test.

Eight patients were tested for evidence of recent Epstein Barr virus (EBV) infection by MONOSPOT test for hetrophilic antibodies. All sera from patients and controls were tested for the presence of antibodies to human immunodeficiency virus (HIV). Sera were first screened with Organon ELISA. Sera found initially positive in this test (41 individuals), were further tested in the Welcome inhibition assay. If they were found consistently positive for antibodies, the result was finally confirmed in Western Blot.

Results

(Table 1) shows the age distribution of the patients with Bell's palsy compared to the general national population.

Table 1

AGE DISTRIBUTION OF 167 PATIENTS WITH BELL'S PALSY

Age Group (Years)	Number	Percent	Percent of General Ethiopian Population *
0-10	16 (1)	9.60	33.90
11-20	42 (8)	25.10	21.60
21-30	40 (8)	24.00	13.70
31-40	28 (2)	16.70	11.10
41-50	16 (1)	9.60	8.10
51-60	14 (0)	8.40	5.30
61-70	10 (0)	6.00	3.50
70+	1 (0)	0.60	2.80
Total	167 (20)	100.00	100.00

The figures in parentheses represent patients for whom viral serological tests were performed.

•Source: Central Statistical Office, Addis Ababa, 1984.

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	10–19	20–29	30–39	40–49	50–59	60–69	70–79	
Male	11	29	22	20	9	10	5	106
Female	2	6	4	4	0	2	0	18
Total	13	35	26	24	9	12	5	124
Percentage	10.5	28.2	21.0	19.4	7.3	9.7	4.0	100

plaques 23% (28), calcified lesions 4% (7) and complicated lesions 3% (5) of the cases. When the three main branches of the coronary arteries, the circumflex, left anterior descending and the right coronary, were considered together 24 male and two female patients were found to have some degree of coronary atherosclerosis.

Moderate to severe atherosclerotic lesions were present in 10 patients. Fatty streaks and fibrous plaques were found in equal proportions. Fatty streak was not found below 20 years of age. Above this age the frequency increased gradually from 14% to 33% by the age group of 50–59 years. Thereafter the frequency of fatty streak decreased rapidly. It affected commonly both coronary arteries.

Fibrous plaque was not found below the age of 40 years. Thereafter the frequency of fibrous plaque gradually increased from 15.7% to 40% by the age group of 70–79 years (Table 4). Calcified lesion with stenosis of the left anterior descending coronary artery was found only in one 60-year-old female patient.

Myocardial infarction

Evidence of myocardial infarction at necropsy was found in eight patients. Four had scars of myocardial infarction larger than 50 mm and four had multiple scars smaller than 50 mm. The age of the eight patients ranged between 35 and 68 years with an average of 50. Two patients died suddenly, three committed suicide and three died of infections. One had severe obstructive hypertrophic cardiomyopathy and two patients had hypertension. The most severe myocardial infarctions occurred in those patients below the age of 45 years. Except one 35-year-old patient who had mild fatty streaks all the rest had moderate to severe fibrous plaques in the three major coronary arteries.

Discussion

In the last two decades, the incidence of CHD in the indigenous African population seems to be gradually increasing.

Table 4. Distribution of atherosclerotic lesions of the coronary arteries by age

Age (years)	Number of cases	Fatty streak	Fibrous plaque	Calcified lesions
10–19	13	—	—	—
20–29	35	5(14.3)	—	—
30–39	26	2 (7.7)	—	—
40–49	24	3(12.5)	4(15.7)	—
50–59	9	3(33.3)	3(33.3)	—
60–69	12	1 (8.3)	5(44.7)	1(8.3)
70–79	5	—	2(40.0)	—
Total	124	14(11.3)	14(11.3)	1(0.80)

Numbers within brackets are percentages
Three patients had more than one type of lesion

Cases report from Africa

In Nigeria, Brockington and Edington[3] in a retrospective review of the records of 6817 autopsies covering the period from 1958 to 1966 found only eight cases of myocardial infarction, four of which were caused by embolism from bacterial endocarditis. In 1971, Williams[4] examined 279 hearts from consecutive autopsied patients aged 10–90 years. He found that one-third of the patients aged between 50 and 60 years had atherosclerotic lesions consisting of mainly fatty streaks. Ogunnowo *et al.*[5] in their study of 111 autopsies at Ife in 1986 found 7.2% moderate to severe coronary occlusion with one case of myocardial infarction which indicated a significant increase in the incidence compared with the findings of Williams[4]. In Ghana[6], a review of 3645 autopsies from 1921 to 1953 revealed only 30 cases of CHD. In 1979, Pobee[7] reported the frequency of CHD to be 3.9% from the Accra Cardiac Register. From Ivory Coast, Bertrand *et al.*[8] reported an increase in the incidence of CHD from 2.2% in 1965 to 5.3% in 1981 which was more than two fold.

Baldachin[9] in 1963 reviewed records of blacks admitted to Harare Hospital and found no cases of myocardial infarction. During the period of 1968–1976, Castle[10] reported 69 black males with myocardial infarction diagnosed at autopsy. In South Africa, Hegginson and Pepler[11] were among the earliest authors to show that atherosclerosis was rare among blacks. However, CHD in black South Africans is not at present as rare as it was 30 years ago. In a review of autopsy records for 1959, 1960 and 1976, Isaacson[12] found that the incidence has risen from 0.13% in 1959 and 1960 to 2.2% in 1976 which is an increase of 15-fold.

From eastern Africa, Ojiambo[13] in 1968 reported the first case of myocardial infarction from Nairobi. In 1966 D'Arbela *et al.*[14] reported three patients with myocardial infarction from Uganda. However, Nhonoli[15] in 1968 found only one patient with CHD out of 226 cardiac patients.

From Ethiopia reviews of admission records of 5013 patients from the Black Lion Hospital in Addis Ababa[16] and the teaching Gondar Hospital[17] between 1963 and 1967 showed only four patients with myocardial infarction.

In 1984, Gebre-Selassie[18] analysed the autopsy records of 256 patients from the Black Lion Hospital performed during the previous six years and found 4(1.6%) patients with myocardial infarction.

In the present series some degree of coronary atherosclerosis was found in 26 (21%) of the patients. Moderate to severe lesions were found in 10 (8.1%) cases. Myocardial infarction was found in 8 (6.5%) of the 124 patients. Compared with previous reports[16-18], the findings in this series indicate a significant increase in the incidence of myocardial infarction in Ethiopia during the last two decades. A rate of 6.5%

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...ardial infarction in a series with a mean age of 37 years, is highly indicative that myocardial infarction is underdiagnosed.

The contribution of hypertension, serum cholesterol levels and cigarette smoking could not be assessed. The mean serum cholesterol level in Ethiopians has been reported to be within the range of 142±36 mg/dl to 208±40 mg/dl in different social classes[19]. From the few available reports, the prevalence of hypertension ranged from 1.8% in rural communities to 12.8% in hospital outpatients[20-22]. Both hypertension and serum cholesterol levels were found to increase with age, urbanization and social class. Cigarette smoking by Ethiopians is on the increase. The overall prevalence is still unknown. However, studies of medical and paramedical students revealed a rate of 25%[23]. The effect of these predisposing factors will be more evident with improvement in the standard of living and with increasing life expectancy of the population.

The findings in this series are similar to those of Isaacson[12] who in a retrospective study found an increase in the rate of CHD from 0.2% in 1960 to 2.2% in 1976 in South African blacks. Bertrand *et al.*[5] found in Ivorians an increase from 2.2% in 1965 to 5.3% in 1981. Ogunnowo *et al.*[5] also reported a significant increase in the incidence of myocardial infarction in Nigerians in the last 14 years. These studies are highly indicative that CHD is in the increase in black Africans.

International comparisons of black African populations have not been made because of inadequate mortality and demographic data. However, necropsy studies in Nigerians[5,24], South African Bantus[25], the International Atherosclerosis Project of blacks and whites in New Orleans, Oslo, Puerto Rico, Sao Paulo and Durban in South Africa[26] and the present study showed that atherosclerosis is fundamentally the same in all ethnogeographic groups. The principal differences were seen in the rate of progression of the different lesions. In the black African fibrous plaques, calcified and complicated lesions occur at a much lower frequency as a result the complications of atherosclerosis are much lower compared with that of the developed countries[26]. However, the rise in the incidence of CHD in the indigenous African population during the last two decades has been distinctively impressive. This rise may be ascribed to the changing life style due to increasing level of prosperity being enjoyed by an increasing number of black Africans.

According to Gillum[27] CHD is the leading cause of death among United States blacks. It would not be too long before it also becomes a major health hazard in black Africans. Therefore, a primordial prevention of CHD, as recommended by the WHO Expert Committee[28] which will be appropriate to the health and economic development of each African country may be necessary.

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HLA-DR and -DQ antigens in malnutrition-related diabetes mellitus in Ethiopians: a clue to its etiology?

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Thirty Ethiopian malnutrition-related diabetes mellitus (MRDM) patients were HLA typed and their HLA antigen frequencies were compared to those of 31 previously typed insulin-dependent diabetes mellitus (IDDM) patients and to 84 controls from the same ethnic background. In comparison to controls, a striking association between MRDM and HLA-DR3 ($X^2 = 15.15$, $p = 0.0001$) was observed, whereas the frequency of HLA-DR4 was non-significantly increased (RR = 1.72). The frequency of DR2, DQw1, and DQw6 was decreased among MRDM. In comparison to IDDM that is associated with both DR3 and DR4 in this population, MRDM showed no significant differences in HLA class II antigens frequencies. Therefore, the genetic basis of susceptibility to MRDM and IDMM in Ethiopia is at least partially identical.

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Tropical diabetes has been recognized, under a variety of designations (Abu-Bakare et al. 1986), as an entity that can be distinguished from Type 1 ((IDM) and Type 2 (NIDDM) diabetes in a number of clinical characteristics. There are at least two variants of it: the J-type first reported by Hugh-Jones from Jamaica (Hugh-Jones 1955) and the pancreatic type first reported by Zuidema from Indonesia (Zuidema 1959). Both variants occur in an environment in which poverty and malnutrition are prevalent. Patients of both types of tropical diabetes are young, commonly male, underweight or cachectic when first seen, present with the classical symptoms of diabetes, require insulin for control (frequently in high doses), but are resistant to ketoacidosis (DKA) upon interruption. In addition, the pancreatic type often shows clinical evidence of exocrine pancreatic dysfunction and pancreatic calcification.

Tropical diabetes has recently been put into a separate category as malnutrition-related diabetes mellitus (MRDM) by the WHO committee on diabetes, the J-type being designated protein-deficient pancreatic diabetes (PDPD) and the pancreatic type fibrocalcific pancreatic diabetes (FCPD) (WHO 1985). But there is as yet no evidence that these types (PDPD in particular) are etiologically

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Table 1.
HLA class II antigen frequencies in Ethiopian malnutrition-related diabetes (MRDM), insulin-dependent diabetes (IDDM) patients and controls.

HLA class II		MRDM		Control		IDDM		MRDM vs CTRL			
Antigen	(split)	+	−	+	−	+	−	RR*	X^2	p*	EF*
HLA-DR1		5	25	16	67	9	21	0.88		n.s.	
2		1	29	22	62	3	28	0.14	6.46	0.01	
3		15	14	12	72	13	18	6.20	15.15	0.0001	0.44
4		10	20	19	65	15	16	1.72		n.s.	
5		1	29	11	73	2	29	0.33		n.s.	
	w11	1	29	5	78	1	30	0.73		n.s.	
	w12	0	30	5	78	1	30	0.23		n.s.	
w6		10	20	28	56	5	26	1.02		n.s.	
	w13	9	21	26	58	4	27	0.98		n.s.	
	w14	1	29	2	78	0	20	1.60		n.s.	
7		6	24	25	56	5	26	0.53		n.s.	
w8		2	28	11	73	3	28	0.56		n.s.	
9		0	30	0	84	0	31	1.00		n.s.	
w10		0	30	6	78	0	31	0.20		n.s.	
w52		23	7	54	30	23	8	1.75		n.s.	
w53		16	13	43	41	14	16	1.17		n.s.	
−DQw1		14	16	62	22	16	15	0.32	7.2	0.007	
	w5	6	22	24	55	9	20	0.65		n.s.	
	w6	8	22	45	39	8	23	0.33	6.17	0.01	
w2		17	11	40	44	21	10	1.67		n.s.	
w3		12	18	29	54	10	20	1.25		n.s.	
	w7	2	28	19	65	4	25	0.30		n.s.	
	w8	8	21	10	74	6	24	2.81	4.08	0.04	
	w9	0	29	2	80	1	29	0.55		n.s.	
w4		1	19	3	80	0	26	1.77		n.s.	

* RR = Relative Risk; p = uncorrected for number of antigens (= 25) tested (Svejgaard et al. 1980, 1983).
EF = etiological fraction.

different from IDDM, and the committee has recommended that further studies be conducted in order to better define their epidemiological, clinical and etiological characteristics, among which should be studies addressing possible HLA associations.

The occurrence of IDDM and NIDDM in Ethiopia is well documented (Lester et al. 1976). In addition, within the MRDM group, a variant with clinical characteristics similar to those of PDPD is also seen, differing from it only in the rarity of insulin resistance (Belcher 1970, Abdulkadir et al. 1987), reported to be common in PDPD (Abu-Bakare et al. 1986). Regardless of this difference, the preponderance of evidence favours its inclusion in the category of PDPD.

IDDM is clearly associated with certain HLA antigens (although exhibiting race-related variations) but NIDDM is not. Inasmuch as the great majority of patients in both MRDM variants are adolescents or young adults and require insulin for diabetic control, they resemble IDDM rather than NIDDM.

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However, there is little information on HLA antigens in MRDM so far. In this study, the HLA pattern in 30 Ethiopian MRDM patients was determined and the findings were compared with those in IDDM from the same ethnic background (Ottenhoff et al. 1987b).

Patients and Methods

Patients and controls

Thirty unrelated MRDM patients who were attending the Diabetic Clinic at the Tikur Anbessa Teaching University Hospital in Addis Ababa were randomly selected for the study. The patients had been diagnosed according to internationally accepted criteria (WHO 1985) and presented with clinical characteristics of PDPD as described above. There were 27 males and three females; the age of onset was below 40 years of age with the exception of two patients (45 and 52 years). Cryopreserved peripheral blood mononuclear cells were shipped on dry ice to Leiden. The 31 IDDM patients used in this study have been previously described (Ottenhoff et al. 1987b) and were from the same clinic as well as ethnic background. The control group consisted of 33 healthy laboratory staff members used in an earlier study (Ottenhoff et el. 1987a) extended with 51 borderline tuberculoid leprosy patients whose HLA class I and class II frequencies have been previously shown not to differ from the 33 healthy controls, as described earlier (Ottenhoff et al. 1987a,b).

HLA typing

Typing for the HLA-A, B and C antigens was performed with a set of 120 well-defined sera using the standard NIH microlympocytotoxicity technique (Van Rood 1979). HLA-DR, -DQ typing was performed with a set of 90 antisera using the two-colour fluorescence test (Van Rood et al. 1976). The recently designated DQ subtypes were defined with monoclonal antibodies IIB3 and TA10 (WHO 1987) and local LB-E13 antisera. DQw1 is now split into DQw5 and DQw6, whereas DQw3 has three subtypes, DQw7 (TA10, DQw3,1), DQw8 (DQw3,2) and DQw9 (Schreuder et al. 1986).

Statistical analysis

Association between HLA phenotypes and MRDM were tested by 2 × 2 contingency tables. Relative risks and their significances were calculated according to Woolf's method as modified by Haldane (reviewed by Svejgaard et al. 1980). Etiological fractions were calculated by the methods of Bengtsson & Thomsen (reviewed by Svejgaard et al. 1983).

Results

The results of the HLA class II typing are shown in Table 1. In comparison to the controls, the frequencies of HLA DR3 and DQw8 were significantly increased ($P = 0.0001$ and 0.04, respectively) and those of DR2 and DQw6 significantly decreased ($P = 0.01$ in each case). DR4 appeared increased (RR = 1.72) and DQw7 decreased (RR = 0.30), but the differences did not reach statistical significance in either case. After correction for the number of comparisons made, only the association between DR3 and MRDM retained statistical significance. There were only two DR3/DR4 heterozygous MRDM patients.

Borderline tuberculoid leprosy patients and normal healthy controls did not differ significantly in this population in either HLA-A, -B, -C or -DR or -DQ antigen frequencies from each other and therefore were pooled as control group for comparison with MRDM patients as shown in Table 1. A separate analysis on MRDM versus normal healthy controls only (33 subjects) was also performed and gave very similar results, namely positive as-

sociations of MRDM with DR3 (RR = 5.4; X^2 = 8.5; P = 0.004), and DQw8 (RR = 4.8; X^2 = 4.7; P = 0.03) and negative associations with DR2 (RR = 0.17; X^2 = 4.4; P = 0.04), DQw6 (RR = 0.34; X^2 = 4.4; P = 0.04) and DQw1 (RR = 0.22; X^2 = 7.7; P = 0.006).

When the MRDM and IDDM groups were compared in a separate analysis, no significant differences in HLA antigen frequencies could be detected (not shown in Table 1). Nevertheless, DR3 was increased and DR2 and DR4 decreased among MRDM as compared to IDDM patients (Table 1). These differences, although not significant, explain the stronger association of DR3 with MRDM as compared to IDDM as well as the lack of association between DR4 and MRDM and DR2 and IDDM, respectively.

When MRDM versus controls were compared for HLA-A, -B and -C antigen frequencies, A1, 24, w66, 29, B8, w63 and w47 were increased and A31 and B5 decreased in frequency but none of these differences remained significant after correction for the number of comparisons made.

Discussion

The results of this study show that Ethiopian MRDM, which is clinically similar to PDPD, is strongly associated with HLA-DR3 (RR = 6.2, P corrected = 0.002) but not with HLA-DR4. No significant differences were found between MRDM and IDDM which is associated with both DR3 and DR4 in the same population (Ottenhoff et al. 1987b). But, unlike the finding in IDMM in this population, the difference in the frequency of DR4 in MRDM was not significantly higher than that in the controls (RR 3.97, P = 0.01 in IDDM compared to controls versus RR 1.72, P not significant in MRDM compared to controls). On the basis of these findings, Ethiopian MRDM appears to share a genetic basis with IDDM but, unlike the latter, its association appears to be with DR3 but not DR4.

Although DQw8 was increased in frequency among MRDM patients, its association did not retain significance after correction for the number of comparisons made. Nevertheless, its increased frequency is interesting given the recently reported identification of DQ molecules as at least one of the susceptibility gene products for IDDM in different races (Todd et al. 1989).

IDDM has indeed been considered a genetically heterogeneous disease, and DR3 but not DR4 was found to be associated with a milder form of IDDM with lesser ketonuria, less often DKA and more often a partial remission in children of different nationalities (Ludvigsson et al. 1986). The relative ketosis-resistance in our MRDM patients, which contrasts to the situation found in IDDM, may well be compatible with such a milder DR3 associated subtype. The lack of DR3/DR4 heterozygous IDDM (Ottenhoff et al. 1987b) as well as MRDM patients in our studies furthermore suggests an independent contribution of both alleles to susceptibility to IDDM/MRDM and, thus, could reflect different subtypes. MRDM patients have a higher residual insulin secretion as compared to IDDM during glucose tolerance test that could be the result of a milder immunologically damaging process in the pancreas. In addition, other factors such as body fat depletion could be involved in DKA resistance.

In sub-Saharan Africa, the HLA pattern in IDMM varies from region to region and is probably related to ethnic heterogeneity (Ottenhoff et al. 1987b). For example, in one study in South Africa no significant association was found with any HLA antigen in black patients (Orren et al. 1985) while in another study there was a significant association with DR4 and DR3 (Omar et al. 1984). In yet another study in Nigeria, the association with DR3 was found to be stronger than

that with DR4 (McDonald et al. 1986). No HLA studies, however, have been reported for MRDM so far. Taking together (i) the striking association with DR3 but not DR4 in our mildly diabetic MRDM group, (ii) the association of both DR3 and DR4 with IDDM, (iii) the milder nature of the DR3 related IDDM subtype in Caucasoids (Ludvigsson et al. 1986) and (iv) the relative lack of DR3/DR4 heterozygous Ethiopian IDDM and MRDM patients, our findings suggest that MRDM is related to the DR3 rather than the DR4 associated subtype of IDDM in Ethiopia, although other studies elsewhere have shown a milder clinical picture in the DR4 related subset (Hoogwerf et al. 1985).

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of Paediatrics and Child Health of the Faculty of Medicine, Addis Ababa University. Morphological changes were analyzed in terms of the frequency of occurrence and age and sex distribution of the patients. Liver cirrhosis was diagnosed on the basis of hepatic fibrosis and nodular regeneration. The type of cirrhosis, however, was not specified in the pathology reports. The diagnosis of porphyria cutanea tarda (PCT) was based on inspection of the biopsy material immediately after removal under ultraviolet light (UVL) using a binocular dissecting microscope illuminated by 111 watt UVL inspection lamp (Allen). Tuberculous granulomata were diagnosed by the presence of caseating granulomata in specimens. Shistosomal granulomata were diagnosed by demonstration of *Shistosoma mansoni* eggs in the specimens. The remaining hepatic granulomata were recorded as unclassified. Since this was a retrospective analysis of liver biopsies as seen in the Pathology Department, data on clinical features such as indications for, and complications of liver biopsies, incidence of hepatitis B surface antigen positivity, and alcohol abuse were not available.

RESULTS

A total of 860 liver specimens were examined in this study of which 156 (18.1%) were inadequate for precise pathologic diagnosis. The remaining 704 specimens were from 482 male and 222 female patients, the male to female ratio being 2.2 : 1. The age distribution and the frequency of the histopathological patterns are shown in Tables 1 and 2. About half of the PHC patients (80/135) occurred in a background of liver cirrhosis.

The highest prevalence of liver cirrhosis and PHC was in patients between 40 and 59 years of age (Table 3).

There was a large male preponderance in involvement of the liver in PCT, 80 of the 87 patients being male. Of the 2[illegible] granulomata in the liver, tuberculosis accounted for 13, and schistosoma for one; the remaining 6 were of undetermined aetiology.

DISCUSSION

The high prevalence of liver cirrhosis and PHC in this report is in agreement with previous clinical and autopsy studies from Ethiopia (1,5,6,7,8). In an analysis of adult medical admissions in Ethiopia, Lester and Tsega (6) found that acute and chronic hepatitis, liver cirrhosis and PHC accounted for 11.6% of all admissions and 33.3% of all adult medical ward deaths. Moreover PHC accounted for 50% of all medical admissions due to malignant diseases. Hofvander (7) and Boshmakova (8), in analysis of medico-legal autopsies, reported the prevalence of liver cirrhosis as 3.7% and 7.5% respectively. The type of cirrhosis was not specified in most of the specimens examined, probably due to inadequate size of needle biopsy specimens. However, autopsy studies have shown post-necrotic, posthepatitic, and mixed cirrhosis to be the predominant types, the histologic features of alcoholic cirrhosis being distinctly less common (7,8).

One major point that differentiates PHC in Ethiopians from cases reported in the United States is its very high prevalence and occurrence at a younger age. The prevalence of 19.2% of liver biopsies in this report is more than fifty times than that reported in the United States in 1953 (9). Moreover patients with obvious malignant diseases are not admitted when they are not treatable. Also a significant number of PHC were diagnosed from extrahepatic pathology, that is secondaries and peritoneal cytology, and if included might well increase the prevalence significantly. Tsega (10) in a prospective study of 100 Ethiopian patients with PHC, noted that half o

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TABLE 1. Age distribution of patients.

Age (years)	No. of patients (% total)
0 - 19	59 (8.4)
20 - 39	280 (39.8)
40 - 59	300 (42.6)
60 - 79	65 (9.2)

TABLE 2. Histologic features, all ages.

Diagnosis	No. of patients (% total)
Liver cirrhosis	179 (25.4)
Hepatoma	135 (19.2)
Porphyria cutanea tarda	87 (12.4)
Hepatitis	62 (8.8)
Secondaries to the liver	32 (4.5)
TB and other granuloma	20 (2.8)
Miscellaneous*	189 (26.8)

* Miscellaneous includes : Portal fibrosis, haemosiderosis, fatty liver, venous congestion, hydatid cyst of the liver, malaria and borrelia in the liver and a few cases of amoebic and pyogenic liver abscesses.

TABLE 3. Histopathologic features by age group.

Age (years)	Liver cirrhosis	Hepatoma	PCT	Secondaries to the liver
	(% total)			"
0 - 19	25 (14.0)	1 (0.7)	-	3 (9.4)
20 - 39	50 (27.9)	34(25.2)	22(25.2)	8 (25.0)
40 - 59	89 (49.7)	73(54.0)	61(70.1)	14 (43.8)
60 - 79	15 (8.4)	27(20.0)	4(4.6)	7 (21.9)

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of disease in families. Sixty-four percent of our patients were clustered in four families and all had direct exposure to diseased animals. The likelihood of disease occurring within multiple members of a family should prompt providers to consider initiation of therapy of entire families prior to the development of symptoms. This is particularly true for villagers from isolated regions of the countryside.

The severity of disease also differed in the various locales. In Bangladesh no deaths were recorded among 27 patients [7], in Zimbabwe 95% of cases were uncomplicated [2], in Gambia the mortality rate was 3% [8]; in Tanzania there were no deaths among 234 patients [6], in Thailand there were three deaths among 24 cases of oral pharyngeal anthrax [5], and in Ethiopia three deaths occurred among the 27 patients. In addition 14 patients (52%) in this series developed significant complications during hospitalization. Of particular interest is the common finding that deaths in Ethiopia and Bangladesh occurred only in patients with incubation periods of less than 24 hours [7].

The question arises as to whether differences or changes in the antigenicity, toxin production, and/or virulence of the bacillus could account for variations in prevalence and morbidity and mortality. Also host specific factors including concurrent infection and nutrition status may have an effect on disease outcome.

It is known that response to infection varies among individuals exposed to the same bacillus. Some develop an antibody response that persists up to a year and others fail to develop any significant response. Antibodies have also been identified in individuals without a clinically apparent infection. However, it appears that serologic positivity is a transient response and lifelong immunity is not conferred by either clinical or subclinical infections [11]. However, continuous exposure might provide ongoing immunity. The epidemic in Zimbabwe, for example, could have been the result of a sudden increase in the prevalence of *B. anthracis* in the environment due to cessation of the cattle vaccination program. Antibody titres to anthrax would have waned during the period of vaccination resulting in a large pool of susceptible hosts. In Thailand the epidemic occurred in association with a large influx of diseased cattle from Burma into a community without endemic infection in indigenous herds. The apparently low prevalence of clinical anthrax in Ethiopia may be due to intermittent subclinical infection with resultant low level immunity. The fact remains however, that factors determining individual and community susceptibility are unclear and further population studies are needed.

The delay in seeking care and the effects of cautery and herbal medicine on the clinical presentation of patients may explain the increased morbidity noted in our series. The isolation of villages and difficult transportation contribute to the dependence of villagers on local healers. The local knowledge about anthrax in Ethiopia has not been assessed but Davies found a generally poor knowledge about the disease in the health care providers in Zimbabwe prior to the onset of epidemics in that country [3].

As the Medical College is a referral center, the true prevalence of anthrax in the general community may be much higher than herein reported. No specific comment concerning morbidity and mortality can be made as the presentation of the disease is variable, especially in children. Spontaneous recovery from mild attacks is known to occur and vital statistics data is not available from the countryside.

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ANTHRAX IN ETHIOPIA

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Abstract. Twenty-seven patients with cutaneous anthrax were identified over a three-year period at Gondar College of Medical Sciences in North Central Ethiopia. Nine patients who delayed seeking medical care presented with severe symptoms and three patients died. Eighteen patients were clustered within four families in which an attack rate of 32% occurred. Ninety-three percent of patients could trace their disease to exposure to the products of a specific diseased animal. Characteristics of anthrax in Ethiopia include a known exposure to diseased animals, occurrence within families, frequent treatment by local healers, and high morbidity and mortality.

Key words: Anthrax, Ethiopia

Introduction

Anthrax is a zoonotic disease rarely reported in the developed world. [1] Although endemic in many developing communities, periodic epidemics of the disease have been reported in a number of countries on several continents [2-7]. These have been associated with the impact of social and political turmoil on human and animal public health practices [2], local customs that include extensive utilization of beef products [5, 6], the migration and death of diseased herds [5], and the use of products from diseased animals by people who are ignorant of the causes of anthrax or are forced by poverty to accept the risk of contracting the disease [2, 7].

Although Ethiopia is a developing nation that is characterized by all of these risk factors, no epidemics have as yet been reported from this country. However, the same forces that place a nation at risk for epidemic anthrax also hinder identification, surveillance, and reporting of the disease. Expansion of trade and tourism, and increasing exchange of professional personnel with Ethiopia and other developing nations increase the international importance and pressure to characterize the epidemiology of anthrax throughout the world.

This is the first published report of anthrax from Ethiopia. Its purpose is to describe the existence and pattern of disease transmission in order to facilitate early implementation of appropriate preventive, diagnostic, and therapeutic measures.

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This study was performed at the Gondar College of Medical Sciences in Gondar City (population 80,000). The Medical College serves much of Gondar province and is one of three medical schools in Ethiopia. Four hundred students are enrolled in a five-year program leading to an M.D. degree. Approximately 30,000 outpatients and 3,000 inpatients are cared for each year.

An attempt was made to identify all patients presenting as in- or out-patients to the Medical College with the clinical diagnosis of anthrax during the years 1983 to 1986. Criteria for inclusion as a case of anthrax included: 1) examination by one of the authors during the period of the study, 2) demonstration of a cutaneous lesion characterized initially as a small macule or papule that developed through a vesicular phase into a painless black eschar, 3) any history of a similar lesion as noted in (#2) that occurred after exposure to a diseased animal and for which herbal medications and/or cautery were used, and/or 4) demonstration of encapsulated gram + bacilli obtained from under the scabs or from vesicular fluid in edematous areas. Cultures were obtained from only ten patients due to the fear by laboratory personnel of contamination. They were plated on blood agar and incubated at 37°C in the ambient atmosphere for 24 hours. Visual identification was based on the finding of non-hemolytic, flat colonies which on gram stain showed large, gram positive rods consistent with *Bacillus anthracis*. Facilities were not available for further biochemical characterization.

Clinical data was obtained and included name, age, sex, address, site and duration of lesion, local herbal treatment or cautery of the skin lesion or adjacent tissue, date of appearance, contact with by-products of domestic animals or consumption of meat, the health status of contact animals, and the number of other individuals potentially exposed to diseased animals.

Results

Twenty-seven patients with cutaneous anthrax were identified. Twenty five were from rural areas and two were urban dwellers. One of the urban dwellers apparently contracted the disease after exposure to relatives with anthrax in a rural area.

Fifteen patients were males and 12 were females. The mean age of males and females was 30 (range 9-75) and 24 (range 1-65) respectively. Eighteen (67%) patients were clustered within four families and nine (32%) occurred in isolation. No family clusters or individuals lived in geographic proximity to one another.

Twenty five of the patients could trace their contact to ingestion of meat from a sick animal and/or contact with its hide. Two patients were unable to identify a likely contagious source.

Among the four families, the ratio of those with clinical disease to those who were exposed was 3/15, 3/17, 3/13, 10/15. This is an attack rate of 32%.

The time between known exposure and appearance of cutaneous lesions varied from one to five days. Fourteen patients presented with lesions of the scalp, face, neck, eyelids, and lip. Seven had lesions on the shoulder, arm, hand, and finger, and the remainder had lesions on the thigh, lower leg, and heel. In two patients edema extended from the upper eyelid to the iliac crest.

Fourteen patients initially received either self treatment or care from a herbal healer. Among these 14 patients were all nine of those that presented with severe symptoms. These symptoms included distorted, painful, and enlarged ulcerations, cellulitis, hypotension, and respiratory symptoms. All fatalities were from this group of nine patients.

All patients received antibiotic therapy. Eleven received intravenous penicillin (24 million units/day). Two patients received intravenous penicillin in combination with chloramphenicol (2 grams/day) and one penicillin in combination with an aminoglycoside. Five received procaine penicillin (1.6 million units/day), and eight received oral ampicillin (2 grams/day). Inpatients were treated for two weeks and

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outpatient therapy was for seven days. Six severely ill patients (hypotension, respiratory collapse, anuria) also received glucocorticoids. The skin lesions of three patients were initially misdiagnosed as allergic dermatitis or insect bites and they also received glucocorticoids and antihistamines.

Three patients died yielding a case fatality rate of 11%. Two patients died within 48 hours of the onset of symptoms due to respiratory failure associated with disseminated infection. The third patient died on the 21st day of illness probably due to cavernous sinus thrombosis associated with a large invasive necrotic lesion involving the entire right face. The incubation period for these three patients was less than one day.

Among the surviving patients, temperature became normal between three and twenty-one days (mean 11 days) and all other symptoms improved by the third week of illness; specifically, soft tissue edema and eschars had resolved leaving only shallow ulcerations with granulation tissue at the base.

Discussion

Ethiopia has many similarities to other countries that have recently experienced epidemic outbreaks of anthrax. However, no epidemics have as yet been reported from Ethiopia despite the endemic presence of the disease and the multiple community risk factors. Recent epidemics in Zimbabwe [2-4] Thailand [5], Tanzania [6] and the Gambia [8] emphasize the need for both ongoing surveillance and public health prevention measures. However, other pressing problems in Ethiopia render such a program a low priority. This further increases the importance of surveillance in order to limit the breadth of a potential epidemic through early recognition and intervention.

In Zimbabwe, for example, only 500 cases of anthrax had been reported between 1923 and 1977 [2]. Identification of sporadic cases had previously initiated both human treatment and vaccination of cattle. Elimination of these programs in the 1970's was associated with the onset of a major epidemic with at least 6,000 reported cases of human anthrax between October, 1979 and March, 1980 [2, 4].

There are similarities and differences among the characteristics of anthrax as described in Ethiopia and other African and non-African countries. The seasonal incidence is similar throughout Africa occurring predominantly during the dry season [2, 6]. In this series there was also an apparent association with the occurrence of Easter, a holiday during which cattle are traditionally slaughtered in great numbers for the Easter feast. However in Bangladesh two outbreaks were reported in consecutive years during the wet summer months [7]. Male : female ratios lean toward a preponderance in males but there is a variation in reported age distributions. Whereas Heyworth *et al.* found no preponderance by age in the Gambia, reports from other countries note fewer children involved [8, 9]. This is probably due to their relative lack of direct exposure to cattle products, especially during their slaughter. Although transmission is known to occur via fly vectors, [10] observations in these studies that relatively few children are affected, despite their constant exposure to insect vectors, and of distinct seasonal peaks for fly vectors and anthrax (exception in Bangladesh), support the view that insect vectors were not an important source of infection. Although Heyworth *et al.* suggest that human to human transmission occurs, it is important to note that there has been no evidence of spread to health workers caring for patients with the disease [4].

This series from Ethiopia is the only published description of the occurrence

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of disease in families. Sixty-four percent of our patients were clustered in four families and all had direct exposure to diseased animals. The likelihood of disease occurring within multiple members of a family should prompt providers to consider initiation of therapy of entire families prior to the development of symptoms. This is particularly true for villagers from isolated regions of the countryside.

The severity of disease also differed in the various locales. In Bangladesh no deaths were recorded among 27 patients [7], in Zimbabwe 95% of cases were uncomplicated [2], in Gambia the mortality rate was 3% [8]; in Tanzania there were no deaths among 234 patients [6], in Thailand there were three deaths among 24 cases of oral pharyngeal anthrax [5], and in Ethiopia three deaths occurred among the 27 patients. In addition 14 patients (52%) in this series developed significant complications during hospitalization. Of particular interest is the common finding that deaths in Ethiopia and Bangladesh occurred only in patients with incubation periods of less than 24 hours [7].

The question arises as to whether differences or changes in the antigenicity, toxin production, and/or virulence of the bacillus could account for variations in prevalence and morbidity and mortality. Also host specific factors including concurrent infection and nutrition status may have an effect on disease outcome.

It is known that response to infection varies among individuals exposed to the same bacillus. Some develop an antibody response that persists up to a year and others fail to develop any significant response. Antibodies have also been identified in individuals without a clinically apparent infection. However, it appears that serologic positivity is a transient response and lifelong immunity is not conferred by either clinical or subclinical infections [11]. However, continuous exposure might provide ongoing immunity. The epidemic in Zimbabwe, for example, could have been the result of a sudden increase in the prevalence of *B. anthracis* in the environment due to cessation of the cattle vaccination program. Antibody titres to anthrax would have waned during the period of vaccination resulting in a large pool of susceptible hosts. In Thailand the epidemic occurred in association with a large influx of diseased cattle from Burma into a community without endemic infection in indigenous herds. The apparently low prevalence of clinical anthrax in Ethiopia may be due to intermittent subclinical infection with resultant low level immunity. The fact remains however, that factors determining individual and community susceptibility are unclear and further population studies are needed.

The delay in seeking care and the effects of cautery and herbal medicine on the clinical presentation of patients may explain the increased morbidity noted in our series. The isolation of villages and difficult transportation contribute to the dependence of villagers on local healers. The local knowledge about anthrax in Ethiopia has not been assessed but Davies found a generally poor knowledge about the disease in the health care providers in Zimbabwe prior to the onset of epidemics in that country [3].

As the Medical College is a referral center, the true prevalence of anthrax in the general community may be much higher than herein reported. No specific comment concerning morbidity and mortality can be made as the presentation of the disease is variable, especially in children. Spontaneous recovery from mild attacks is known to occur and vital statistics data is not available from the countryside.

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HISTOLOGICAL EXAMINATION OF BLOOD VESSELS IN PERIPHERAL GANGRENE AMONG PATIENTS WITH SPORADIC OUTBREAK OF ERGOTISM

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Abstract. During the academic year 1985-1986 at Gondar College of Medical Sciences Hospital gangrenous ergotism was clinically diagnosed in seven patients (5 males, 2 females) ranging in age from 20 to 45 years. Amputation and subsequent histological examination of the blood vessels revealed occluded tibial arteries by acute thrombosis without cellular reaction or inflammatory lesion of the arterial wall in 3 patients. Endangitis with organized arterial thrombosis and focal recanalization of the vessels was noted in the remaining four patients. The smaller arterial branches including the dorsal pedal artery appeared to be contracted with knobby projections into the lumen. The latter was occluded by chronic, organized thrombosis in all patients. The present finding indicates that thrombosis and its organization could be another pathogenic factor in the development of gangrene due to ergotism, which is a histological picture similar to that of thrombangitis obliterans.

Key words: Histology; ergotism; Ethiopia

Introduction

Ergotism, the poisoning with the alkaloids of the ergot fungus *Calviceps purpurea*, occurs as an acute or chronic condition. The principal manifestations of this poisoning are convulsions and gangrene.

Acute poisoning arising from ingestion of food prepared from grain contaminated with ergot fungus, injection or application of alkaloids to mucous membranes leads to vomiting, diarrhoea, dizziness, rise or fall of blood pressure, slow and weak pulse, dyspnoea, convulsions and loss of consciousness.

Chronic poisoning arising from the same conditions includes two types of manifestation which may occur together or separately. Those resulting from contraction of blood vessels and reduced circulation include numbness and coldness of extremities, tingling, pain in the chest, oliguria from reduced renal blood flow and peripheral gangrene. Those resulting from nervous system disturbances include vomiting, diarrhoea, headache, tremors, contractions of facial muscles and convulsions.

Ergotism was once a major problem in Europe and Asia, the last notable outbreak in Europe was recorded in the small South French town Pont St. Esprit in 1951 [1]. However it still occurs sporadically in certain areas of the world; particularly associated with times of scarcity of food [2]. King [3] and Demeke *et al.* [4] reported an outbreak of gangrenous ergotism in the Wollo Administrative Region of Ethiopia in 1977-1978.

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During the academic year 1985-1986 seven patients with a unilateral (two) and bilateral (five) peripheral necrosis of the lower leg due to ergotism were admitted to the hospital of the Gondar College of Medical Sciences. This is the first report of a histological examination of blood vessels in peripheral gangrene among patients treated during a sporadic outbreak of ergotism in Ethiopia.

Methods

Five male and two female patients between 20 and 45 years from drought areas in Gondar, Ethiopia were admitted to the Gondar College of Medical Sciences Hospital with a diagnosis of ergotism during 1985-1986. Symptoms of the disease started at least three weeks prior to admission. After amputation of the necrotized legs the anterior and posterior tibial arteries, the dorsal pedal artery and concomitant veins were investigated histologically by transverse sections. Histological slides were stained by haematoxylin-eosin and the connective tissue staining procedure as described by Goldner [5].

Results

The clinical picture was characterized in all patients, by sharply demarcated necrosis of the forefoot, the whole foot, and in five of the patients with bilateral foot necrosis (*figure 1*). However, in one case the entire lower limb was completely mummified (*figure 2*). The diagnosis was based on the patients clinical presentation as well as the epidemiology of the disease in the area. In the five patients without severe bacterial superinfection the amputation was performed slightly above the line of demarcation. Wound healing occurred in all patients by primary intention without complications. In the two patients with a more marked bacterial superinfection, amputation was performed more proximally from the demarcation line. This is quite different from the clinical experience with wound healing after amputation of extremities due to atherosclerotic and diabetic gangrene.



Figure 1. Sharply demarcated bilateral necrosis of the feet in a 30 year-old-woman.

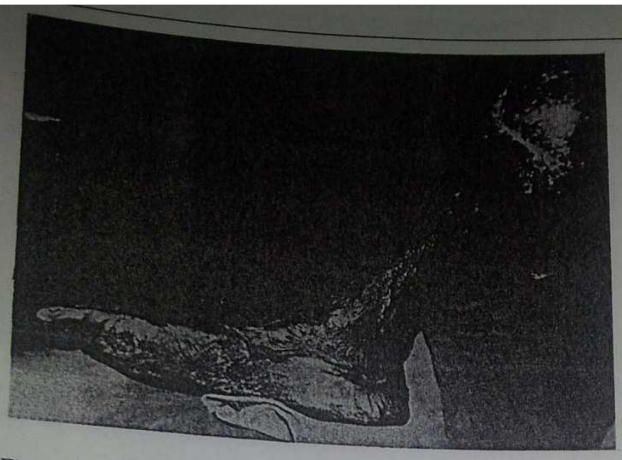


Figure 2. Complete mummification of the right lower limb in a 46 year-old-man.

Histological examination revealed the following results: In three cases the larger arteries (A. tibialis anterior and A. tibialis posterior) were occluded by acute thrombosis without cellular reaction or inflammatory lesions of the arterial wall. The other four patients were characterized by endangitis with organized thrombosis and recanalization of the larger arteries at the periphery of the old thrombus (*figure 3*).

Smaller arterial branches including the dorsal pedal artery appeared to be contracted with knobby projections into the lumen. The A. dorsalis pedis was found to be occluded by chronic organized thrombosis in all cases (*figure 4*).

Findings varied in the concomitant veins. Some appeared to be affected, others were found to be occluded by acute thrombosis and again others showed organized thrombosis with obliteration of the lumen. Ischemic damage to the surrounding skeletal musculature was noted in all patients.



Figure 3. Posterior tibial artery with endangiitis characterized by an organized thrombus with recanalisation of the vessel (Goldner, 42 x).

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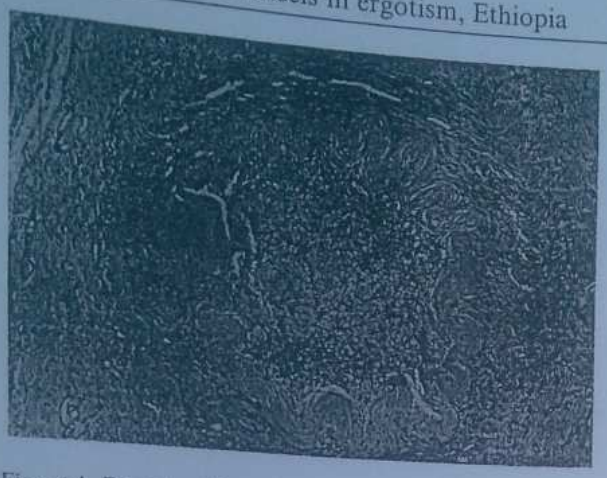


Figure 4. Dorsal pedal artery with contracted appearance of the intimal layer and obstruction of the lumen by an organized thrombosis (HE, 53 x).

Discussion

In chronic ergotism the peripheral gangrene is believed to be due to prolonged spasms of medium size arteries and small nutrient vessels. However a hypercoagulability state has also been reported and may be a factor in the causation of the gangrene. Although thrombangiitis obliterans (Winiwarter-Buerger) is in the differential diagnosis, no infiltration by polymorphs or fibrinoid necrosis of the vascular walls was found. However, inflammatory signs may subside in this lesion, and as discussed by Kaunitz [6] based on the similarity of the morphology of the vascular changes, may itself be a cause of thrombangiitis obliterans. Heavy cigarette smoking has been described as the single most important predisposing factor for thrombangiitis obliterans but was not noted in our patients. Idiopathic peripheral gangrene of the tropics is another entity in the differential diagnosis. This lesion usually occurs in previously healthy men between 20 and 40 years of age but has also been reported in children and older age groups from several parts of Africa [7-10]. The gangrene is often symmetrical and frequently affects the lower extremities. The aetiology is unclear and there is no report of thrombangiitis in these patients.

In summary the following points are advocated: (1) The role that acute and chronic thrombangiitis play in the causation of ergotism in peripheral gangrene should be further investigated. (2) However, we believe thrombotic episodes could be the primary cause of the disease. (3) Better definition of the relationship between ergotism and angiitis obliterans is necessary. (4) Ergotism must be considered in the differential diagnosis of gangrene. It may be more common than expected. (5) Early diagnosis may limit the extent of amputation. (6) Outbreak of ergotism may be produced during periods of drought.

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