THE ETIOLOGY AND TREATMENT OF ERYTHRASMA*

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Erythrasma is much more common that had been supposed. Twenty-two per cent of 107 subjects selected at random showed evidence of the infection in their toe webs (Fig. 1). Mild, subclinical forms of the classical genito-crural type are frequently missed and the generalized form, though rarely encountered in temperate climates, is seen fairly often in hot and humid regions.

We have recently found evidence to suggest that erythrasma is of bacterial origin and that it responds to systemic treatment with certain antibacterial antibiotics.

HISTORICAL

The condition was first described in 1859 by Burchardt (1) who suggested that the delicate filaments and numerous granules found in the scales were of fungal origin and were the cause of the disease. The term erythrasma was coined in 1862 by von Bärensprung (2), Burchardt's teacher, who named the causative organism *Microsporum minutissimum.*

Köbner (3) (1884) succeeded in reproducing the disease for the first time in 1866, by applying to the skin of one of his pupils epidermal scales affected by erythrasma. The rare reports of cultural isolation of the causative organism have not been confirmed. The numerous names under which the causative organism of erythrasma has appeared in the literature include *Microsporum minutissimum*, *Nocardia minutissima*, *Sporotrichum minutissimum*, *Microsporoides minutissimus*, *Oospora minutissima*, *Actinomyces minutissimus*, *Leptothrix epidermidis*, *Discomyces minutissimus* and *Microsporum gracile.*

In discussing the etiological factors, Poehlmann (4) (1928) considered, in addition to local factors such as site, humidity and bodily secretions, also individual predisposition, a tendency to sweating and a delicate integument. Three of our series of 14 patients with widespread erythrasma of the trunk suffered from diabetes mellitus.

INCIDENCE, CLINICAL PICTURE AND FLUORESCENCE

Erythrasma is seen in all parts of the world, but is commoner in tropical climates. It was said never to occur in children, but we have observed a case of erythrasma of the toe webs in a one-year-old child. We believe that this form is not uncommon in the younger age group and may account for some hitherto unexplained cases of scaling and fissuring of the clefts which are not due to fungus or monilia and which may not yield any growth on standard culture media.

The clinical picture of classical erythrasma is well known. Mild forms of this condition are common and may pass unrecognized. The subclinical form was found in 9 of 25 normal male subjects examined.

The generalized form, characterized by well-defined, scaly, lamellated plaques on the trunk and proximal parts of the limbs was seen, in Miami, predominantly in middle-aged Negro women.

The Wood's light is of diagnostic value in erythrasma. Various shades of red fluorescence are seen over the affected areas (Gougerot and Duché, 1941 (5), Michaelides and Shatin, 1952 (6)).

We have found the Wood's light invaluable, particularly in confirming the diagnosis of erythrasma of the clefts and in identifying fluorescent colonies in cultures of erythrasma organisms.

BACTERIOLOGY

Direct Examination

Potassium hydroxide preparations demonstrate the organisms in the scales. Stained preparations (with methylene blue, Gram, Giemsa or periodic acid Schiff), examined under the oil immersion lens, are preferable. Stained imprints of the horny layer, using slides coated with an adhesive solution (Goldschmidt and Kligman, 1961 (7)), are

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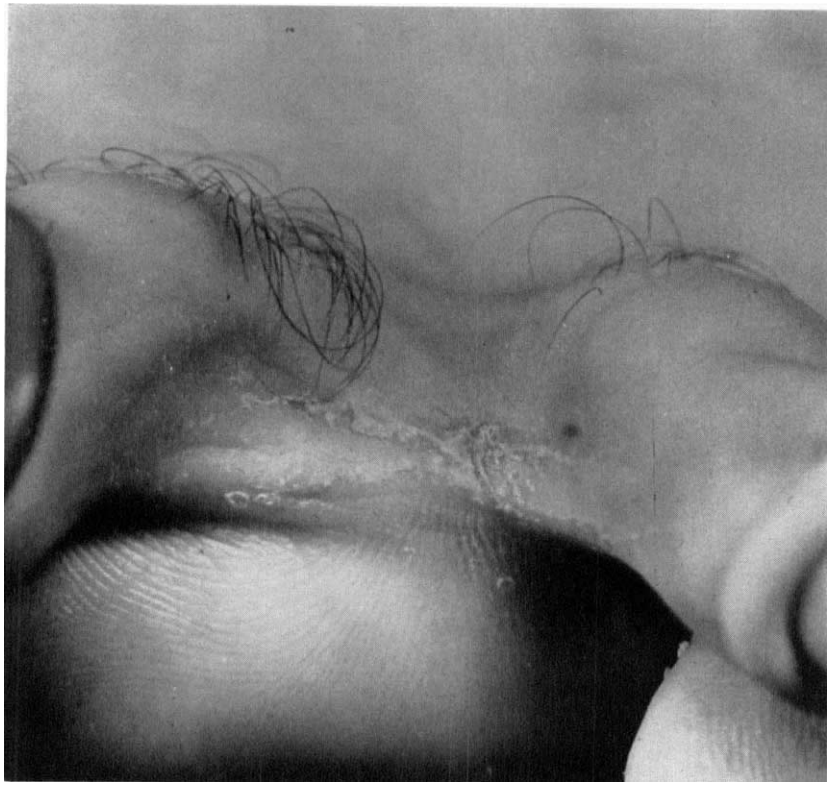

FIG. 1. Erythrasma between the toes of an adult. There was red fluorescence under Wood's light

particularly suitable for diagnostic purposes (Fig. 2a). These show rod-like organisms, filaments and coccoid forms. The relative proportion of these organisms varies in different areas examined and, sometimes, only bacteria-like rods are seen (Fig. 2b).

Electron microscopic examination of the scales from erythrasma has shown bacteria-like organisms lying within the cells of the horny layer (Fig. 3).

Cultures

Cultural isolation of the organism from the scales of erythrasma was accomplished at some time in all our cases. Our culture medium contains 20 per cent fetal bovine serum, 78 per cent tissue culture medium No. 199, incorporating phenol red as an indicator (Morgan, Morton and Parker*) and 2 per cent agar. The pH of the medium is adjusted to 6.8 to 7.2 with tris (hydroxymethyl) aminomethane (0.05 per cent). Within twelve to twenty-four hours, at 34° C., small (1 to 2 mm.), shiny, moist, whitish-grey, translucent, slightly convex colonies develop (Fig. 4), producing varying degrees of coral red to orange fluorescence under Wood's light. The fluorescent material diffuses into the medium in the immediate neighborhood of the colonies. There is no visible pigment in daylight. The fluorescence resembles that seen over erythrasma-affected areas *in vivo*, but in culture it disappears completely by the end of ninety-six hours. The task of identification and selection of colonies was made easier with a dissecting microscope, using Wood's light illumination.

Subcultures of the organism grow on a fairly large number of bacteriological media. They also thrive on the chorio-allantoic membrane of ten-day-old embryonated eggs incubated at 38° C. However, we have found that tissue culture medium No. 199 with 20 per cent fetal bovine serum appears optimal for the production of red fluorescence. The only other media on which subcultures occasionally produced some fluorescence were blood-containing media, *i.e.* chocolate agar and sheep blood agar, but the results were too inconsistent to be of value.

The Organism

Gram stain of a smear from a colony shows gram-positive rods 1 to 2 μ by 0.3 to 0.6 μ (Fig.

* Purchased from Microbiological Associates, Inc., Bethesda 14, Maryland.

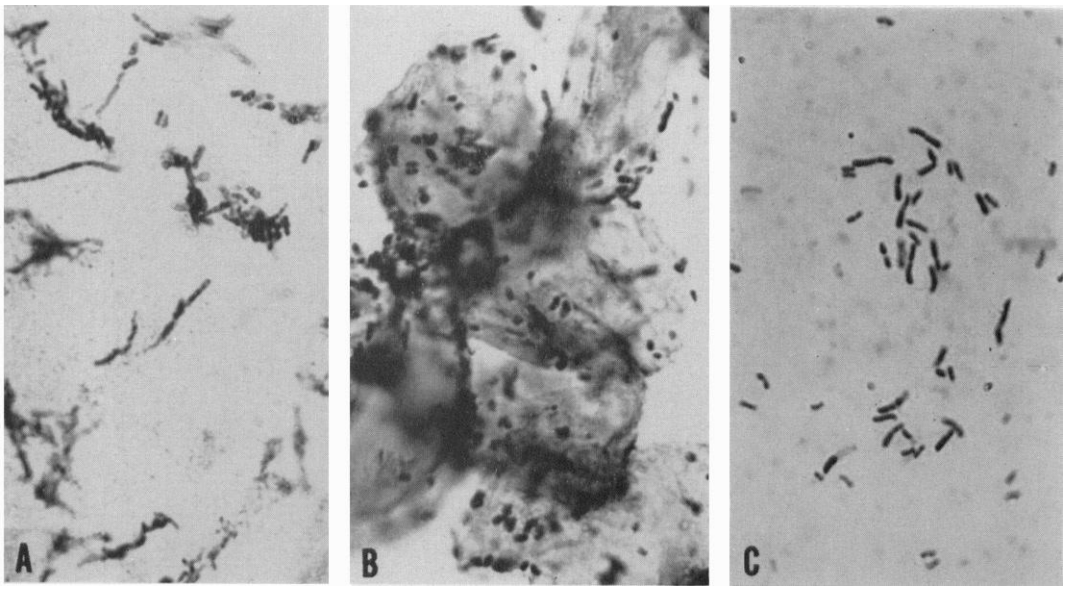

FIG. 2a. Gram stain of horny layer from erythrasma of the groin. (× 900)
FIG. 2b. Gram stain of scale from toe web. (× 900)
FIG. 2c. Gram stain of smear from culture. (× 900)

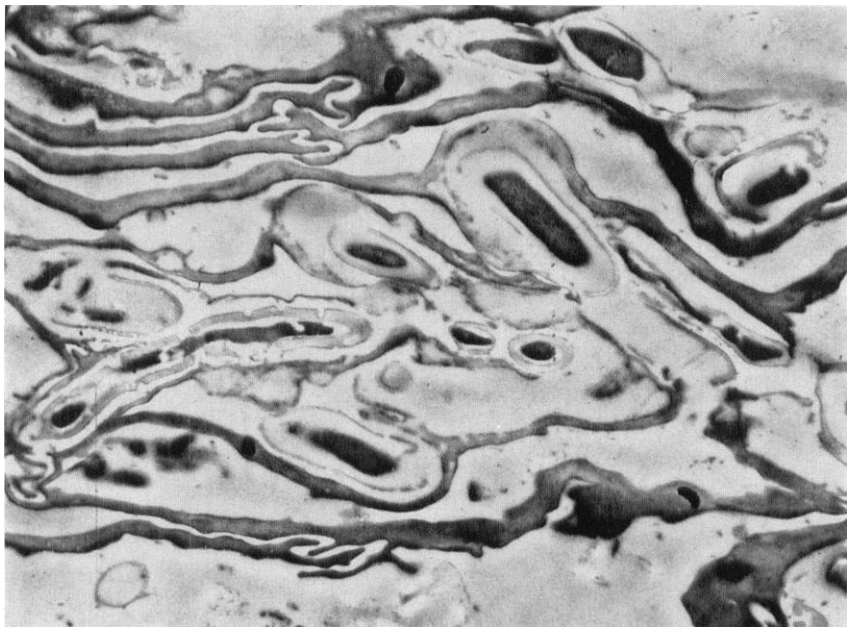

FIG. 3. Electronmicrograph of ultrathin section of scale from erythrasma of the trunk. (Osmium fixed. × 10,000.)

2c). The organism tends to become pleomorphic and gram-negative in old cultures, showing well-marked gram-positive subterminal granules. There is occasionally an additional centrally located granule. These changes are accompanied by loss of fluorescence of the colonies. The bacteria are non-motile and are not acid fast. Dark-field microscopy shows typical bacilli with well-

rounded ends and a marked outer wall. It produces acid from dextrose, sucrose and maltose, but not lactose.

In vitro sensitivity tests, carried out on solid and liquid media, show that the organism is maximally sensitive to erythromycin and relatively more resistant to penicillin. The minimum inhibitory concentrations depend to a marked degree on the nature of the medium employed for the test.

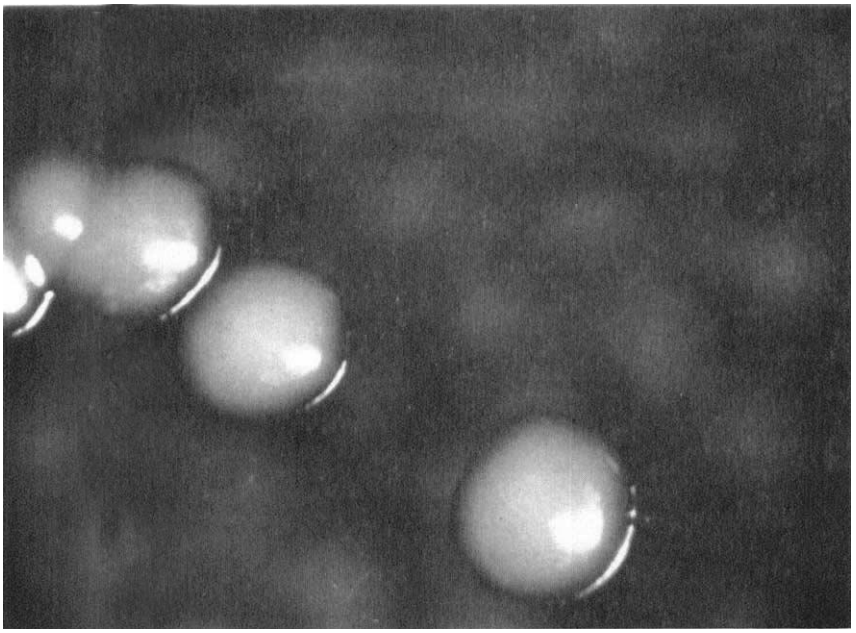

FIG. 4. Close-up appearance of colonies. (× 20)

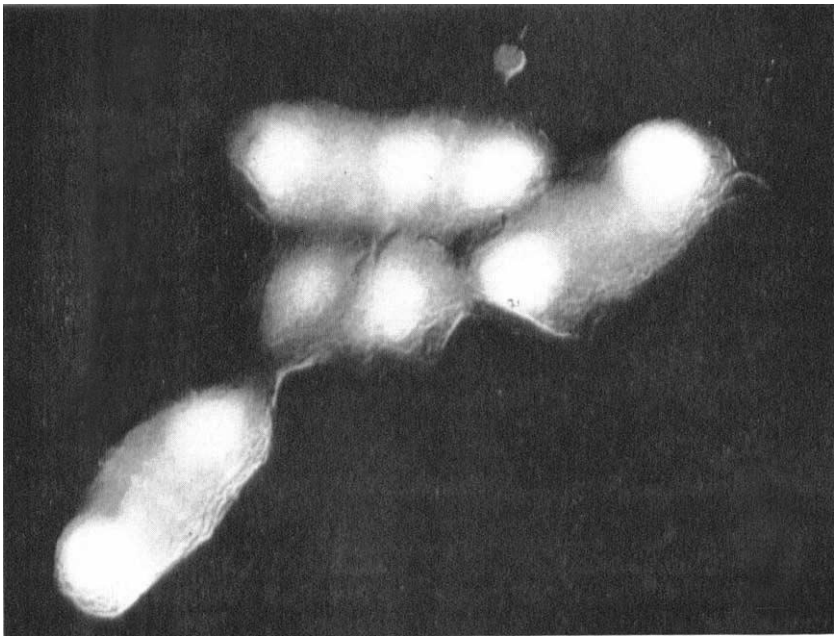

FIG. 5. Electronmicrograph of organism. (Osmium fixed, palladium shadowed. × 32,000)

Electron microscopic studies of the unfixed dried organism from a fresh culture show bacilli with well-marked electron dense granules. Osmium fixed, palladium shadowed preparations demonstrate a definite cell wall and spherical granules (Fig. 5).

Experimental Infections

Five inoculations in 4 human subjects, using pure isolates, resulted in three positive reactions. In one of the subjects, who had been successfully treated for erythrasma of the groins with a systemic antibiotic previously, the technic consisted in applying small amounts of pure culture material to the inner aspect of the thighs on:

(1) intact normal skin
(2) scarified skin
(3) skin stripped to glistening with Scotch tape.

The area was covered with a double layer of Saran wrap which was held in place for three days with adhesive tape. Scales from a known case of erythrasma were applied to similarly prepared sites.

At the end of 72 hours there was scaling and red fluorescence at the site of application of the culture material over the stripped and the scarified areas; however, the diseased scales produced an exactly similar picture over the stripped areas only.

The fluorescence faded 24 hours later and the scaling cleared in a matter of a few days. A KOH preparation of scales from the artificially infected patch showed fine filamentous rods as seen in erythrasma. Gram stain of the scale showed gram-positive short rods and gram-negative rods with subterminal gram-positive granules. There were also coccal elements. Culture of the scale yielded fluorescent colonies containing gram-positive bacilli with subterminal granules.

In two subjects, application of culture material to stripped areas of the forearm, covered with parafilm and held in place with adhesive tape, failed to produce visible changes.

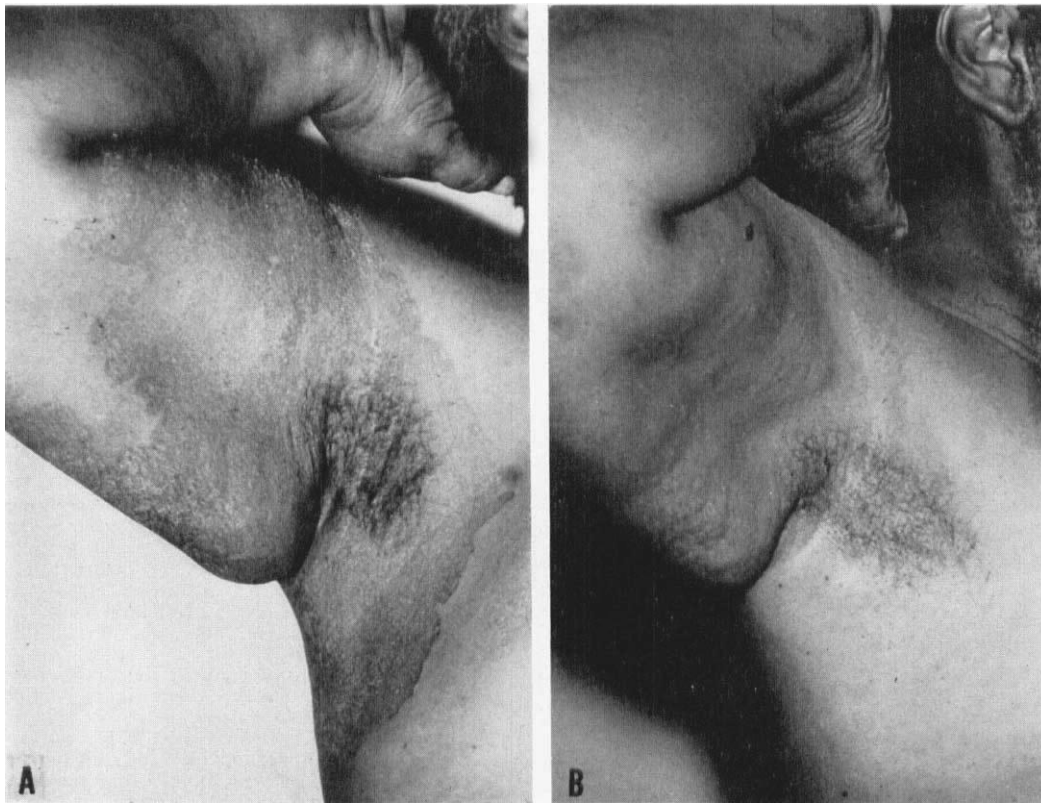

FIG. 6a and 6b. Erythrasma of 25 years' duration before and after treatment with oral erythromycin

In the fourth subject, application of pure culture material from a case of erythrasma to a stripped area on the thigh produced scaling and red fluorescence. On a second occasion, scaling and red fluorescence were produced on the thigh by application of pure culture material obtained from a case of erythrasma of the toe clefts and held in place in the usual manner by a layer of parafilm with the help of adhesive tape. Although the fluorescence was of relatively short duration (approximately 24 hours), the scaling persisted for one week. Culture of the scales at 54 hours yielded markedly red fluorescent colonies containing bacilli of characteristic morphology.

Exacerbation of mild erythrasma of the groins was produced experimentally in one subject on two occasions. The mildly fluorescent and scaling affected area was occluded with parafilm which was kept in place with adhesive tape for three days. On removal of the occluding parafilm there was a marked increase of scaling and fluorescence. Examination of the scales showed a striking increase in the number of the filamentous forms. This subsided spontaneously to approximately the same proportions as had been noted previously. We have found that mild, subclinical forms of erythrasma of the groins can commonly be detected by careful examination with Wood's light. It would seem that occlusion and increased humidity favor the growth of the causative organism and that these are important etiological factors.

No detailed animal experiments were carried out and we do not know whether species other than humans are susceptible to the disease.

TREATMENT

We have treated successfully 15 patients suffering from erythrasma with systemically administered erythromycin, chloromycetin or the tetracyclines. Complete clearance of the disease over all areas except the toe webs followed a five-day course of oral erythromycin given in a dose of 1 gm. daily. The condition had cleared within two to three weeks of administration of the drug (Figs. 6a and 6b). One patient's erythrasma has relapsed so far during a follow-up period of six months.

Systemic penicillin was tried in two patients without success. Systemic griseofulvin had been used in one of the patients with a negative result. Erythromycin and chlortetracycline topically applied did not clear the lesions completely.

SUMMARY

Evidence is put forward to show that erythrasma is a common bacterial infection of the skin. The strikingly high incidence of erythrasma in the toe webs has lent new importance to its study and understanding. The evidence for its bacterial nature is as follows:

1. The scales of erythrasma always contain gram-positive rods and/or filaments with granules.

2. Colonies of bacteria cultured from scales show red fluorescence under Wood's light which resembles the fluorescence seen in vivo over erythrasma-affected areas.

3. Electron microscopic examination of the scales and the organisms grown on culture confirms that the organisms are bacteria containing electron dense granular elements.

4. Inoculation experiments with pure culture have produced scaly lesions showing red fluorescence. These were of relatively short duration and failed to persist as clinical erythrasma.

5. Further evidence for the bacterial nature of the disease is provided by the dramatic response of erythrasma to some systemically administered antibacterial antibiotics, particularly erythromycin.

REFERENCES

1. Burchardt, Max: Ueber eine bei Chloasma Vorkommende Pilzform. Medicinische Zeitung, **2** (No. 29): 141, 1859.
2. von Bärensprung: Neue Beobachtungen über Herpes. Annalen des Charité-Krankenhauses, Berlin, 10, 1862.
3. Köbner, Heinrich: Erythrasma. Monatshefte für Praktische Dermatologie, **3** (No. 12), Dec., 1884.
4. Poehlmann, August: Erythrasma. Handbuch der Haut und Geschlechtskrankheiten Jadassohn, pp. 711–728, 1928.
5. Gougerot, H. and Duché, Jaques: Les Trois Teintes Brune, Brun-Violacé, Rouge de L'erythrasma a la Lumière DeWood. Annales de dermat. et syph., **1:** 277–280 (July–Aug.) 1941.
6. Michaelides, P. and Shatin, H.: Erythrasma fluorescence under the wood light. A.M.A. Arch. Derm. **65:** 614, 1952.
7. Goldschmidt, H. and Kligman, A. M.: Surface biopsy: A new method for studying normal and pathologic horny layers read at 22nd annual mtg. of The Soc. for Invest. Dermat., June 27, 1951.

DISCUSSION

DR. J. GRAHAM SMITH, JR., (Durham, North Carolina): I would like to congratulate Dr. Sarkany and his coworkers. Certainly it is a unique experience to see a disease which has for years been thought to be well understood completely redelineated and at one time Koch's postulates satisfied, the etiologic agent identified and cultured, and an appropriate therapeutic measure brought forth.

In April of this year, Dr. John Tindall and I were visiting in Dr. Blank's laboratories in Miami and at that time Dr. Sarkany was kind enough to give us a presentation very much like the one you have heard today. On our return to Duke University, Dr. Tindall investigated four patients with clinical lesions of the feet which appeared clinically to be dermatophytic; however, he could not get a positive KOH examination, nor was he able to culture a dermatophytic fungus. He was able to demonstrate the characteristic coral red fluorescence with a Wood's light which Dr. Sarkany has shown so beautifully; and in all four of these patients complete clinical cure ensued following treatment with erythromycin.

DR. JACOB H. SWARTZ: (Boston, Mass.). I want to congratulate Dr. Sarkany and the collaborators of this paper. However, I would like to make the following observations.

The clinical picture of erythrasma described in this apper and the localization does not correspond to the accepted descriptions of this disease. The common sites are the areas in contact with the scrotum and the axillae. Occasionally there is involvement in the periumbilical area, intergluteal fold and submammary areas. The eruption is superficial, resembles tinea versicolar in color and type of scaling. No vesicles, papules or moist lesion are observed. The cases shown today did not show such distribution except in one case. The character of the lesions in the cases shown today varied from dry to moist oozing lesions. We usually interpret the latter findings which are rare, as the result of irritation from treatment or superimposed bacterial infection.

Did the authors do direct microscopic examinations of the skin scales in each case and find a microscopic picture usually seen in erythrasma or did they rely only on culturing the scales? If they relied on cultures only, then the question is whether they cultured the causative organism or a secondary invader. Did they reproduce the clinical picture which has been accepted as erythrasma or the scaly, moist oozing lesions which the presenters interpret as erythrasma? Did the presenters find on direct microscopic examination of the skin scales from the reproduced lesions a picture which is accepted as the organism causing erythrasma or did they only culture the material from the reproduced lesions and find the organism they describe. If the latter is the case, then one can argue that they have reproduced a secondary invader which can produce the clinical picture which they describe.

I can confirm the coral fluoresence on examination of erythrasma lesions with Wood's light. This finding is interesting and the presenter and his collaborators should be congratulated on calling it to our attention.

The statement that the response of this disease to bacterial antibiotics is further proof that the causative agent of erythrasma is a bacterial rather than a fungous organism can be challenged. Infections caused by nocardia may respond to some antibacterial agents.

DR. E. WILLIAM ROSENBERG (Miami, Florida): I had the advantage of working in the laboratory where all this was going on and I would like at this time, particularly in view of Dr. Swartz's comment about the feet, to tell you of one patient that I saw within the last several weeks.

He was a young man of sixteen who had had a chronic crusted eczema between the toes of both feet, more prominently on foot, for about two years. Some fungus had been identified. He had been treated previously for a year with griseofulvin, but he still had 90 per cent of his trouble.

Examination under Wood's light showed the characteristic pink fluorescence on his feet. A culture was made from this boy's feet and placed on the special medium which Sarkany, Taplin and Blank have been using. The growth grew out almost a pure culture of the same organism which these workers have found from the lesions of erythrasma.

This boy, by the way, had been treated with penicillin without success.

In vitro studies were done on this one case. Penicillin was found to be ineffective, but erythromycin and tetracycline were both found to be effective. He was treated for some two

weeks with erythromycin by mouth; no topical therapy was used at all.

He cleared completely, I was very impressed by the dramatic effectiveness of erythromycin in this case and the fact that the lesion responded to the same drug which worked on the cultured organism *in vitro*; it would all seem to be Sarkany's erythrasma organism.

DR. DONALD S. SCHUSTER (Palo Alto, California): I would like to ask what your results were when you attempted to recover this organism from normal skin and from other skin lesions.

DR. CARL T. NELSON (New York, New York): I would like to ask Dr. Sarkany if he has any data on the biochemical activities of these isolates—oxygen requirements, fermentation reactions and so on.

DR. ROBERT STOLAR (Washington, D. C.): What other microbiologic examinations have been made?

DR. I. SARKANY (in closing): I should like to thank all who took part in the discussion. Dr. Schwartz's comment that some of the forms of erythrasma with which we are dealing are not the classical types usually quoted in text books, is no doubt pertinent. However, others have previously described the widespread variety of erythrasma (McCarthy, 1943; Gonçalves and Mangeon, 1960) and erythrasma between the toes was reported by Rabeau and Guerra (1936).

In reply to Dr. Schuster, we have not been able to culture this organism from areas of normal skin or from scales of other skin conditions, both naturally occuring and following trauma.

REFERENCES

McCARTHY LEE, Tropical Mycoses, J.A.M.A., **123:** 450, 1943.

PADILHA GONÇALVES A., e MANGEON, GILBERTO: Eritrasma Multiplo e Extenso não intertriginoso. Trab. Soc. Portuguêsa de Dermat. e Sif. 18–11, 1960.

RABEAU H. AND GUERRA P.: Sur une localisation Peu Connue de L'érythrasma. E. interdigital des pieds.
Bull. de la Soc. Fr. de Dermat. et de Syph. **43:** 464, 1936.