Original Articles.

KERATOLYSIS PLANTARE SULCATUM, A LESION DUE TO AN ACTINOMYCOTIC FUNGUS.

By HUGH W. ACTON,

LIEUTENANT-COLONEL, I.M.S.,

Director, Calcutta School of Tropical Medicine and Hygiene,

and

C. McGUIRE, D.T.M.,

Under the Indian Research Fund Association.

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THIS lesion was described by Castellani as "a peculiar pitting of the hands and feet," and in the 3rd edition of his text-book, Castellani and Chalmers (1920) on page 2258, he gives it the name of keratoma plantare sulcatum. At first the lesion was considered to be a manifestation of yaws. Castellani (1922) states that framboesia may be a causal factor in certain cases, and notes that mercury and potassium iodide have no effect on the malady, and hence it is not of syphilitic origin. Gutierrez (1923) thought it was a manifestation of yaws, and describes it under the name of keratosis palmaris et plantaris, and again in 1925 under the name of keratodermia palmaris and plantaris sulcatum. In 1917 Chalmers and Kamar described a non-follicular localised hyperkeratosis of the palms without acanthosis or markedly dilated papillary vessels under the name of keratodermia punctata, and Castellani (1920) states that he described this lesion before Chalmers as keratodermia cribrata. Chalmers' report is based on a single case in a barber woman, who was apparently healthy and had not suffered from syphilis or taken arsenic internally. These two different lesions, keratoma plantare sulcatum (Castellani) and keratodermia cribrata (Castellani), have been very much confused by many workers with late manifestations of yaws. The former lesion is caused by an actinomycotic fungus, and the latter is a late manifestation of syphilis, for we have seen a large number of cases, and the Wassermann reaction has always been markedly positive in them. In fact, we regard keratodermia cribrata as a pathognomonic lesion of syphilis. About its relationship to yaws, we are not in a position to judge, as this disease is not seen in Bengal. The term keratoma given to the lesions on the feet is a misnomer; what actually happens is that the horny layer is dissolved or eroded by the fungus into deep pits, these coalesce and form furrows, hence the name keratolysis plantare sulcatum which we propose to give it, as in our opinion it is more appropriate. We believe that the lesion is only one of the clinical manifestations of this fungus, but the point will be dealt with more fully in a subsequent paper, when we will be able to produce more evidence to support this view.

Synonyms.—In Bengal the condition is generally known as *chaluni*, a sieve, owing to the pitted appearance of the soles. Sometimes it is spoken of as *haja*, which means sodden, a name also applied to intertrigo of the toes, i.e., mango toe.

Ætiology.—The lesion was first described by Castellani from Ceylon, and later from Macedonia; it has also been seen in the Philippine Islands. In Bengal, it is extremely common during the monsoon months, especially in persons walking bare-footed and whose occupation necessitates walking on damp earth, e.g., rice cultivators, servant girls, etc. The villagers think that it is caused by walking on damp earth contaminated with animal fæces, e.g., of horses, cattle, etc. We have twice seen the lesions in Europeans; they were both chief officers on coastal steamships, who were admitted in our hospital suffering from tinea violaceum and tinea cruris infections respectively. As a rule, these people never come to hospital for the disease, as the only symptom it causes is a certain amount of tenderness of the feet after standing or walking on them for a long time. In Bengal yaws does not occur, and hence cannot play any part in the causation of the lesions; neither does syphilis, as the cases admitted into hospital have consistently given a negative Wassermann test.

Symptoms and signs.—The lesion known as keratolysis plantare sulcatum is seen mainly on the feet and attacks the thickened epidermis of the heel and tread of the foot, see Plate I, fig. 1; more rarely does it attack the thick skin of the palm, see Plate II, fig. 3.

The lesion commences as a small pit which gradually deepens, the edges being irregular and dark in colour. These pits or depressions coalesce and form irregular furrows, giving rise to an appearance like the surface of a moderately coarse sponge. After washing the feet well, the thick horny epithelium of the heel and tread is yellow in colour and pitted all over with depressions, see Plate I, fig. 1. The sides of the pits are dark in colour, and at the base of the furrows the white or pinkish colour of the prickle cell layer is seen. The condition is not one of hyperkeratosis, but a lysis of the thickened epidermis by an actinomycotic fungus. The lesions on the hands are very rare, compared with keratodermia cribrata, (see Plates II and III, figs. 3 and 4), and they have the same character as seen on the feet, but less marked, and the pits do not usually coalesce to form furrows. In keratolysis plantare sulcatum, there is never any localised hyperkeratosis as in keratodermia cribrata, where these horny plugs can be lifted up, leaving small pits. Although the patients usually complain of some tenderness of the feet, when standing or walking about on them for a

long time, there is no sign of any local inflammation. We have found the same fungus microscopically in cases of intertrigo between the toes and paronychia, see Plate II, fig. 4. Whether it is the same fungus that gives rise to all these different conditions remains to be proved by us.

The causation of these lesions.—For the last three years, as opportunities have arisen, we examined the first seventeen cases of this disease thoroughly by making cultures on various media and using numerous inseminations of the scales on each medium. We were able to grow a black Aspergillus in 12 of these cases, and a green coloured one in three cases, giving a result of 15 positive cultures for Aspergillus in 17 cases. At that time, we suspected that this Aspergillus was the cause of the lesion, owing to the black colour around the sides of the pits.

In scrapings taken from the side of these pits and cleared by 40 per cent. caustic potash, we were unable to find any hyphæ of the Aspergillus fungus. This was rather a blow against the Aspergillus theory, so we thought we would be able to prove it by studying the keratolytic action of the fungus on the epidermis of the heel. From post-mortem material the skin of the heel was first sterilised by alcohol, etc., then removed aseptically, placed on plaster of Paris platforms kept moist by water in a sterile Petri dish, and inseminated with this Aspergillus. The Aspergillus colony spread all over the skin of the heel without liquefying the epidermis. So we had to abandon this view. Later on we found that if we attempted to make cultures after allowing these patients to walk from the hospital to our laboratory, we invariably grew Aspergilli from their feet, as this fungus is always present in the dust of floors, etc., during the monsoon months. Last year, we realised the danger of using the caustic potash method for studying any fungi invading the glabrous skin, as it always destroys the more friable fungi like the Malassezia, Actinomyces, etc., besides producing numerous artifacts, which simulate hyphæ. We therefore no longer use it for this purpose of study. The junior author found that by using a modification of Ponder's stain by increasing the strength of the toluidin blue from 0.02 per cent. to 1 per cent. and dissolving it in 2 c.c. glacial acetic acid, 4 c.c. absolute alcohol and 93 c.c. of water, the thick bits of epidermis could be cleared in glycerine afterwards. The fungi were stained at once without any damage to the hyphæ, and the glycerine cleared the epithelial scales so that one could see through fairly thick pieces of tissue. The specimen can be examined in the wet stage with or without glycerine, a coverslip being put on if the slide has to be examined by the high power lens. These cases were studied after staining by McGuire's method, using the one-twelfth objective, and in all the eight cases recently seen we were able to find fine segmented hyphæ of an actinomycotic fungus in the scales. This method has enabled us to study more exactly these fungi as they grow in the glabrous skin as well as in cultures, and it should be the method of choice in all work on fungi invading the glabrous skin.

The mycology of the fungus.—Microscopically when stained by McGuire's method the fungus is seen in the scales as very fine segmented hyphæ; these are apt to break up into individual segments, at first sight resembling bacteria, see Plate I, fig. 2. This mistake is easily rectified as the individual segments are short stout forms almost as broad as they are long. In cultures, the hyphæ are seen as a non-segmented branching mycelium, the ends of the hyphæ carrying numerous slightly stained oval conidia; see Plate I, fig. 3. In the ordinary stained specimen, i.e., fixation by heat, and staining with Manson's methylene blue, conidia are not usually found, and the mycelium consists of a network of non-segmented branching hyphæ.

These morphological appearances in cultures are exactly similar to the type culture we possess of *Actinomyces bovis* from the American Type Culture Collection.

Cultivation.—Out of the last eight microscopically positive cases, we have been able to cultivate an actinomycotic fungus twice. The reason of our failure has been due to the growth of certain spore-forming bacilli and an Aspergillus fungus. Certain precautions must be taken and the patient's foot should be thoroughly scrubbed with soap and warm water, and then washed well with sterile saline, in order to get rid of all extraneous dirt from the feet. The cultures should be made before the patient leaves his bed, after scrubbing his feet. The edges of the pit are first scraped with a fine sharp scalpel, in order to remove the black stain of the wall. Small pieces are then dug out after washing thoroughly in sterile saline and planted on whey agar medium, i.e., a medium which the senior author has used since 1906 and of the following composition, whey, 2 per cent. agar, 1 per cent. peptone, 0.2 per cent. urea and 4 per cent. saccharose. About 50 inseminations are required as any contamination prevents the growth of the fungus, for the growth is very slow, about 10—15 days must elapse before visible colonies appear on the surface of the media.

The fungus grows best under aerobic conditions, and at blood heat, 37.5°C. Within 3 to 4 days on secondary cultures visible colonies appear on the different media. The characters of the colonies on different media are as follows:—

In ordinary peptone broth, a flocculent white precipitate forms which falls to the bottom.

In peptone water, puff ball white colonies grow at the bottom and sides, the few surface colonies kept up by capillary attraction are red in colour, Plate I, fig. 4, No. 6.

Sabouraud's media, black or red limpet shaped colonies on the surface with deep roots into the media, Plate I, fig. 4, Nos. 1 and 2.

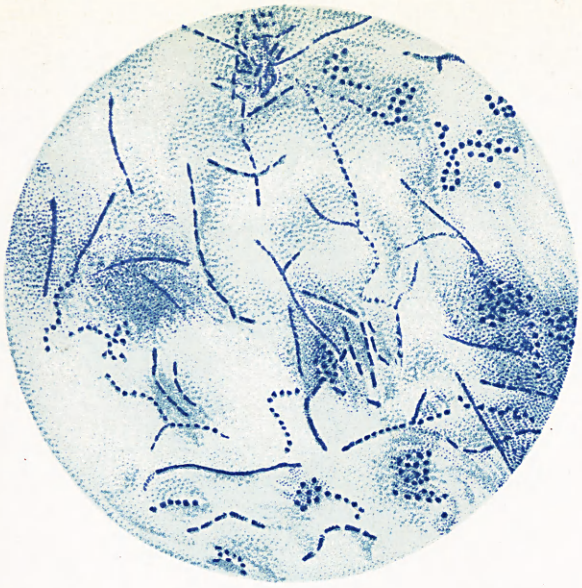

Fig. 2.—Objective 1|12th, ocular 10. Scrapings of the scales from the sides of the pits, and stained by McGuire's method. Note the segmented and non-segmented hyphæ. The segmented hyphæ look rather like chains of bacteria.

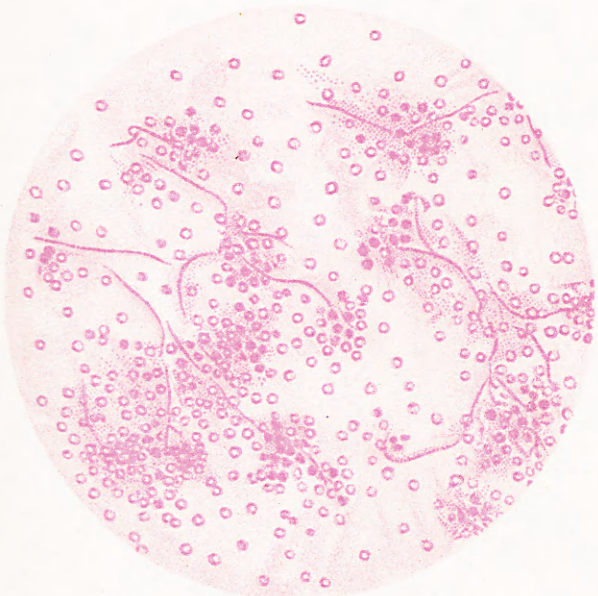

Fig. 3.—Objective 1|12th, ocular 10. Culture stained by McGuire's method. Note the non-segmented hyphæ and the numerous lighter stained conidia.

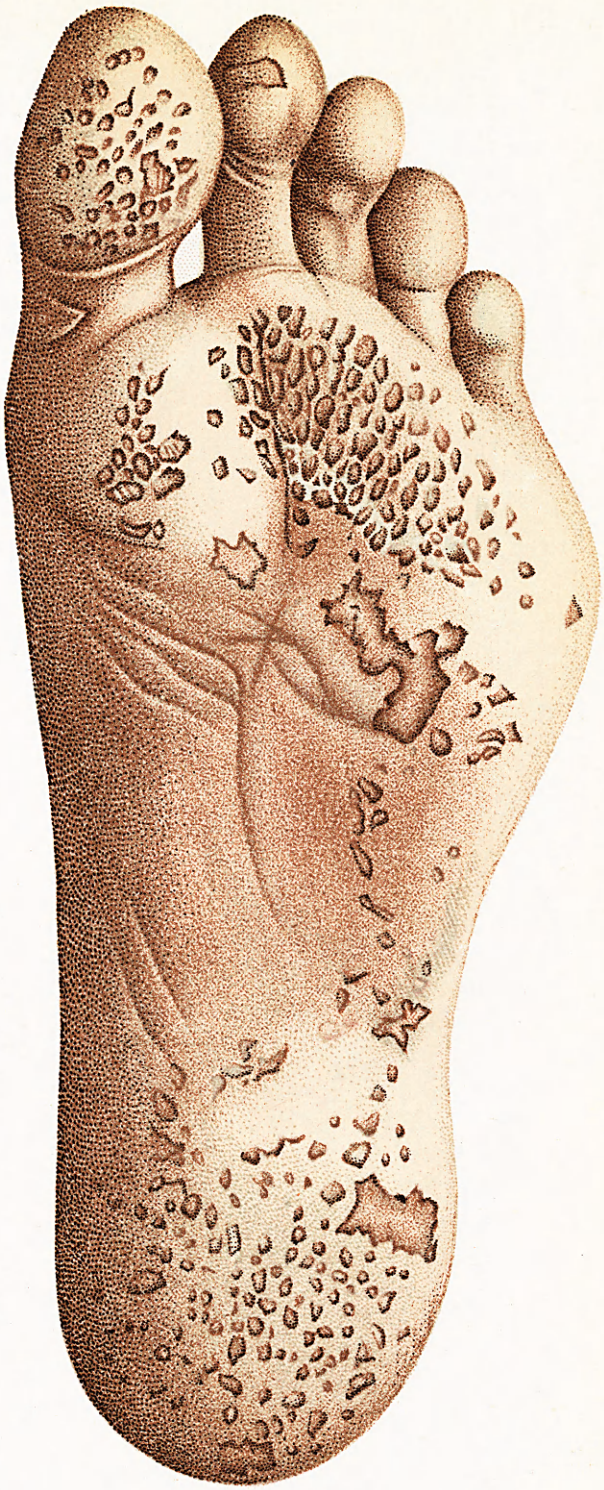

Fig. 1.—The appearance of the lesion known as keratolysis plantare sulcatum. Note the pit-like depression with darker staining of the sides.

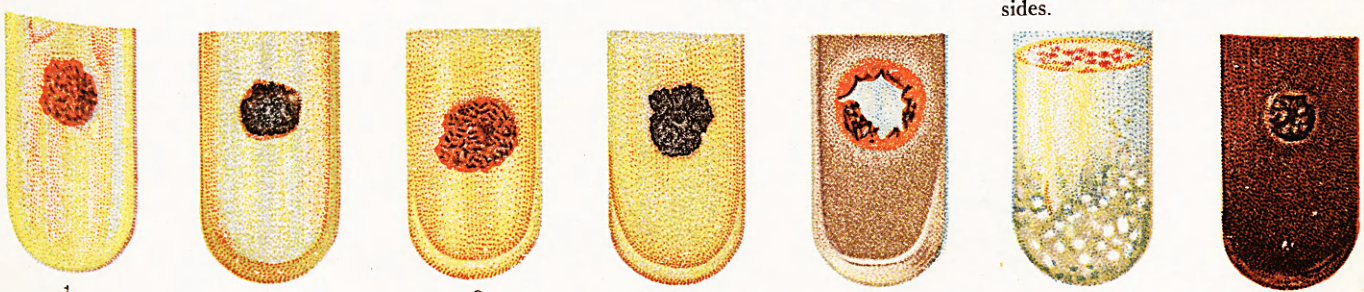

Fig. 4.—The cultural appearances on the different media. Nos. 1 and 2 Sabouraud's test media; note red and black limpet-shaped growths. Nos. 3 and 4 on whey agar, similar appearance, but more profuse growth. No. 5 coagulated serum. Note degree of liquefaction. No. 6 on peptone water. The colonies at the bottom form white puff balls and the surface colonies red. No. 7 on blood agar, black growth surrounded by a zone of hæmolysis.

Whey agar, red or black limpet shaped surface growth with deep roots, see Plate I, fig. 4, Nos. 3 and 4.

Ordinary agar, limpet shaped surface growth with deep roots black or red.

Coagulated serum.—Marked pit-like liquefaction with a small black growth at the bottom of the pit, see Plate I, fig. 4, No. 5.

Blood agar.—Black limpet shaped surface colony, with a small clear hæmolysed zone round the colonies, Plate I, fig. 4, No. 7.

The cultural characters are exactly similar to the red and black fungi which we have obtained from cases of mycetoma of the foot (Madura foot).

The value of colour as a character to identify the species of these fungi.

We have been taught that in the clinical differentiation of these fungi, mycetomas may be classified according to the colour of their granules or growths, i.e., black, red and white, whilst the actinomyces have yellow or white granules, and very rarely red ones. Now it is obvious that there are no such colours as black or white. The former only indicates the depth of the primary colours, thus a deep red which may be so deep that it is visualised as black, and when less deep as a red, whilst when no pigment is produced the growth is achromatic or white. There are three primary colours, red, yellow, blue, and the mixtures of these give the various secondary colours, viz., orange, green, violet. So that colour value of the fungi as a differentiating character of a species can only be of value when primary colours are seen, i.e., red, yellow and blue. Thus we can have a red Mycetoma, or a yellow Actinomyces as a colour character of value to identify species. Black and white only indicate when the conditions for pigment production are favourable or totally unsuitable; compare the growth on blood agar and on peptone water, see Plate I, fig. 4, Nos. 6 and 7. The yellow colour of the agar combines with a light red to produce orange or lemon colours, as these are secondary colours. Blue with yellow produces green as is seen during the growth of the *Pseudomonas pyocyaneus.* As far as we know at present, about the genus *Actinomyces* we can only differentiate those colour values that are sufficiently characteristic to enable us to identify a species, viz.:—

(*a*) Those fungi that are white in colour and never produce pigment on any media used in the cultivation of these fungi.

(*b*) Those that are red or black in colour, in one or more of these media.

(*c*) Those that are yellow to lemon in colour, in one or more of these media.

When the depth of the red or blue passes into the invisible end of the visual spectrum of light, the colour must be black. As far as we know no pathological Actinomyces produces a blue pigment. Secondary colours such as orange, lemon are of no value in differentiating species.

Differential diagnosis.

This has been simplified by our clinical description of these lesions, and we can confirm the diagnosis by microscopical examinations by using McGuire's stain, when the fungi can be seen in the scales. In cases of hyperkeratosis no fungi are found, and the nuclei of the horny cells are large, stain well, and have a granular appearance.

In keratolysis plantare sulcatum, the lesions are seen commonly on the thick skin of the tread of the feet, forming pits or furrows with darker sides and are due to a lysis of the horny cells. The lesions are rare on the hands. There is no localised or generalised hyperkeratosis, whilst scrapings made from the sides and stained by McGuire's method show segmented hyphæ forming the mycelium. The lesions appear during the monsoon months and disappear in the winter. There is no evidence that syphilis or yaws is a causative factor.

There are various hyperkeratoses, localised or generalised, of the palms and soles that have been mistaken for this lesion.

(1) Symmetrical hyperkeratosis of the palms and soles, known also as tylosis or mal de Meleda. The hyperkeratosis involves the whole palm and sole with immense thickening of the horny layer, and accentuating most of the furrows on the hand, so that the hands and feet cannot be extended fully, see Plate III, fig. 1.

(2) Keratodermia of the hands or feet with moderate hyperkeratosis and deep fissuring. Most of these cases are associated with special occupations; thus cultivators have lesions on the feet, i.e., cracked heels; and betel sellers, etc., on the palms. Some of these cases are due to the hyperkeratosis of syphilis, and others to ringworm, see Plate III, figs. 2 and 3.

(3) Localised plaques of keratodermia on the hands and feet. Some of these are due to ringworm and others to an Actinomyces. In many text-books they have been described as gouty eczema, etc. The fungi can be found by McGuire's method, see Plate II, fig. 2.

(4) Keratodermia cribrata (Castellani) or keratodermia punctata (Chalmers) forming localised areas of hyperkeratosis. These can be removed or fall out, leaving shallow pits as if a split seed has been lifted out of the epidermis. In India the condition is always due to syphilis, but it may also be due to yaws according to Gutierrez (1923 and 1925) see Plate III, fig. 4.

There should be no difficulty in diagnosing these different conditions of hyperkeratosis from keratolysis of the horny layer of the palms and soles of the feet. Moreover the fungus can readily be demonstrated in these cases of keratolysis.

Treatment.—In hospital, the condition can easily be cured by painting the lesion over with 5 per cent. formalin, as the patients have the opportunity to keep the soles of the feet dry for they are not walking about on damp soil. Prevention is possible by painting the thick skin of

the soles of the feet with 5 per cent. formalin as the fungus is very slow in growth. This could be done once a week during the monsoon months, i.e., from July to the beginning of October.

Discussion.

Although the title of this paper deals with a single clinical lesion called keratolysis plantare sulcatum (Castellani), a lesion very common in the rural districts of Bengal, this study of its causative agent is going to yield very valuable results in the classification of the Actinomyces. The confusion that exists in the literature of Madura-mycosis is too awful for words; the following genera have been cultivated:—*Aspergillus, Sterigmatocystis, Glenospora, Madurella, Indiella,* etc. Many have been cultivated from septic sinuses, as we did when cultivating *Aspergillus nigra* from cases of keratolysis plantare sulcatum. These fungi have been further subdivided according to the colour of the granules, black, red or white. Furthermore, slight variations in the colour and character of the growth have been considered sufficient to subdivide the genus into two separate species. Often the growth of a fungus has been accepted as proof that it is the causative organism, without testing its pathogenicity in animals. We have been able to find an Actinomyces fungus in such different lesions as keratolysis plantare sulcatum, onychia of the nail, intertrigo, hyperkeratosis of the nail bed and plaque-like lesions of the hands, similar in appearance to each other in microscopical examination by McGuire's method. Whilst the microscopical appearances of the cultures from keratolysis plantare sulcatum are identical with the *Actinomyces bovis* type culture, the culture appearances of this fungus are very like those obtained from Madura foot. The question arises whether the same fungus can produce mycetoma on deep inoculation, and keratolysis plantare sulcatum when the horny layer is macerated by dampness. Mycetoma in India is correlated with two factors, a dry sandy soil and the presence of babul thorns (*Acacia babuli*). In Bengal the soil is water-logged and suitable for rice cultivation, whilst deep injuries of the foot are not common and rarely go further than the prickle cell layer on the thick skin of the tread of the foot. The present classification of the Actinomyces adopted by Bergey is very unsatisfactory. He divides them under three heads, (*a*) pathogenic to man, (*b*) plant parasites, and (*c*) saprophytes. Now we know that the *Bacillus pestis,* causing rat plague, can be transmitted to man as bubonic plague, whilst the saprophytic *Staphylococcus albus* can produce superficial stitch abscesses. The pathogenic Actinomyces are divided by Bergey into those that produce club-shaped ends in the tissue and those that do not do so, as well as by their growth on various media, and their pathogenicity for animals. We would suggest that the following tests should be adopted for their study.

(A) Morphology, *appearance in the tissue* as segmented or non-segmented hyphæ. The unsegmented hyphæ indicate that conditions are favourable for growth and the mycelium is young, whilst segmentation indicates age or unfavourability.

In cultures.—A study of young and old cultures on different media. Uusually one finds unsegmented hyphæ, branching, and later on conidia. The latter may be absent if the medium is not favourable for conidia production, and difficult to see if not stained properly.

(B) Staining reactions. Examination of the fungus in the tissue as well as in culture media by McGuire's method, and also for acid-fast rods. As these are higher fixed plants, there is no need to study whether they are motile or non-motile.

(C) Cultural characters. The general characters should be first considered, whether these fungi are anaerobes, facultative anaerobes, or strict aerobes, and whether they grow best at blood heat or at room temperature. Their growth on the different media should next be studied.

(1) In fluid media, such as peptone water, ordinary peptone broth and litmus peptone broth, some fungi can form pigment from litmus, whereas they fail to do so in ordinary liquid media.

(2) On solid media—agar slopes, potato, acid and alkaline, and carrot.

(3) Solid media containing sugars—whey agar containing saccharose, Sabouraud's test medium of glucose and maltose. Most of the fungi-forming pigment do so on one or other of these media.

(4) Lytic action. The Actinomyces have a lytic action on most proteids, etc. This is of more importance than the reduction of sugars or the formation of pigment. Thus the true Actinomyces clinically do not rarefy bone or dissolve the horny layer of the skin, whilst the Maduromycosis apparently do so, hence it is necessary to study their action as regards their different enzyme action, i.e.—

(*i*) Proteolysis on gelatin, milk, egg and serum.

(*ii*) Amylolytic action on starch.

(*iii*) Keratolytic action on the horny layer of the epidermis.

(*iv*) The rarefaction of bone in culture.

(D) The pathogenic effects in animals, taking into consideration these various methods of infection on the skin surface and in the deeper tissues. Moreover we do not know whether these fungi are only infective in certain stages of their growth, i.e., by conidia, hyphæ, etc.

Moreoyer Pallacci and Nannizzi (1926 and 1927) have shown that for certain ringworm fungi, asci and ascospores are formed when the fungus grows at room temperature on hair, feather, leather or damp soil. In the same way, these fungi will have to be studied on media

PLATE II.

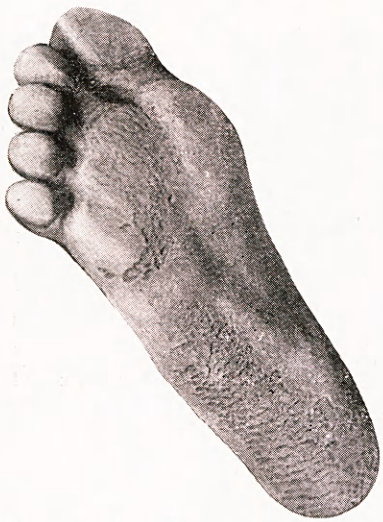

Fig. 1.—A very marked case of keratolysis plantare sulcatum. Notice the furrows on the tread of the foot.

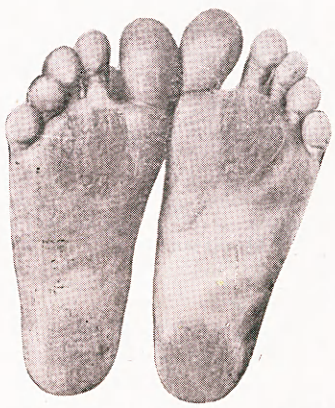

Fig. 2.—A plaque type of hyperkeratosis that showed an actinomycotic-like fungus.

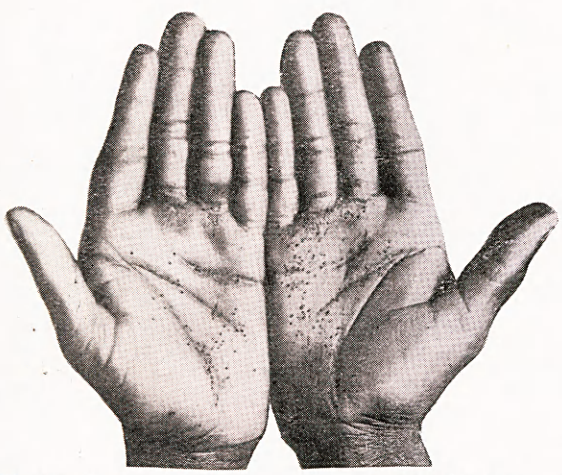

Fig. 3.—Keratolysis palmare. There are no furrows, and notice the dark staining at the sides of the pits.

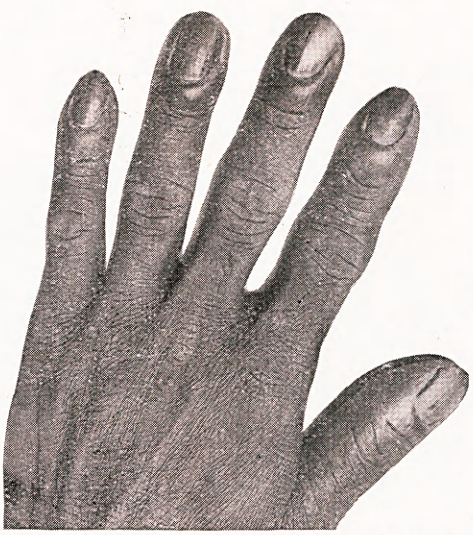

Fig. 4.—Paronychia of the nails produced by a similar fungus.

PLATE III.

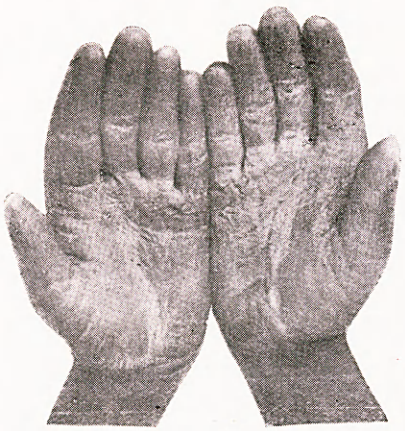

Fig. 1.—Symmetrical hyperkeratosis of the hands and feet. Note the thickening of the skin and the accentuation of the main furrows.

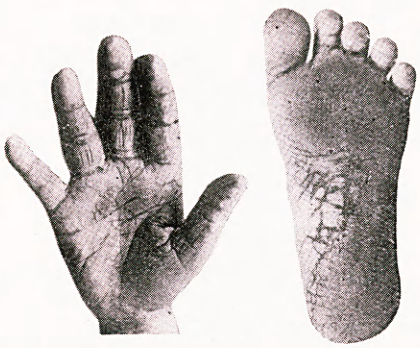

Fig. 2.—Hyperkeratosis of the hands and feet. Secondary to ringworm and associated with certain occupations—betel sellers, cultivators, etc.

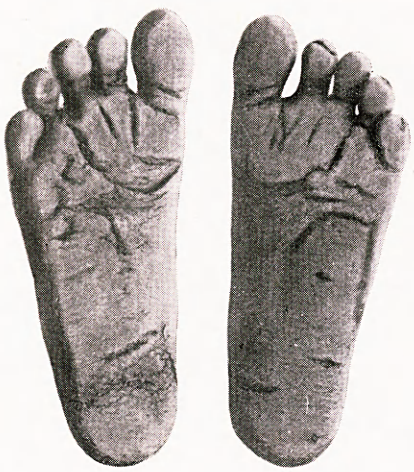

Fig. 3.—Syphilitic hyperkeratosis of the feet. Note the numerous deep cracks extending down to the prickle cell layer.

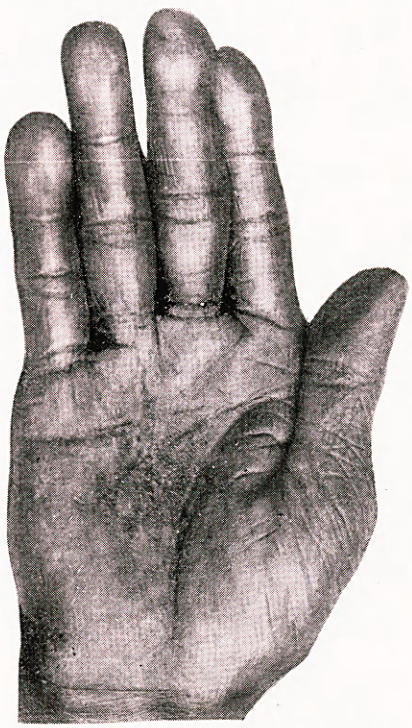

Fig. 4.—Keratodermia cribrata, a late syphilitic manifestation. Note the pit-like depressions in the centre of the palms.

other than those commonly used in the laboratory, such as thorns, etc. There is a good deal of work to be done before we can clear up the exact clinical relationship of such diverse lesions, as mycetoma, actinomycosis, keratolysis plantare sulcatum, some cases of paronychia, intertrigo, and plaque-like areas of hyperkeratosis on the palms and soles. We would be very grateful for any cultures of these fungi obtained from pathological lesions.

CONCLUSIONS.

(1) The lesion known as keratoma plantare sulcatum (Castellani) is not one of the hyperkeratosis, but is caused by a lysis of the horny layer of the thickened epidermis of the soles of the feet, and more rarely of the palms of the hands.

(2) The name keratolysis plantare sulcatum is a better one for describing the lesion.

(3) The lesion is not a manifestation of syphilis or yaws, but is due to an Actinomyces.

(4) In eight cases, examined by McGuire's method, we have found the fungus in all of them.

(5) We have obtained successful cultures in two of these cases.

(6) Microscopically, the cultures resemble the *Actinomyces bovis* of the American Type Culture Collection.

(7) The limpet shaped growth on the surface of the different media used, with deep penetrating roots, which may be black or red resembles those we have grown from cases of Madura foot.

(8) Microscopically we have found similar fungi in certain cases of intertrigo, paronychia and plaque-like hyperkeratosis on the palms and soles.

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ON RHEUMATIC INFECTION AS A CAUSE OF MITRAL STENOSIS AMONGST YOUNG INDIANS.

By H. STOTT, M.D., M.R.C.P.,
LIEUTENANT-COLONEL, I.M.S.,
Professor of Pathology, King George's Medical College, and Physician to King George Hospital, Lucknow.

DOES acute rheumatic arthritis affect Indians? Is unrecognized subacute rheumatic infection in childhood responsible for the mitral stenosis and chronic congestive heart failure of young Indian adults?

My interest in these questions was first aroused by observing a series of some 20 cases of chronic heart failure in young Indian males, mostly between 12 and 18 years of age, in the medical wards of King George's Medical College Hospital, Lucknow, during the past seven years. They were the victims of congested heart failure following progressive stenosis of the mitral valve. What was the cause of this chronic mitral fibrosis? Was it an evidence of subacute rheumatic infection during childhood? Before this problem could be decided, the question as to whether rheumatic fever exists amongst Indians at all required consideration.

Former views.—The impression formerly held was that Indians were not susceptible to rheumatic fever. Authorities who had examined the cause of chronic valvular disease amongst young Indian adults had concluded that the chronic valvular disease affecting them was a sequel of preceding pneumococcal or streptococcal inflammation. Moreover it was an impression amongst those who had given a thought to the world distribution of rheumatic fever that rheumatic infection would not, in general, exist in such warm climates as in India, Africa, and especially in Egypt. So far as was then known it was confined mainly to such cold and damp climates as are typically experienced especially during the autumn and also during the spring of the British Isles—and of the coast line of North Western Europe.

But acute articular rheumatic fever does affect young Indian adults. I use the word "articular" because an acute febrile infection with multiple hot red swollen joints, exquisitely painful, and affected in rapid sequence, in a young adult, in whom other causes of acute synovitis have been excluded, and when the infection has often followed exposure to cold and damp and has responded to rest and salicylates, forms a clinical syndrome the significance of which is quite clear. I have in mind three such cases in young Indian adults where such a pathognomonic picture was typical. Moreover one of these cases was observed in hospital to develop rheumatic pericarditis and another rheumatic mitral endocarditis. In one case the patient had been soaked in the monsoon rain and had slept on the sodden earth throughout a night preceding his attack. I have seen further cases where a diagnosis of acute articular rheumatic fever was justified, but in these three cases there could be no dispute as to the undoubted evidence they afforded of the existence of acute articular rheumatic infection in young Indian adults. Lieut.-Col. Sandes, I.M.S., Physician to the Medical College Hospital, Calcutta, tells me he frequently recognizes acute rheumatic infection in Indians in his wards. The answer to our first problem is therefore that acute arthritic rheumatic infection does attack young Indian adults.