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MYCETOMA INFECTION: AN APPEAL FOR MATERIAL.

A NEW science has arisen of recent years in tropical medicine, and is rapidly coming to the front; that of medical mycology. Many of the skin diseases of the tropics are due to infection with fungi, and recent articles by Lt.-Col. H. W. Acton, I.M.S., and his assistants, Dr. C. McGuire, Dr. Ganapati Panja and Dr. K. P. Bannerji, show how important this infection is in general medical practice in India. Cryptococcus infections are extremely prevalent in birds and animals, and have been reported in man from time to time. *Rhinosporidium seeberi* is essentially an Indian disease. *Sarcocystis* infection is possibly of fungoid origin. It is possible that the mysterious Rickettsia bodies which are responsible for typhus fever, for spotted fever of the Rocky Mountains, and for the seven-day fever of Japan are of fungoid nature. Granuloma inguinale has long been suspected to be of fungoid origin. Fungi—such as *Blastocystis hominis*—frequently parasitise the intestinal tract of man, where they seem to be non-pathogenic, but are especially associated with indigestion due to starchy food-stuffs.

There is one special fungoid infection of man, however, concerning which our ideas as to causation, classification and treatment are still in a state of chaos, viz., mycetoma infection (commonly referred to as "Madura foot," though it may affect the hands also). From time to time, severe cases of this infection are reported in our columns. Yet it is clear that cases are so infrequent that no one observer within his lifetime will see a sufficient number of cases thoroughly to work out the aetiology, pathology, and treatment of this disease. Hence the present appeal.

We have previously commented in these columns on the fine work which has been carried out in the Skin Out-patient Department of the Calcutta School of Tropical Medicine, financed by the generosity of the Indian Research Fund Association. And—in response to a request by Lt.-Col. H. W. Acton, I.M.S.—we now desire to broadcast an appeal for help in studying the problems of mycetoma infection. If workers all over India will collaborate in sending in material, clinical notes, information and photographs of cases, there is very little doubt that within the course of a few years sufficient information can be collected to render a standard account of this rather rare disease possible, and to indicate the best measures of prophylaxis and treatment.

Turning to the history of the disease, Madura foot, as it has hitherto been reported in India, it is stated to be common in the following areas:

Bombay Presidency; Larkana, Sukkur, and East Khandesh.
Madras Presidency; South Kanara, Guntur, South Arcot and Ramnad.
Mysore State; in South Kanara.
Hyderabad State, Deccan; Aurangabad.
Delhi Province.

It is stated to be rare in—

Bengal; where it occurs at Pabna.
Assam; the Garo Hills, Kamrup and Sibsagar are reported to be infected.

Bihar and Orissa; in the Santhal Parganas.
Burma; in Mandalay and Sandoway.
The Punjab; where it has been reported from Karnal, Gujrat and Shahpur.

The Central Provinces; reported from Yeotmal, Bhandara, Bilaspur and Jubbulpore.

The method of classification generally adopted is that of Chalmers and Archibald. This classification is followed by Brumpt, Langeron, Castellani and Chalmers and other workers in their manuals. They subdivide the mycetoma infections into two broad groups, as follows:—

(a) The actinomycoses. These are forms of mycetoma infection in which the grains are composed of fine, non-segmented mycelial filaments, in which the walls are usually not well-defined as apart from the contents, and in which chlamydo-spores are absent.

(b) The maduramycoses. In this type of infection the grains are composed of large, segmented mycelial filaments possessing well-defined walls and chlamydo-spores.

The actinomycoses are caused by organisms belonging to a genus which is usually termed the genus *Actinomyces*, though it is termed *Discomyces* by the French workers, and *Nocardia* by many British workers. These are organisms which grow in the form of a much branched mycelium, which may break up into segments that function as conidia. They are sometimes parasitic, and infect animals as well as man, the radiating threads showing prominent clubbed ends. Some are anaerobic. The following species have been isolated from cases of mycetoma infection in man:—

(i) *Actinomyces bovis* harz. Three cases in Brazil. The colour of the granules is not reported.

(ii) *Actinomyces asteroides*. From the Argentine, Europe and Brazil; the colour of the granules is not reported.

(iii) *Actinomyces convolutus*. From Khartoum; granules orange coloured.

(iv) *Actinomyces bahiensis*. From Brazil; granules yellow.

(v) *Actinomyces mexicans*; from Los Angeles; granules yellow.

(vi) *Actinomyces indicus*; from the Sudan; granules yellow.

(vii) *Actinomyces maduræ*; from Greece, Algiers, the Argentine and Cuba; granules white.

(viii) *Actinomyces somaliensis*; from Somaliland and the Sudan; granules yellow.

(ix) *Actinomyces yazbebi*; from Brazil; granules white.

(x) *Actinomyces pelleteri*; from Brazil, Egypt and India; granules red.

(xi) *Actinomyces verrucosus*; from Switzerland; granules white.

The above list will be sufficient to show the confusion which at present surrounds the whole subject, and one cannot help wondering whether the white, yellow, black and red strains are not possibly analogous to the different colour strains of *Tinea cruris*, and whether in fact they cannot be reduced to a common denominator on a suitable synthetic medium; whether they are not local varieties or sub-species of one and the same organism. Further, infections with *Sterigmatocystis*, *Aspergillus*, and other species are common. Are these secondary contaminating fungi, or are they pathogenic? The point remains to be worked out. Is Madura foot a clinical entity caused by several different species of fungi; or is it due to a certain genus of fungus which causes localised periostitis?

Castellani divides the actinomycoses into the following genera: (i) *Nocardia*, (ii) *Cohni-streptothrix*. The fungi of genus *Nocardia* are stated to grow best under aerobic conditions, are usually cultivated very readily, and produce arthrospores. The genus *Cohni-streptothrix* Pinoy, 1911, grows best anaerobically, is difficult to cultivate, and does not produce arthrospores. He recognises black, white or yellow, and red varieties of actinomycosis infection, with granules of corresponding colour, and then differentiates different species within these groups. The white or yellow variety of actinomycosis may thus be caused by an organism of either the *Nocardia* or *Cohni-streptothrix* groups. The red variety is due only to *Nocardia indica*.

Turning to the maduramycoses, here the grains show large, segmented mycelial filaments, possessing well-defined walls, and usually chlamydospores. Seventeen different species, belonging to different classes and genera, have been reported as causative agents. They have been classified as follows:—

Fungi imperfecta.

- Genus *Madurella*; 6 species.
- Genus *Indiella*; 3 species.
- Genus *Glenospora*; 2 species.
- Genus *Scedosporium*; 2 species.

Ascomycetes.

- Genus *Allescheria*; 1 species.
- Genus *Aspergillus*; 1 species.
- Genus *Sterigmatocystis*; 1 species.
- Genus *Penicillium*; 1 species.

Castellani again divides the maduramycoses into black, white or yellow, and red varieties, with grains of corresponding colour. According to its geographical distribution, he sub-divides the black variety into European, African, Asian and American strains. This classification seems needlessly complicated; especially since Nicolle and Pinoy have experimentally produced both black and white grains by injecting *Sterigmatocystis nidulans* into pigeons' feet. Castellani also divides the white or yellow maduramycoses into European, African and Asiatic strains.

As far as can be observed from the literature, black maduramycosis may be produced by the

different genera *Aspergillus*, *Madurella*, *Sterigmatocystis* and *Glenospora*.

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It is obvious, from the above outline, that the whole subject of mycetoma infection in man (as also in animals) is at present in a state of confusion. Sir Aldo Castellani deserves the utmost credit for his pioneer work on the subject, which now merits fuller attention and study.

The material asked for is (a) cultures, and (b) infected tissues for section.

In cultivating, the greatest care should be taken to take cultures only from sinuses which have not been opened up previously, since open sinuses are very apt to become secondarily contaminated. If the pustule is open, the grains removed should be well washed in saline, then heated in saline at 56°C. for ten minutes to kill secondary, contaminating bacteria, and two grains planted on each tube of culture medium. At least three such cultures should be taken from each case. The media used should be either Sabouraud's Maltose Agar, which has the following composition:—

- Maltose 4 per cent.
- Peptone (Chassing) 1 per cent.
- Agar 2.5 per cent.
- Distilled water 100 c.c.

With a pH of 6; or Whey Agar. The method of preparation of this is as follows:—

- Whey 250 c.c.
- Peptone 5 grms.
- Saccharose 7.5 grms.
- Urea 3 grms.
- Agar 2.5 grms.
- Distilled water 250 c.c.
- pH. 7.4

Whenever possible, grains should be taken from unopened pustules. The skin over the unopened pustule is first washed with absolute alcohol; then the pustule is punctured and the grains squeezed out, and after washing in saline two grains are planted on each tube of medium. This medium can be obtained from the Calcutta School of Tropical Medicine.

Three or four expressed grains should also be sent in normal saline in order to study whether actinomycetes or maduramycetes infection is present. Tissues for section should be sent in a solution of formalin, 5 per cent. in normal saline, and the sections should be cut very thin, not more than 4 to 5 mm., if possible.

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This is the first time that we have utilized these columns in an appeal for material; but we hope that it will not be the last. The problem in question is a most interesting one: it can only be solved by the co-operation of a number of willing workers. What one man cannot hope to carry out in a single lifetime, may readily be carried out by team work by a number of helpers. We would like to express our gratitude to those who have responded to Colonel Acton's first appeal, which was privately circulated; but the problem is so big, that we invite the co-operation

of the whole medical profession in India. It only remains to add that cultures or material, case notes, photographs, etc., should be sent to Lt.-Col. H. W. Acton, I.M.S., Director, Calcutta School of Tropical Medicine, Central Avenue, Calcutta.

CORRIGENDA.

Page 282, Col. 2, The Prescriber's Companion for Price Rs. 15-12, read Price Rs. 5-12.

Page 370, the third author should be B. N. Banerji and not B. N. Bagchi.

SPECIAL ARTICLE.

THE TREATMENT OF INTÉSTINAL AMÉBIASIS: (AN ANALYSIS OF RESULTS, AND A REVIEW OF THE LITERATURE.)

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SINCE the introduction of emetine into medical practice by Sir Leonard Rogers (1912)—following the lead given by Bardsley (1829) of Manchester, who had used the drug generally in dysentery, Tull Walsh (1891), who used it in the treatment of dysentery in Calcutta, but reported that it did not give better results than other drugs, and Vedder (1911), who tested its action on free-living amœbæ, and suggested its therapeutic use—the treatment of acute and sub-acute amœbic dysentery has become a relatively simple matter. The patient is put to bed and daily injections of emetine are given. The result in almost every case is very rapid clinical improvement; indeed, there is hardly any medicinal line of treatment which gives more immediately gratifying results; on the day of admission the patient may be in real misery; twenty-four hours later he may be in comparative comfort. On the other hand, there is ample evidence to show that, whilst this line of treatment effects a clinical cure in the vast majority of patients, it fails to eradicate the infection in some 70 per cent. or more of infected persons, and that the "cured" patient is all too liable to suffer from one or more relapses at a later period.

But there is another condition due to infection of the mucosa of the colon with *Entamœba histolytica*, and that is *chronic intestinal amœbiasis*, and the successful treatment of this condition is one of the most difficult and pressing problems in the practice of medicine in the tropics. There are so many vaunted "cures" for this condition on the market to-day, that the medical practitioner is positively embarrassed in his attempt at choice. Yet, the efficacy of any or all of them, seems very much open to question. We shall discuss the pathology of the carrier state later in this memoir, but we may here state that the trend of evidence of recent years goes to show that infection with *E. histolytica* may be of any grade of severity; it is possible that in some persons the amœba lives for only a short period in the lumen of the gut, causing no symptoms, and that the infection is speedily got rid of. In the great majority of cases, however, the parasite lives in and at the expense of the mucous membrane of the colon, and the patient's symptoms may vary from a mild carrier condition which is nearly (but not quite) symptomless, to a state of affairs in which he suffers from frequent or incessant relapses, and in which he may be tortured with dysentery for years on end.

Since the opening in 1921, of the Carmichael Hospital for Tropical Diseases (116 beds), attached to the Calcutta School of Tropical Medicine, certain routine tests have been applied to the great majority of all persons admitted; no matter what the disease from which they were suffering. Thus, thin and thick blood films are examined for blood-inhabiting protozoa; thick blood films are taken at night and examined for filarial infection; the Widal and the Wassermann reactions are performed; the total and differential leucocyte counts are observed; the agglutination reaction of the serum against the bacilli of Shiga and of Flexner is tested; and often a routine blood culture, both in glucose broth for blood-inhabiting bacteria and in N. N. N. medium for *Leishmania donovani* infection, is taken. The stools of every newly admitted patient are examined (a) in the Protozoology Department for intestinal protozoa; (b) in the Bacteriological Department for pathogenic bacteria; and (c) in the Hookworm Research Department for helminthic infections. These routine tests afford a means of making a general assessment of the patient's state of health, whilst very frequently secondary infections—for which the patient has not been primarily admitted—are discovered.

The examination of the stools in the Protozoology Department shows a general incidence of infection with *E. histolytica* of about 14 per cent. Thus in 1927, the stools of 1,030 persons were examined, once only, and *E. histolytica* infection was found in 145;