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## MYCETOMA IN AMERICA

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Although mycetoma, or Madura foot, was described by Kaempfer<sup>1</sup> in 1712, its occurrence, or rather its recognition, in America is of quite recent date. Of the cases originating in this country, that described by Adami and Fitzpatrick<sup>2</sup> is probably the first. Their patient was a French Canadian, 21 years old, a native of Montreal who had never been outside of Canada. Parkes' patient<sup>3</sup> had previously resided in India, and in the case described by Kemper and Jameson<sup>4</sup> the course of the disease was so rapid and the pain so great that, in the absence of corroborative microscopic evidence, a diagnosis of mycetoma may safely be excluded. In the example reported by Hyde and Senn<sup>5</sup> the patient was a dental student, 20 years of age, a native and resident of Iowa. Artwine and Lamb's<sup>6</sup> case occurred in a Mexican laborer, 45 years old, and Pope and Lamb's<sup>7</sup> patient also was a Mexican laborer, aged 27. The fifth, and last, American case that I have been able to find a record of is the one on the study of which Wright<sup>8</sup> largely based his admirable contributions to the subject of mycetoma. The patient was an Italian woman, 26 years of age, on Dr. H. H. A. Beach's service at the Massachusetts General Hospital.

The two following cases of Madura-foot disease have recently been under observation in Kansas City:

**CASE 1.**—The patient, A. D., laborer, single, aged 24, was an employee of the Missouri Pacific Railway Company, and was referred to my associate, Dr. J. P. Kanoky, the company dermatologist. Dr. Kanoky being absent from the city, I diagnosed and treated the case, and am indebted to him for permission to report it. The patient is a native of Padua, Mexico, and formerly resided at Aransas Pass, Texas. He has never before suffered from a skin disease, and the cutaneous history of his family also is negative.

**Present Illness.**—Three years prior to the time of consultation, while walking barefooted across a pasture, the patient stepped into a depression in the soft ground that had been left by an old mule track, and at the same time sustained a slight punctured wound of the sole of the left foot, beneath the arch.

1. Kaempfer: *Amaentum exotitarum, Lemgoviae, 1712*, III, 561; cited by Scheube, *Die Krankheiten der warmen Landen*, 1903, Ed. 3, p. 735.

2. Adami and Fitzpatrick: *Tr. Assn. Am. Phys.*, 1895.

3. Reported by Hyde: *A Practical Treatise on Diseases of the Skin*, Phila., 1888, p. 406.

4. Kemper and Jameson: *Am. Pract. and News*, 1876, p. 577.

5. Hyde and Senn: *Jour. Cutan. Dis.*, 1896, p. 1.

6. Artwine and Lamb: *Am. Jour. Med. Sc.*, 1899, cxviii, 393.

7. Pope and Lamb: *New York Med. Jour.*, lxxiv, 386.

8. Wright: *Jour. Boston Soc. Med. Sc.*, 1897, II, 128; *Tr. Assn. Am. Phys.*, xlii, 471; *Jour. Exper. Med.*, 1898, p. 422; *Buck's Reference Handbook of the Medical Sciences (under Actinomyces)*, 1900, I, 101; *Publications of the Mass. General Hosp.*, Boston, 1905, I; *Oster's System of Modern Medicine*, 1907, I, 344.

He thinks that the wound was probably made by a cactus thorn. The lesion gave rise to but little pain or inconvenience, and was almost forgotten until about a month afterward, when a small, hard lump appeared beneath the skin at the site of the injury. The tumor was incised, but no pus escaped, and no foreign body could be discovered. The tumefaction gradually increased, however, until the depression beneath the arch was replaced by a large, boggy swelling. There was little or no associated pain. In the course of about fourteen months, a minute, oval opening appeared near the site of the original wound, and small amounts of "grainy," yellowish pus escaped. Since then, a number of other openings have developed, until, at present, there are a hundred or more scattered over the sole and sides of the foot. At no time has the pain been severe. A feeling of fulness is present occasionally, especially in cold weather, but the patient did not entirely cease work until the spring of 1912.

**Examination.**—The patient was a slight, nervous man, 5 feet and 4 inches tall, and weighed 124 pounds. The skin on parts other than the left lower limb was normal and unscarred. There was no response to a von Pirquet application of tuberculin, and the Wassermann serum test was negative. A radiograph, made by Dr. C. F. Martin, showed the bones to be apparently normal. The affected foot was greatly swollen and misshapen, the deformity being principally confined to the region of the instep. The circumference of the left foot at this point was over 50 cm., while the right measured only 27 cm. The dorsal surface of the affected part was almost constantly covered with large drops of perspiration, the plantar surface being dry or only moderately moist (Fig. 1). The right foot was normal in this respect. There was some tenderness on deep pressure, but fluctuation could not be obtained. The sinus openings were about the diameter of an ordinary pin, many being capped by a round or oval, reddish or brownish, tightly adherent crust (Fig. 2). Small amounts of yellow, fish-roe-like matter, suspended in an oily, puriform fluid, could be squeezed out of the majority of the sinuses. The fungi, which morphologically were identical with those found in the ochroid variety of mycetoma, were easily found in this expressed material and in the crusts after thorough soaking in a solution of potassium hydroxid. Cultures of the organism were not so readily secured, however, our experience in this regard coinciding with that of previous observers. Even scrapings from the sides of two of the canals, removed by means of a small, sharp spoon, after thorough anesthetization of the part with cocaine, failed to prove productive. Repeated attempts on the part of Dr. W. K. Trimble, Dr. Frank Hall and myself having been without result, it is very probable that no viable organisms will be secured until the foot is opened and fresh, moist material, which has not been exposed to the action of antiseptics, is obtained.

For histologic study, a small piece of tissue was excised from the sole of the foot at the outlet of one of the sinuses. The material was stained with hematoxylin and eosin, alone and in combination, methylene-blue (Unna-Pappenheim), Weigert and Gram-Weigert. The prickle-layer was somewhat increased in thickness, with many open spaces between the cells. Some of these intercellular cavities contained polymorphonuclear leukocytes, round cells, and, occasionally, a granular deposit which stained with eosin. The grains, or

"druses," were irregularly scattered through the corium in the neighborhood of the sinus. Under the low power, these bodies appeared as rounded, oyster-like masses, the central and pericentral portions of which stained fairly well with hematoxylin, and the outer zone of which reacted to eosin only. Histologically, the bodies consisted of a central, granular appearing portion, with radiating mycelial threads which extended almost to the periphery, the entire mass being encompassed in a glassy, hyaline shell. The separate filaments stained so faintly that it was not possible to ascertain, with any degree of accuracy, whether or not either branching or segmentation was present. The tissue changes in the immediate vicinity



Fig. 1.—Case 1.—Character of deformity and distribution of sinuses. The dorsal surface of the foot and the ankle are covered with perspiration.

of the druses were such as one might expect to find in a chronic inflammatory process of this nature—vascular generation and dilatation, the latter often accompanied by endothelial proliferation, with connective tissue and epithelioid infiltration of the vessel walls, and collections of plasma and epithelioid cells in the cutis, together with occasional giant cells.

**Treatment.**—In the districts where Madura-foot disease most frequently occurs, it has been found that the only successful treatment is amputation of the affected part. In this instance, however, the patient refused operation, and we were compelled to resort to other measures. Of these, dependence has been placed, for the most part, on remedies which have proved helpful in the treatment of actinomycosis. Potassium iodid, in gradually increased doses, copper sulphate, 0.02 gm., in water, after each meal, as originally suggested by Bevan,<sup>9</sup> and the x-rays, as recommended by Stelwagon<sup>10</sup> and by Zeisler.<sup>11</sup> Locally, various preparations of iodine have been employed. After two months of treatment along these lines, the foot is somewhat less swollen than at first, but the degree of improvement is very slight.

**CASE 2.**—The patient, J. H. C., married, housewife, aged 23, was under the care of Dr. John W. Perkins, of this city, and was treated by him. It is through his courtesy that I am enabled to include the history in this report. The patient was a native resident of Texas. Her cutaneous history and that of her family were negative. She had never gone barefooted, but frequently bathed in a stream where many cattle drank. Dr.

Perkins first saw the patient Sept. 5, 1906. Nine years previous to that time, a horse had stepped on her left foot, but the skin apparently was not broken. About one year after this accident, several small excrescences appeared near the base of the great toe and discharged slightly. These nodules gradually increased in size and number, and the foot became greatly swollen (Fig. 3). The pain was more or less constant, and quite severe. In 1902, an incision was made and some of the metatarsal bones were scraped. This procedure was repeated in 1904, but at that time appeared to aggravate the condition. On September 6, Dr. Perkins opened the foot, and removed the second toe and the second metatarsal bone. The sinuses were cauterized with a Paquelin cautery and dry dressings applied. A bacteriologic examination made at this time, by Dr. Frank Hall, showed the *Streptothrix maduræ* to be present in large numbers. The after-treatment consisted of thorough cleansing with solutions of hydrogen peroxid and potassium permanganate, and the injection into the sinuses of iodoform emulsion. November 12, the third, fourth and fifth toes were removed, and the lesions on the dorsum of the foot curetted and dressed with iodoform (Figs. 4 and 5). A small sinus just anterior to the internal malleolus was incised, and cauterized with nitric acid. Iodin was injected into the drainage tubes for a fortnight. The patient was sent home late in December, with the lesions on the dorsal surface of the foot healed, and only a slight ulcer remaining on the inner surface of the ankle, where the nitric acid had been applied.

Dr. Perkins did not see the patient again until September, 1907. At that time there was a small ulcer on the inner side of the instep, a second just beneath the arch, and a tiny, blister-capped sinus 2 inches back of the fourth metatarsophalangeal articulation. There was no pain, and only slight tenderness on deep pressure. No fungi could be found in the discharge. The sinuses were again cauterized, and dressed with a 5 per cent. solution of phenol (carbolic acid). Later, an iodoform emulsion was injected daily. The patient returned home November 26, her condition apparently much improved. Seven months later, she again applied for treatment. After reaching home, she had walked on the foot, and had suffered very little inconvenience in any way until April, 1908, when a constant, throbbing pain developed and gradually increased in severity. In May, she was compelled to use crutches. At the time of examination, she was unable to place her foot on the floor. Several sinuses had ruptured on the dorsum and sole of the foot, and on the sides of the ankle. A blood analysis made July 12, 1908, showed: Hemoglobin, 100 per cent.; erythrocytes, 5,600,000; leukocytes, 25,900, with a differential count of: Polymorphonuclears, 69.3 per cent.; mononuclears, 18.5 per cent.; small lymphocytes, 4.5 per cent.; transitionals, 3.1 per cent.; eosinophils, 3.3 per cent.; basophils, 0.6 per cent.

A bacteriologic report, received from Dr. Edward N. Tobey, of Harvard University, Sept. 2, 1908, read as follows: "Cultures made from specimen received show fine radiating growths giving the characteristic puff-ball appearance of *Streptothrix maduræ*. Microscopic examination shows long, branched filaments, some with club-shaped ends."

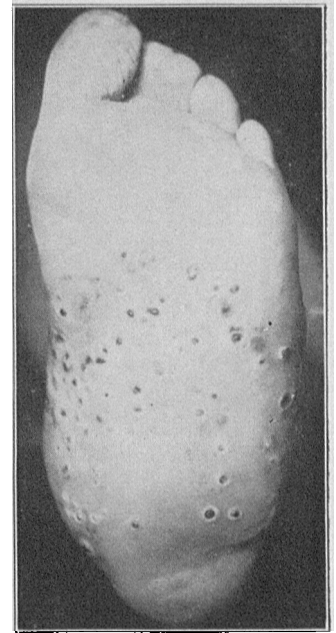


Fig. 2.—Case 1.—Sinus openings on sole. Many are capped by round or oval, tightly adherent, brownish crusts.

9. Bevan: Treatment of Actinomycosis and Blastomycosis with Copper Salts, THE JOURNAL A. M. A., Nov. 11, 1905, p. 1492.

10. Stelwagon: Diseases of the Skin, W. B. Saunders & Co., Phila., Ed. 6, 1910, p. 1111.

11. Zeisler: Tr. Am. Dermat. Assn., 1906, p. 104.

The foot was amputated in July, and the stump healed promptly and smoothly. Cross-sections made before hardening the tissues showed that the sinuses followed the tendon sheaths, and were filled with a soft, gelatinous material which, in most instances, had entirely replaced the tendon. The tendons that remained were soft and atrophied.

The fact that both of the patients whose histories are here recorded were in the habit of living active, outdoor lives in a subtropical country is of interest. In a statistical study of one hundred cases of mycetoma, Bocarro,<sup>12</sup> of the Hyderabad Medical School, found that

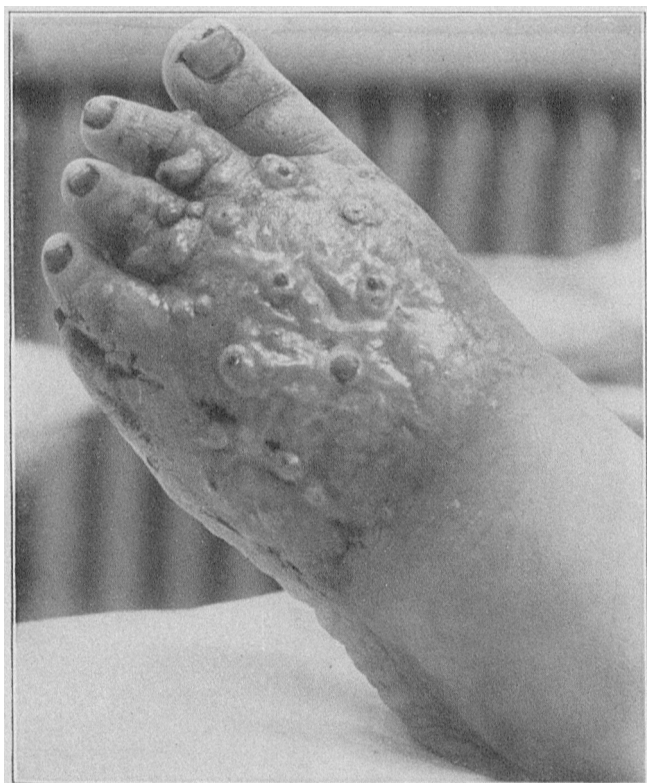


Fig. 3—Case 2.—Condition of dorsum of foot at time of first examination (courtesy of Dr. John W. Perkins).

91 per cent. of the patients were tillers of the soil, and that the remaining 9 per cent. spent the greater portion of their time barefoot in the open air (boatmen, porters, beggars, etc.). Eight of the patients were females, seven being the wives of agriculturists. The disease occurred most frequently between the ages of 21 and 40. Crocker<sup>13</sup> states that a history of previous attack of guinea-worm disease is often present, but Bocarro found that the causative organism most frequently gained entrance through the wound left by a thorn prick. While the disease usually affected the feet, other exposed parts, especially the hands and the knees, occasionally were attacked.

Clinically, mycetoma may be divided into three varieties, the yellow or ochroid, the black and the red, so named because of the color of the small masses or granules suspended in the oily, seropurulent discharge from the sinuses. The ochroid is the most common type, while the red is exceedingly rare. Except Bassini's<sup>14</sup> Italian case, I can find no record of the occurrence of either the black or red forms outside of India.

Bacteriologically, the consensus of opinion would indicate that the yellow and the black, the two varieties that have been most exhaustively studied, are due to different organisms. Jackson<sup>15</sup> has found that the ochroid organism, when grown in association with pyogenic cocci, on steamed potato, will sometimes, after a month or two, take on a rose color, or even a red color. It may be that this explains the origin of the much-discussed red growths of the streptothrix isolated and studied by Vincent<sup>16</sup> and, later, by Gémy and Vincent.<sup>17</sup>

Vandyke Carter,<sup>18</sup> to whose masterly monograph we owe much of our knowledge of this disease, believed that the pale particles represented an evolutionary stage of the same organism found in the black variety. Kanthack<sup>19</sup> studied three cases of the black form and twelve of the yellow, and concluded that both were due to the same fungus, an actinomyces. Boyce and Surveyor,<sup>20</sup> while acknowledging the similarity of the organism found in these two varieties of mycetoma and in actinomycosis, believe that the two forms differ distinctly in etiology. They examined seven cases of the black type, and found the particles to consist of a brown pigment-substance, readily removable in Javelle water, and containing a large, branching, septate fungus. No organisms of fructification were observed. In Adami

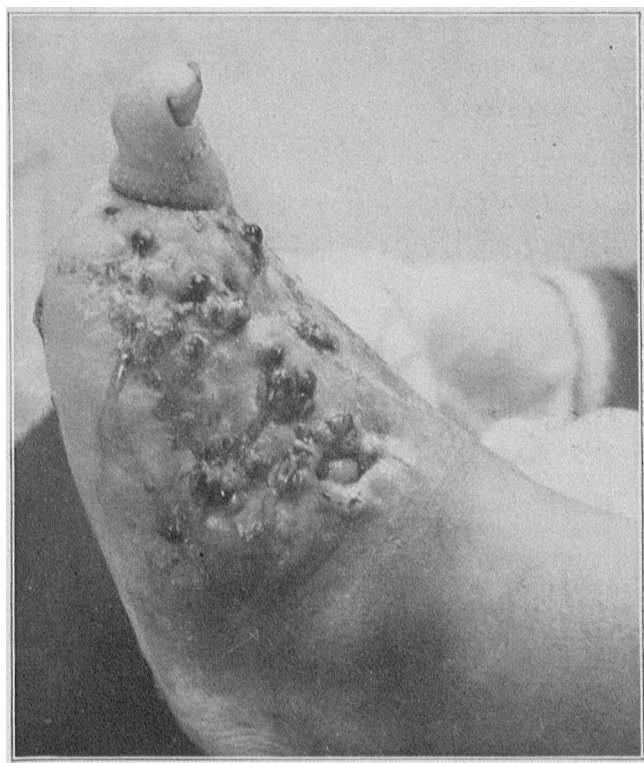


Fig. 4—Case 2.—Condition of dorsum of foot at time of amputation, July, 1908 (courtesy of Dr. John W. Perkins).

and Fitzpatrick's<sup>2</sup> case, the fungi were identical in general appearance with actinomyces but the clubs were much larger. Oppenheim,<sup>21</sup> who obtained his material from the Tametsee Djidjishboy Hospital in Bombay.

15. Jackson: *Tropical Medicine*, P. Blakiston's Son & Co., Phila., 1907, p. 496.

16. Vincent: *Ann. de l'Inst. Pasteur*, 1894, p. 129.

17. Gémy and Vincent: *Ann. d. Dermat. et de Syph.*, November, 1897, vii.

18. Carter, Vandyke: *Mycetoma or the Fungus Disease of India*, Churchill, London, 1874.

19. Kanthack: *Jour. Path. and Bacteriol.*, 1893, p. 140.

20. Boyce and Surveyor: *Tr. Royal Soc. London*, 1894.

21. Oppenheim: *Arch. f. Dermat. u. Syph.*, 1901, lxxi, 299.

12. Bocarro: *Lancet*, London, Sept. 30, 1893, p. 797.

13. Crocker: *Diseases of the Skin*, P. Blakiston's Son & Co., Ed. 3, ii, 1348.

14. Bassini: *Arch. per le sc. med.*, 1888, p. 300.

made a comparative histologic and bacteriologic study of the yellow and black varieties. Clinically, and in their main histologic features, he found them very similar, in fact, practically identical. In the yellow form there was apparently a somewhat greater tendency to connective-tissue proliferation, while in the black type abscess formation and liquefaction were more prominent features. Bacteriologically, however, the two conditions were very dissimilar. The organism from the yellow variety he believed belonged to the actinomyces group, while that isolated from the black was more of the nature of an odium.

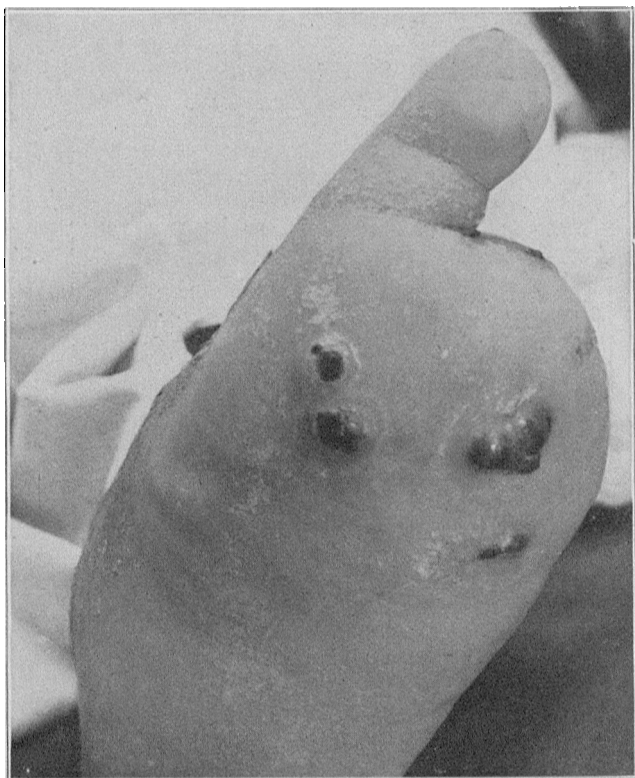


Fig. 5—Case 2.—Condition of sole at time of amputation, July, 1908 (courtesy of Dr. John W. Perkins).

Wright found that the granules in the yellow variety were composed of microorganisms from the streptothrix group, to which the actinomyces is now generally thought to belong, and not to the more highly organized hyphomycetes. He considered it not unlikely that many of the oehroid cases were nothing more nor less than actinomycosis.

Unna,<sup>22</sup> in his work on actinomycosis and its possible relation to Madura-foot disease, found that the causative fungi in the two affections, while resembling each other culturally and morphologically, possessed marked tinctorial differences, the actinomyces, when first fixed by anilin xylol and then decolorized with anilin, staining readily with acid fuchsin, while the adult *Streptothrix maduræ* was affected but little, or not at all, by prolonged contact with this dye.

Later Unna and Delbanco<sup>23</sup> again investigated the subject, both from a histologic and bacteriologic standpoint, and finally arrived at conclusions coinciding, in the main, with those which Unna reached in his first research.

McLeod<sup>24</sup> believes that Vincent's streptothrix is the etiologic agent in the yellow variety of mycetoma, and that this organism is allied to, but differs from, the actinomyces.

The black species of Madura foot he thinks is due to a degenerate form of the same fungus.

One of the most recent and valuable investigations that has been made regarding the etiology of mycetoma is that of Musgrave and Clegg.<sup>25</sup> Their material was obtained from a typically clinical case of the oehroid variety, of three years' duration, in a Filipina woman, 30 years old. With an organism which they isolated, and to which they gave the name *Streptothrix freeeri*, they performed inoculation experiments on forty monkeys, guinea-pigs, rabbits, dogs and pigeons. In three instances, typical examples of Madura foot developed in monkeys after the injection of cultures of the organism into the tissues of the foot. On the other hand, in no instance was a progressive disease produced by inoculation into other parts of the body.

Variations in the color of the granules were occasionally noted, and in one instance, in which the subject was a monkey (*Cynomolgus philippinensis* Geoff), a fair number of small, black granules were produced in the tissues following a subcutaneous inoculation of the organisms.

The statement, which has often been repeated, that the oehroid variety of mycetoma is actinomycosis is not supported by the weight of evidence in the literature, and is positively disproved by the results of Musgrave and Clegg's work.

As these investigators conclude, it is probable that all types of mycetoma are due to streptothrix infection,

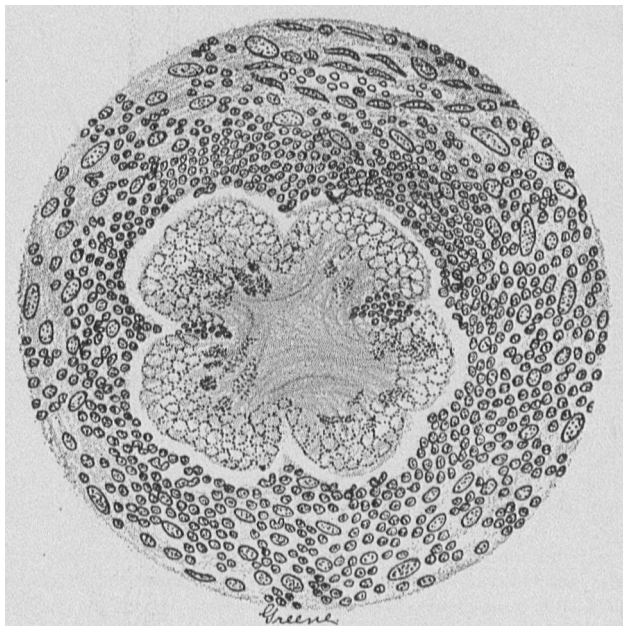


Fig. 6—Case 2.—Organism with surrounding zone of cellular infiltration (drawing by Dr. Marle Greene; courtesy of Dr. John W. Perkins).

but whether all forms are caused by an infection with the same organism, or whether more than one species plays a part in the disease cannot at this time be stated positively.

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22. Unna: Deutsch. med. Ztschr., 1897, p. 49.

23. Unna and Delbanco: Monatsch. f. prakt. Dermat., 1903, xxxi, 545.

24. McLeod: Allbutt's System of Medicine, Ed. 2, 1907, II, 754.

25. Musgrave and Clegg: Philippine Jour. Sc., December, 1907, II, No. 6, Sec. B.