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The Fevers of Africa

6. Leishmaniasis South of the Sahara

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Leishmaniasis was first described from India as the visceral form kala azar; since then this disease has been found to occur in China, Central Asia, Arabia, North Africa, the Sudan. Kenya and sporadically across Africa south of the Sahara to the West Coast.

Different varieties of the disease have been described on clinical, epidemiological and parasitological grounds, but these differences are possibly caused by varying degrees of immunity in the human host and the differing habits of the sandfly vector.

Varieties of Leishmania

In the Old World three different leishmanial parasites have been described in man: *L. tropica* confined to the skin, *L. donovani* confined to the viscera, and *L. infantum* from North Africa. No morphological differences can be found and animal infections show no marked differences, though Adler (1931) has claimed to distinguish *L. tropica* from *L. donovani* on serological grounds.

In Mice.—L. donovani and *L. tropica* inoculated intravenously and intraperitoneally produce a general infection, but when inoculated intracutaneously cause a local skin lesion (Laveran, 1914; Row, 1914).

In Monkeys.—L. donovani when inoculated intracutaneously causes a local skin lesion, but when inoculated intraperitoneally general infection results (Row, 1912).

In Hamsters.—In Chinese hamsters lesions in the skin and subcutaneous tissue can be produced by *L. donovani* (Hindle and Thomson, 1928). In the European hamster intracutaneous inoculation of *L. donovani* and *L. tropica* causes local lesions (Mayer, 1929) as well as a visceral infection.

In Dogs.—In North Africa both a generalised visceral or a skin infection with or without ulcers can result, and these dogs are considered to be the reservoir of infection in North Africa for *L. infantum* which produces a general infection in man. In Persia and Iraq the dog is considered to be the reservoir of infection for *L. tropica.*

Other Animals.—In Central Asia both visceral and cutaneous leishmaniasis in man have been found to be a zoonosis with a reservoir in gerbils and possibly jackals (Viem, 1940).

Varieties of Leishmaniasis

The clinical and epidemiological picture of leishmaniasis in the Old World varies in eight main features:—

(1) The age group affected.
(2) Skin or viscera only, or both affected.
(3) Frequency of leishmania in the peripheral blood.
(4) Response to treatment with trivalent antimony compounds.
(5) Frequency of relapses.
(6) Frequency, incubation period and duration of post kala azar dermal leishmanoid.
(7) The presence or absence of an animal reservoir.
(8) The species of sandfly vector and its habits.

(1) *Oriental Sore or Cutaneous Leishmaniasis.*—In oriental sore the skin only is affected; there are no leishmania in the viscera; sandflies must be infected from the cutaneous lesion. The distribution differs from that of the visceral disease except in East Africa and the Sudan. In Iraq the dog and in Central Asia gerbils are the animal reservoirs.

(2) *Indian Kala Azar.*—In Indian kala azar the age group 14-18 is chiefly attacked; the viscera only are involved, except in post kala azar dermal leishmanoid. Leishmania can easily be found in the peripheral blood from which sandflies can be infected. The disease responds well to trivalent antimony compounds and relapses are not common. Post kala azar dermal leishmanoid is common, occurs one to two years after treatment and lasts for some years. There is no known animal reservoir. The vector is *Phlebotomus argentipes,* a house-haunting sandfly, so that the disease is urban.

(3) *North African or Infantile and Chinese Kala Azar.*—In Mediterranean kala azar infants chiefly are attacked, though adult immigrants also suffer. Leishmania in multiple areas of the skin without apparent lesions have been described by Benhamou *et al.* (1935), Cash and Hu (1927). Parasites are seldom found in the blood. *Phlebotomus major, perniciosus* and *chinensis* are infected from the skin of dogs who form the reservoir of the disease. These are domestic sandflies, so that the disease is urban. The response to trivalent antimonials is poor and the incidence of post kala azar dermal leishmanoid does not appear to be heavy.

(4) *Sudanese and Central Asiatic Kala Azar.*—In Sudanese and Central Asiatic kala azar,

adults as well as children are affected. Parasites are extremely scanty and often absent from the peripheral blood. Skin lesions in association with visceral disease are commonly found (Kirk and Drew, 1938; Mirzoian, 1941). There is little or no response to trivalent antimony compounds, and relapses are extremely common. In Central Asia kala azar is a zoonosis with an animal reservoir in gerbils and jackals (Viem, 1940). In the Sudan so far no animal reservoir has been found, nor has the sandfly vector been identified, but the disease is sporadic and rural (Kirk, 1955; Kirk, 1956).

DISTRIBUTION OF LEISHMANIASIS SOUTH AND EAST OF THE SAHARA

The distribution of leishmaniasis south and east of the Sahara is more extensive than was at first thought.

Visceral Leishmaniasis or kala azar has been found in Eritrea (Ferro Luzzi, 1943), British Somaliland (Annual Medical Report, 1922), Somalia (Timms), the Sudan in the Kapoeta and Fung districts (Archibald and Mansour, 1937), in Kenya, the Northern Frontier district (Anderson, 1943), the Kitui district (Fendal, 1952), the Elgeyo reserve (*East African Medical Journal*, 1934), where it has recently been active, Brazzaville (Malbrant, 1940) and the Gambia (Walters, 1949).

There must be other foci connecting these places in the savannah lying south of the Sahara. An increase in population and immigration to new areas, with the increasing development of water supplies, could bring an increase in the incidence of kala azar, its appearance in new areas and a repetition of its recent remarkable increase in Kenya (Heisch, 1954).

Cutaneous Leishmaniasis or Oriental Sore.—Oriental sore has been found in Abyssinia (Poggi, 1937), British Somaliland (Annual Medical Report, 1922), the Sudan (Kirk and Drew, 1938), Kenya (Cole, 1942), Kisumu, Kenya (*East African Medical Journal*, 1934), and a surprising though apparently quite genuine autochthenous case from Portuguese East Africa (Ziemann and Wagner, 1930), the North Cameroons (Rageau, 1951), South Cameroons (Herve, 1937) and Nigeria (Dyce Sharp, 1925; Elmes and Hall, 1944), where it is apparently not uncommon. The distinction between visceral and cutaneous leishmaniasis in Kenya and the Sudan is not clear.

Canine Leishmaniasis.—Canine leishmaniasis has been found in Eritrea (Ferro Luzzi, 1943), Brazzaville (Malbrant, 1940), Dakar and the Niger Province (Mornet, 1940), but so far in neither the Sudan nor Kenya.

VISCERAL LEISHMANIASIS

Epidemiology.—The epidemiology of kala azar south of the Sahara has been studied by Kirk (1956) in the Sudan and by Heisch (1954) in Kenya. The disease is entirely rural, being found in small isolated foci, though quite extensive epidemics may occur (Heisch, 1954). In Kenya the disease occurs below the 2,000 feet level and there is a seasonal variation, with a maximum incidence about six months after the rains. The vector has not been identified in the Sudan or Kenya, though Kirk (1955) suspects *Phlebotomus clydei* and *orientalis* in the Sudan and Heisch (1956) *Phlebotomus garnhami* and *martini* in Kenya. The habits of the sandfly have an important influence on the epidemiology of the disease, and Heisch (1954) believes in Kenya that the vector lives in termitaries with small mammals and lizards in a complicated ecological association. Young adults in the 14-18 age group are affected, although the disease is sporadic when it invades a new area, or in the presence of famine, extensive epidemics may occur with a high mortality rate, recalling the first appearance of kala azar in India in the middle of the nineteenth century. Such an epidemic has occurred (Fendall, 1952) and is still continuing in the Kitui district of Kenya, where the disease will probably become endemic.

Clinical Features.—In East Africa three main clinical types of kala azar are met with (Manson-Bahr and Heisch, 1956). Acute toxic, mild or ambulant, and typical kala azar.

(1) *Acute Toxic Kala Azar.*—When kala azar invades new areas, acute toxic forms are found and some such cases have been admitted to King George VI Hospital, Nairobi. These cases show the typical features of acute toxic kala azar; often an acute haemorrhagic disease with bleeding from the mucous membranes, severe toxaemia and little or no splenomegaly. When occurring sporadically they may be very difficult to diagnose, unless the possibility of their occurrence is borne in mind. A variety of this type is nephritic kala azar, with gross oedema, albuminuria and fever resembling a type 2 nephritis; such cases were found in East African soldiers during the late war (Cole, 1944) and have also been described from India (Napier and Krishnan, 1931).

(2) *Mild and Ambulant Kala Azar.*—Mild or ambulant cases with no symptoms, but showing an enlarged spleen, and leishmania in the viscera, occur not infrequently, and one such case has been described (Manson-Bahr, 1955). There is a varying degree of splenomegaly with some lymphatic glandular enlargement, but no fever. These cases are of considerable import-

ance, as they may form a reservoir of infection. and in a recent survey in the Kitui district at a time when the disease was as its lowest ebb, ten cases were found among 448 people examined at random. Several of these cases had skin lesions.

(3) *Typical Kala Azar.*—Typical kala azar is a chronic disease showing little or no fever, with splenomegaly, lymphatic glandular enlargement, a small degree of hepatomegaly and moderate anaemia. Intercurrent respiratory infections bring the patient to hospital, and Leishman Donovan bodies are found in the skin in association with visceral disease in a percentage of cases. Over half the cases occur in young adolescents between the ages of 14 and 20 years, in males and females in about equal proportions.

The onset of the disease is gradual and the majority of the patients seek treatment about three months after the onset. The main symptoms are pain beneath the left costal margin from the enlarging spleen, cough and sputum due to intercurrent respiratory infections, epistaxis, diarrhoea and tinnitus.

The main signs are splenomegaly of varying degree, sometimes of considerable amount, little or no fever, lymphatic glandular enlargement chiefly of the inguinal and femoral groups, but more significantly of the axillary glands, which are not usually enlarged in normal Africans; these lymphatic glands are not greatly enlarged, but can be felt discrete and shotty. The liver is usually just palpable and hard. Signs of associated nutritional deficiencies are common and invariable in the late stages, dry skin with pavementing of the shins, and rarely peripheral neuritis. Oedema where present is more likely to be due to an associated nephritis and albuminuria and casts in the urine are present in about 10 per cent. of cases. A toxic jaundice is found in 5 to 10 per cent. of cases.

Skin Lesions.—The skin lesions found in visceral leishmaniasis may be divided into two groups:—

(a) Solitary skin lesions containing leishmania with concurrent visceral disease.

(b) Post kala azar dermal leishmanoid.

(a) *Solitary Skin Lesions.*—Small solitary skin lesions associated with visceral infection are not uncommon in East African kala azar and are found in 10 to 20 per cent. of cases. In the Sudan, Kirk (1942) has described skin lesions in 30 per cent. of cases. In Kenya these lesions are solitary and are found in first and second attacks of kala azar, usually on the legs below the knees, though occasionally the back may be affected. The lesions appear as small hyperpigmented areas about ½ to 6 cms. in diameter, often with a small depigmented scar in the centre, and look exactly like healed tropical ulcers, from which they can only be differentiated by finding leishmania in skin scrapings. The nature of these lesions is in doubt and can be explained either as a primary lesion at the site of the infecting sandfly bite or by the settling of leishmania in an area of skin which has already been damaged.

(b) *Post kala azar dermal leishmanoid.*—This complication is not common and occurs in a small proportion of cases treated, though the number will probably increase as the disease becomes more endemic, as has occurred in Assam, India. The eruption consists of two distinct lesions, a depigmented petechial rash and a papular eruption starting on the face and neck, later spreading to the arms and legs. This leishmanoid is exactly comparable to that described in India by Napier and Das Gupta (1930). Leishmania are frequently absent from skin smears and are only scanty in others. This eruption appears shortly after treatment and lasts about a year; in Sudanese kala azar (Kirk and Sati, 1940) the eruption appears during or shortly after treatment and lasts a comparatively short time. In Indian kala azar the eruption does not appear until one or two years after treatment and lasts as long as two years.

CUTANEOUS LEISHMANIASIS OR ORIENTAL SORE

Pure cutaneous leishmaniasis or oriental sore is not common in East Africa, though it is quite common in parts of the Sudan and Nigeria. An isolated indurated painless ulcer on the forehead or nose, more rarely the arm, without any associated visceral infection. Sometimes these lesions are multiple.

MUCOCUTANEOUS LEISHMANIASIS OR ESPUNDIA

Mucocutaneous lesions like Espundia in South American leishmaniasis are not uncommon in the Fung district of the Sudan (Kirk, 1942). These lesions are usually associated with visceral disease. A typical case of espundia without visceral disease has been described from Kenya by Piers (1947).

SPECIAL INVESTIGATIONS

Leishmania are readily found in smears from the spleen, liver, marrow and less commonly lymphatic glands. In the blood leishmania can

be recovered by culture, though they cannot be found in blood films. There is a moderate normochromic normocytic anaemia with a leucopenia. In the early stages of the disease the total white cell count may be normal, but the neutrophils are reduced.

The formol gel test performed on the serum is of great value in diagnosis and a positive reaction as measured by complete solidification with egg white opacity developing within twenty minutes is invariably found after the disease has been present for three months. A negative reaction is found in the first three months. An intradermal reaction can be performed using an antigen prepared from a culture of leptomonad forms. A positive reaction is found after 72 hours.

DIFFERENTIAL DIAGNOSIS

Acute toxic kala azar must be differentiated from other acute fevers, typhoid, typhus, essential thrombocytopenia (onyalai), pulmonary and miliary tuberculosis.

Typical kala azar must be differentiated from other causes of gradual enlargement of the spleen, schistosomiasis mansoni, chronic brucellosis, cirrhosis of the liver and rarely chronic malaria. Other causes of wasting must also be excluded, such as starvation and tuberculosis. The diagnosis is made by finding the leishmania in smears from the spleen, liver, marrow or lymphatic glands. The formol gel test is positive only in kala azar, an indefinite result sometimes being found in splenomegaly due to schistosomiasis mansoni.

TREATMENT

The treatment of leishmaniasis south of the Sahara is difficult, as the disease is of such a relapsing nature. In the Sudan, Kirk and Sati (1940) and in the cases contracted near Lake Rudolph (Cole, 1944), trivalent antimony compounds are of little use. The chief drugs that have been used are the pentavalent antimony compounds urea stibamine and pentostam and the diamidine compound pentamidine isethionate. The drug of choice (Fendall, 1952) is urea stibamine, and this drug is now given in daily intravenous injections up to 1½ grains to a total of 30 grains for an adult and 15 grains for a child. Pentostam is used extensively and is given as a daily intramuscular injection of 4 cmls. (0.4 g.) for an adult and 2 cmls. (0.2 g.) for a child for ten days. Pentamidine isethionate is given in daily intramuscular injections of 0.2 g. for a total of ten injections concurrently with pentostam, but by itself is of little use in treatment of kala azar.

RELAPSES

Relapses in kala azar as found south of the Sahara are extremely common. This disease is extremely resistant and frequently two or more courses of treatment are required before a cure is obtained. Test of cure should be strict, and a case cannot be regarded as cured until the formol gel test is negative and the spleen has been reduced until it is almost impalpable. In spite of strict critera of cure, many cases relapse up to twelve months after apparent cure, and 15 to 50 per cent. of the monthly number of cases recorded in the Kitui district are relapses.

SUMMARY

(1) The different forms of leishmaniasis in Africa are described.

(2) The distribution of leishmaniasis south of the Sahara is discussed.

(3) The clinical and epidemiological features of the disease in this area are described.

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