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ON REFRACTORY SUBCUTANEOUS ABSCESSES CAUSED BY A FUNGUS POSSIBLY RELATED TO THE SPOROTRICHA.

By B. R. Schenck, M. D.

(From the Pathological Laboratory, Johns Hopkins University and Hospital.)

On November 30, 1896, A. W. presented himself at the surgical clinic of the Johns Hopkins Hospital with an infection of the right hand and arm of an unusual nature. The primary point of infection was on the index finger, whence it extended up the radial side of the arm, following the lymph channels, and giving rise to several circumscribed indurations, which were in part broken down and ulcerated.

One of these indurated areas was incised, and deep in the tissues a thimble full of gelatinous, puriform material was found. A culture from this fluid was made on gelatin. At the end of four days there was a growth of the staphylococcus epidermidis albus, besides which several other distinct, white colonies, raised from the surface of the medium appeared. Cultures made on agar from the latter colonies showed after three days in the thermostat, an abundant growth of an organism, not resembling the bacteria and evidently present in pure culture.

On December 7, under aseptic precautions, an indurated area just above the elbow was incised, and a small piece of tissue removed for microscopical examination. Two cultures were taken on slant agar from the puriform contents of this nodule. In three days both tubes showed a growth in pure culture of the peculiar organism previously obtained.

On December 14, Dr. Finney made the following note: "Ulcerated area, size of finger nail, over dorsal surface of second joint of index finger—right hand. Edges much undermined. Sero-purulent, gelatinous discharge on surface. A second, similar ulceration between second and third metacarpal-phalangeal joints. An indurated line, 1 to 1.5 cm. in diameter, follows along dorsum of hand and forearm, with here and there ulceration.

On the arm there are two indurated points, which have been excised, the highest one being in the middle of the arm. At the junction of the upper and middle thirds of the forearm there is an indurated spot, the size of a bean, situated to the outer side of the main line.

Epitrochlear gland not involved. Axillary glands palpable, but not especially enlarged."

Dr. Finney then removed with aseptic precautions a second, larger piece of tissue for microscopical examination.

The patient gave the following history: Age 36. Marked family history of tuberculosis. Patient has suffered from phthisis for past twelve years.

During the latter part of August, 1896 (3 months before visit to the Johns Hopkins Hospital Dispensary), while working at the iron worker's trade in St. Louis, the patient scratched the index finger of right hand, on a nail, while reaching into a red lead keg. Shortly after this a small abscess formed which was opened with a pin. A slight amount of watery fluid escaped, which patient thinks did not look like pus. In about three weeks the ulcer between the second and third metacarpal-phalangeal joints appeared. This was treated at the St. Mary's Dispensary (St. Louis). The inflammation traveled up the arm, and in about seven weeks after the infection seven similar abscesses had formed. These were opened, and a watery discharge escaped. About this time a "waxen kernel," size of a walnut, appeared in the axilla. It was not especially tender and disappeared in two days. While in St. Louis the arm was bandaged daily with bichloride and carbolic dressings. The patient thinks that he had no fever, and says the pain was very moderate. Being unable to work he returned to his home in Baltimore late in November.

Physical examination on entrance showed evidences of advanced tuberculosis of the lungs, and the sputum contained numerous tubercle bacilli.

The infection involving the hand and arm proved very refractory to treatment, the last lesion, at point of primary infection, not granulating until late in February, 1897.

The organism which was assumed to be in etiological relationship to the above-described lesions was obtained in three cultures from two different foci of the disease: Once from one of the lesions in the forearm, admixed with the skin coccus, and twice from one of the lesions in the arm, in pure culture.

Cultural Characteristics.—Cultures were made on all our common media, including plain, glycerine and sugar agars, plain and sugar bouillon, plain and acid gelatin, milk and potato. With the exception of the milk all the cultures developed luxuriantly.

Agar.—At 37° C. the growth is first apparent at the end of 48 hours, when the tract of the needle is marked by a faint line, slightly opaque, which under a low magnifying power is seen to be made up of minute colonies, with feathery outline, resembling somewhat minute snowflakes. At the end of 72 hours, the line of inoculation is sharply marked by an opaque, white, moist growth, having well-defined edges, raised from the surface of the media. Here and there at the periphery are isolated colonies. As the age of the culture increases—about five days—the growth extends very much in thickness and but little peripherally. The surface is corrugated, the edges lobulated and sharply defined (Plate I, Fig. b).

In cultures of ten days and older the growth is very thick; the surface is rough, corrugated, and stained a dark brown color, the shade at the periphery being deeper than in the centre. The medium also becomes stained.

Colonies of three days appear to the naked eye as round, raised, moist dots, 0.5 to 1 mm. in diameter. Under the low power they appear to be made up of a feltwork of minute fibrillæ, dense in the centre, lighter at the periphery, with a feathery outline. Scattered through this meshwork are many minute dots, consisting of the conidia.

Colonies of ten days are characteristic. They are round, sharply circumscribed, and elevated from the surface of the medium. The surface of the colony is brownish, and marked

by radiating lines proceeding from centre to periphery, evidently caused by the drying and shrinking of the growth (Plate I, Fig. a).

By a comparison of the development on glucose, lactose and saccharose agars, little difference is to be made out during the first two weeks. In cultures older than 14 days, however, the growth continues longer and becomes heavier on glucose than on plain agar, and in all the sugar media there is more discoloration both of the growth and of the substratum.

Gelatin.—The growth in stab cultures develops slowly. It is much more abundant in the upper part and spreads laterally over the surface, while the development in the depth is feeble, being scarcely perceptible in the lower third. At the end of six days there is slight liquefaction of the medium. The organism grows somewhat more luxuriantly in acid gelatin, and the liquefaction is greater.

Bouillon.—Growth in bouillon is fairly abundant in three days, and appears as little, cottony tufts which settle to the bottom of the tube, leaving the supernatant fluid perfectly clear. As growth proceeds, it tends to spread up the side of the tube. The reaction of the bouillon is not altered.

Potato.—At the end of 48 hours the growth is abundant. It is elevated, the surface is moist and the edges lobulated. After several days the surface of the growth becomes rough and wrinkled, the edges discolored and the potato darkened.

Milk.—There is no change produced in the tint of litmus milk at the end of seven days, and no coagulation takes place. The organism does not seem to thrive in this medium, film preparations showing only very small numbers.

Fermentation Tests.—Stab cultures in glucose, lactose and saccharose agars show no gas bubbles. Glucose, lactose and saccharose media, made from sugar-free bouillon, prepared according to the method of Theobald Smith, placed in fermentation tubes, give an abundant growth in the aërobic bulb, the anaërobic tube remaining clear. There is no gas formation.

Relation to Oxygen.—No growth develops in culture placed in the Buchner jar.

Vitality.—Growth which has remained on potato for eleven months again develops when placed in sterile bouillon. Agar cultures retain their vitality for at least nine months. To test the resistance to low temperatures, portions of growth from bouillon were placed in sterile water and allowed to remain in cold storage, at a temperature of 28° F., for ten weeks, after which they proved to be alive. In these cases actual congelation did not take place. When frozen for this length of time, however, they lose their vitality.

The vitality of cultures is destroyed by exposure to a temperature of 60° C. for five minutes.

The optimum temperature for development is between 20° and 37° C.

Morphology and Development.—For many of the points relating to the morphology and development of the organism, I am indebted to Dr. Erwin F. Smith, of the United States Department of Agriculture, Washington, who has given much time to the working out of the more difficult and obscure points pertaining to its life history and classification. I take this opportunity of acknowledging the great value of his help and advice, and of expressing my appreciation of his kindness.

Cover-glass preparations made in the ordinary way, from agar and bouillon cultures, show two forms: (1) a thread-like, branching form, or mycelium, and (2) oval, spore-like forms, or conidia. In an unstained specimen the mycelium is seen to be made up of a doubly contoured thread, branching irregularly, but not very profusely, and never dichotomously. The protoplasm appears granular. The diameter of the threads presents considerable differences, with an average of 1.5 to 2 microns. The conidia are elliptical or ovate, many of the latter forms being distinctly apiculate. They are also doubly contoured and granular. The spores from the solid media are rounder and smaller than those developing in bouillon. They vary in length from 3 to 5 microns.

The organism stains well in all the basic dyes, and is not decolorized by the Gram method. Stained preparations show marked irregularities in the coloring, especially of the mycelium. The conidia frequently show a small unstained area near the smaller pole of the spore.

In smears made from agar or bouillon it is not possible to determine the relation which the conidia bear to the mycelium. Occasionally, however, one or two spores are seemingly attached by the smaller end to the side or end of the mycelium. This relation can be much more clearly brought out by observing their development in hanging-drop cultures, the description of which I quote from Dr. Smith's report of April 13th. The drawings are also reproduced from Dr. Smith's sketches. "When a little of the bouillon containing the colorless, elliptical or cylindrical conidia was inoculated into hanging drops of alkaline beef broth, and set away under a moist bell jar for forty-eight hours, there was an abundant growth of the fungus, the spore-bearing branches of which, being undisturbed, retained their spores in the normal condition, and the appearance of the fungus under such conditions is shown in the sketches (Figs. 1 to 3). Here from three to six or more spores were to be found, quite commonly clustered at the tips of the spore-bearing branches. Naturally, if the fungus had been disturbed by shaking or lifting out into a drop of water, most of these spores would have been readily washed away, leaving only one or two, that is, leaving such appearances as are shown on the drawings made directly from the bouillon cultures" (Figs. 4 and 5).

The life history of the organism was studied from bouillon cultures and from hanging drops. The conidia germinate by sending out one or more straight, unbranched germ tubes, sometimes from the end, again from the side. These germ tubes give off spores of the same character, the attachment being either terminal or lateral, by means of short pedicles or sterigmata (Figs. 6 and 7). Other seemingly similar spores push out into the branched mycelial forms, which in turn produce a new generation of conidia.

The existing classification of the fungi is a purely artificial one and is incomplete in many particulars. On this account it is often very difficult to determine where an organism is to be classed. Dr. Smith has kindly gone over the points in

regard to the classification of this organism, and his conclusions are as follows:

"It is a conidial fructification only, and on this account it is impossible to give more than a guess as to its position in the natural system of classification. To determine this the perfect spore form would have to be obtained. It can only be put into a form genus, in other words, into some artificial system of classification, until the natural one is known. It seems to me that it might be classified in either of these genera, according to the system given in Saccardo's *Sylloge Fungorum*, which is the commonly accepted standard of the artificial classification.

(1) It is not unlike the *Botrytis bassiana*, the muscardine, or calicino disease of silk-worms, and might therefore be regarded as a Botrytis. Against this classification, however, it is the fact that the spore-bearing branches are not erect, which is a rather trifling distinction. It might also be classed as (2) *Sporotrichum*, but inasmuch as it becomes dusky when it is old it might also be classed as (3) *Trichosporium*. Saccardo separated out the dusky forms of Sporotrichum into a separate genus under this name. The mere difference in color, as we know from cultures of many fungi, is often a very trifling matter, the early stages of a fungus often being white and the later stages dusky or even brown. On this ground I think that his distinction is of no value, and I think that we may throw out the genus Trichosporium altogether. As regards the other two, my own judgment would be that it fits best into *Sporotrichum*. In his *Sylloge Fungorum* Saccardo describes more than one hundred species of *Sporotrichum*, but most of them are described very imperfectly, and I cannot identify this fungus as belonging to any one of them."

The tissues removed for microscopical examination present the characteristics of a chronic abscess, consisting of inflammatory and cicatricial tissues. On the inside is a layer of necrotic material, next a zone of leucocytes, and outside newly-formed connective tissue, in which are several minute secondary abscesses.

Numerous sections stained by the Weigert and Gram methods failed to reveal any micro-organisms whatever. Sections stained for the tubercle bacillus by the carbol-fuchsin method were also negative.

Animal Experiments.—4 dogs, 6 guinea-pigs, 1 rabbit, 1 wild mouse and 2 white mice were employed. The results were as follows:

Dog I. The external jugular vein was opened, and 1 cc. of a suspension in salt solution of the organism was introduced. The dog remained well, and was killed on the 30th day. Nothing unusual was made out at the autopsy. All cultures were negative. The microscopical examination of the organs revealed nothing abnormal.

Dog II. Inoculated subcutaneously on the abdomen with 2 cc. of a 36-hour plain bouillon culture. On the next day there was an induration at the point of inoculation, followed in 24 hours by the formation of a tumor about 3 cm. in diameter, which on palpation gave evidences of fluctuation and tenderness. This remained practically unaltered for ten days, and then gradually became smaller and firmer to the touch. The dog remained apparently well, but was killed on the 28th day. Nothing was made out in the internal organs, and cultures from these were all negative. The tissues around the point of inoculation were excised and found to consist of firm scar tissue, in the centre of which was a small cavity containing a few drops of a gelatinous fluid. Agar tubes, inoculated with several loops scraped from the walls of the cavity, showed on one six colonies and on the other eight colonies of the organism. Bouillon cultures were also positive. However, no organisms could be demonstrated in cover-slips.

Microscopical sections through the wall of the cavity showed advanced cicatricial tissue. Numerous sections, stained according to the Gram and Weigert methods, failed to reveal the organism.

Dog III. Inoculated subcutaneously over the abdomen in a manner similar to Dog II. A second series of injections was made over the thigh in order to ascertain whether or not enlargement of the inguinal lymphatic glands would follow. Induration developed at the points inoculated, followed in two days by fluctuation and tenderness, the process increasing until the end of the first week, when the tumors became firmer and smaller. At no time were the inguinal glands palpable. Dog killed on the 21st day. The internal organs appeared normal; cultures from them remained sterile. Microscopical examination of the organs negative. At the local lesions nodules of fibrous tissue, containing small cavities similar to those in Dog II, were found. These little pockets contained a scanty amount of gelatinous material.

Smears from the cavities were negative.

Cultures from both lesions were positive, the organisms being rather few in number. They were, however, more abundant than in cultures from Dog II.

Microscopical examination of the fibrous tissue revealed the same condition as already mentioned and micro-organisms could not be demonstrated.

Dog IV. Inoculated subcutaneously in a similar manner, the induration and swelling took place as before, and on the fourth day, when the process seemed to have reached its height, the lesion was excised. The nodule was larger and less firm than the preceding ones, the cavity was greater and was completely filled by a thick, yellowish-red, gelatinous material, smears from which showed fibrin and red-blood corpuscles in small amounts, large numbers of polymorphonuclear leucocytes and a few objects similar in size and shape to the conidia characteristic of the organism introduced. None of these bodies were seen in leucocytes, all being extracellular.

Cultures from the walls of the cavity showed a very abundant characteristic growth of the organism.

Microscopical examination of the excised tissue shows the lesion to be a focus of inflammation. The walls are made up of the subcutaneous areolar tissue, forming a loose meshwork, the spaces of which are filled with coagulated albuminous material and leucocytes. The pus cells also infiltrate the connective-tissue stroma. At the edges of the cavity the connective tissue is denser and the infiltration of the leucocytes more marked. The cavity is lined by a mass of coagulated serum and necrotic pus cells. In specimens stained with hæmatoxylin and eosin, it is not possible to make out the organisms; but sections

stained by the Weigert method reveal them in large numbers, situated principally between the inner layer of cell detritus and the adjoining zone of infiltrated connective tissue which forms the wall of the cavity. For the most part they are associated in clumps of from six to thirty elements, but many occur singly and in groups of two or three. They occur mainly close to the edge of the cavity, but now and then may be situated singly or in clumps in the connective tissue stroma.

The organisms are of irregular shapes and sizes. In form they are round, oval and club-shaped, the last predominating. The smallest round forms are from one to two microns in diameter, while the long, club-shaped forms vary from two to four microns in length. These club forms are of irregular diameter, swollen at one end and tapering at the other; the staining is slightly irregular, there being often a small area near the centre taking the stain less intensely. The oval and round appearing forms correspond in size to the varying diameter of the club forms, and give one the impression of being cross-sections of the latter. These organisms are frequently seen within the bodies of both leucocytes and large connective-tissue cells. Many, however, are extracellular (Plate II, Figs. 1, 2, 3).

In the dog then, the inoculation of fluid cultures, either intravenously or subcutaneously, produces no evident constitutional symptoms and no internal pathological changes. When introduced subcutaneously there is a local lesion at the point of inoculation, consisting of a circumscribed inflammation and abscess formation. When allowed to remain for from three to four weeks absorption of the contents of the abscess takes place, and a mass of scar tissue containing a small cavity alone remains. In the cavity organisms are present probably in very small numbers as is shown by the failure of cover-slip preparations and the small number of colonies developing in cultures.

If, however, the nodule is excised at the height of the process, signs of active inflammation are obtained—an exudation of serum and white-blood corpuscles having taken place, as well as an infiltration of the adjacent connective tissue with leucocytes. The micro-organisms are abundantly present, being seen in cover-slips, and developing luxuriantly upon cultures, while sections from the lesions stained by the Weigert method reveal them in large numbers.

Rabbit.—One rabbit was inoculated intravenously with 1 cc. of a 36-hour plain bouillon culture. The animal developed no evident symptoms and remained apparently well for five months.

Guinea-pigs.—Six guinea-pigs were inoculated without result. In three the organisms were introduced subcutaneously. No induration followed at the point of inoculation. In three the inoculation was into the peritoneal cavity. No appreciable symptoms resulted. Five of these six animals died at periods ranging from six days to seven weeks after the inoculations, but in none was anything to be seen at autopsy, and all cultures from the organs were negative. At the time of these experiments numerous guinea-pigs kept at the pathological laboratory died of some unknown cause, and apparently the death of these animals was not due in any way to the organisms introduced.

Mice.—White Mouse I. Inoculated subcutaneously with 0.3 cc. of a suspension made in sterile bouillon, from agar growth. On the second day the mouse appeared ill, sat in the corner of the cage, refused to eat and scarcely moved when the cage was shaken. Death took place on the sixth day. At the point of inoculation there was an area 0.5 cm. in diameter, raised, soft, and gelatinous in consistency, and paler than the surrounding tissues. This involved the subcutaneous tissue and muscle. On section the intestines were hæmorrhagic and the spleen enlarged. The other organs appeared normal.

Smear preparations from the point of inoculation showed abundant oval and long forms of the micro-organisms, the latter varying from two to four microns in length. These stain irregularly, having usually a more or less clear area at one end. The same forms were present in smears from the lungs and liver, but in much smaller numbers. Those from the peritoneal cavity, spleen and heart's blood were negative.

Cultures from the local lesion, lung and liver showed the micro-organism in pure culture. The culture from the spleen was contaminated, while those from the kidney and heart's blood remained sterile.

Microscopical examination of the tissues.—Point of inoculation. The subcutaneous connective tissue is infiltrated with large numbers of the organisms situated in clumps, some around the blood-vessels, and others having no apparent relation to the blood-supply. The leucocytes are fairly abundant, and often contain several organisms within their protoplasm. Numerous larger phagocytic cells appear. Deeper down in the tissues the organisms are very abundant, and lie in large masses between the muscle bundles. The organisms do not invade the muscle, and there is no apparent increase in the muscle nuclei. Sections stained in hæmatoxylin and eosin show hyaline degeneration of the muscle fibres.

Liver.—In the liver many organisms appear in the larger blood-vessels and capillaries. Throughout the organ are minute focal necroses and degenerated liver cells, the organisms being in the capillaries of the diseased area and occasionally within the necrosed liver cells, and in leucocytes. The organisms have the same characteristics as those above described.

Sections of the lung and spleen appear normal except for the presence of the organisms in small numbers both within and without cells. They appear for the most part in small clumps containing numerous elements, but also occur here and there singly.

No pathological changes were made out in the kidney sections and no organisms could be demonstrated.

Lymphatic glands.—The lymphatic structures throughout the body showed the most striking and characteristic appearances. The organisms were readily demonstrable in the peribronchial, perinephritic and peritoneal glands, which contained immense numbers of them. They presented the same characteristics as before, and occurred for the most part outside of and between the lymphatic cells, although at times they are seen within the cells (Plate II, Fig. 4).

White Mouse II. Inoculated in a manner similar to Mouse I. Death occurred on the 10th day. The autopsy revealed

the same soft, semi-caseous area at the point of inoculation and a similar hæmorrhagic condition of the intestines.

The microscopical findings were the same as in the previous experiment.

Mouse III. A wild mouse was inoculated with 0.3 cc. of a 36-hour bouillon culture. Animal appeared to be unaffected until the fourth week, when it became less active and refused to eat. Died on the 38th day. Around the point of inoculation there was a very extensive induration, the tissues being hard, shrunken and dry. This sclerosed condition involved the whole posterior third of the back extending down the thighs and to the root of the tail. Internally the intestines were adherent and the testicles involved in the cicatrix.

Cover-slips and cultures were negative.

Microscopical examination of the tissues removed from the local lesion showed exceedingly dense scar tissue. No organisms were demonstrated. Examination of the organs was negative.

SUMMARY.

The condition in the human subject reported here seems sufficiently unusual to warrant publication.

It is further of interest in view of the evidence given, which would indicate that the skin abscesses and indurated lymphatic glands were due to infection with a micro-organism, differing markedly from the bacteria, but agreeing with certain of the fungi.

The cultural characteristics of the organism are similar to those of many fungi and yeasts, and the imperfect life history which could be determined renders it not improbable that it may belong to the genus *sporotricha*. But for the present the exact classification of the parasite must be left undecided.

The experiments upon the dog and the mice prove the pathogenicity of the organism, and indicate that, under different circumstances, it may remain local in its development and effects (dog), or it may invade the internal organs and produce a sort of pyæmia (mouse).

The etiology and pathology of many fungoid affections in man and animals receive a new interest in the light of the more recent studies of the pathogenic yeasts and their possible relation to tumor formations. It may be mentioned that the pathological conditions met with did not in any instance suggest any other than a simple inflammatory process.

I take pleasure in acknowledging my indebtedness to Dr. Flexner for advice and assistance in the course of the study recorded here.

EXPLANATION OF FIGURES.

Plate I.

Fig. a. Colonies of 10 days. Glucose agar. From lung of white mouse I.

Fig. b. Growth on glucose agar. 3 days. Photograph by Dr. J. F. Mitchell.

Fig. c. Cover-glass preparation from glucose agar. × 1000. Photograph by A. H. Eggers.

Figs. 1 and 2. Growth in hanging drop of bouillon. 60 hours.

Fig. 3. Same. 4 days. Reproduced from camera sketches by Dr. E. F. Smith.

Figs. 4 and 5. Cover-glass preparations from bouillon.

Fig. 6. Swollen and germinating conidia, from hanging drop of bouillon. 30 hours.

Fig. 7. Germ tubes with conidia attached, from hanging drop of bouillon. 3 days.

Plate II.

Figs. 1, 2 and 3. Sections of wall of abscess in subcutaneous tissue dog. Leitz obj. $\frac{1}{6}$ (Fig. 1), $\frac{1}{8}$ (Fig. 2), and $\frac{1}{12}$ (Fig. 3).

Fig. 4. Peribronchial lymph glands of white mouse. Carmine and Weigert's stain. Leitz obj. $\frac{1}{7}$ inch.

ŒDEMATOUS CHANGES IN THE EPITHELIUM OF THE CORNEA IN A CASE OF UVEITIS FOLLOWING GONORRHŒAL OPHTHALMIA.

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Oedema of the corneal epithelium with various changes and distortions of the epithelial cells due to pressure of fluid in the intercellular spaces, has been observed by many workers in the pathology of the eye, and has been described and depicted more or less thoroughly since Arlt's[1] original observations in 1855. He described the œdematous changes taking place in the corneæ of eyes affected with choroiditis accompanied by increased intraocular tension.

Fuchs,[7&8] Fridenberg,[6] Birnbacher and Czermak,[3] Klebs[12] and other observers have seen these changes occurring in glaucomatous and staphylomatous eyes.

Some experimental work has been done; Leber, Gutmann, and others have produced artificial œdema in the corneal epithelium. Leber[13] succeeded by injecting oil of turpentine under the anterior epithelium in producing, without any roughening of the surface, a corneal opacity which closely resembled the haze of glaucoma. On microscopical examination he found numerous vacuoles in different layers of the epithelium with a pronounced dilatation of the intercellular spaces. More recently, Gutmann[5] by injections of a solution of asphalt in chloroform, demonstrated a communication between the lymph spaces of the corneal matrix and the finer system of channels in the anterior epithelium, and produced a condition similar to that found by Leber.*

The corneal œdema of glaucomatous eyes (causing haziness and the appearance of rainbow colors around a flame at night)

*Bizzozero,[4] in his excellent article, first demonstrated the presence of a series of intercellular spaces or clefts forming a system of minute channels for transporting nutritive fluids to the individual cells and containing a small amount of viscid cement substance. Pflüger[14] and Gruber[10] have also described the nutrition of the corneal epithelium through these channels.

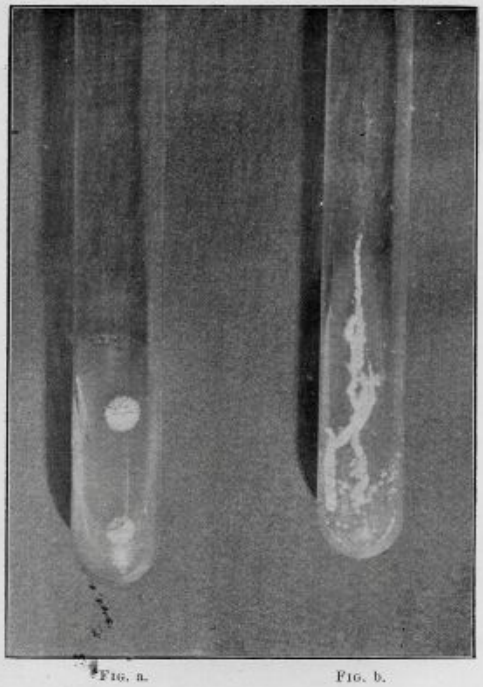


Fig. a. Fig. b.

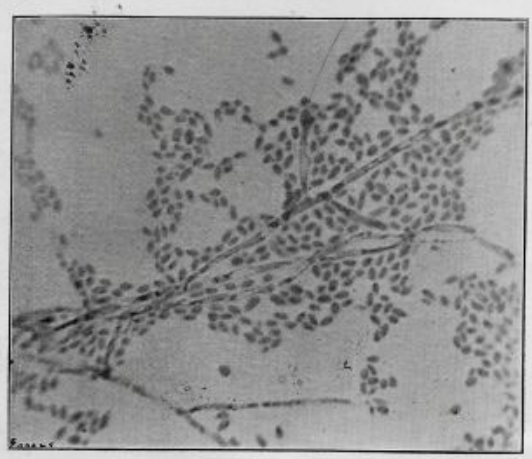


Fig. c.

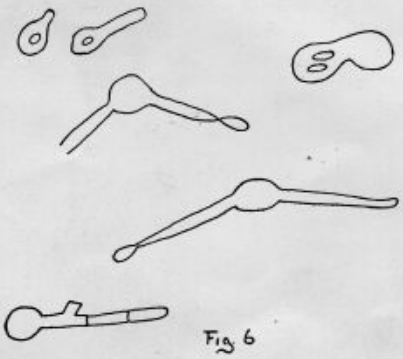
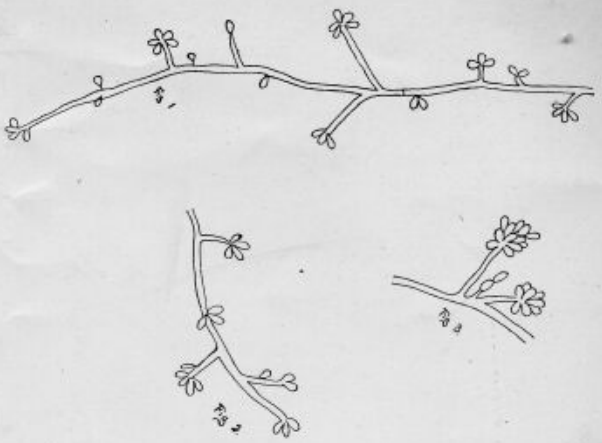


Fig 6



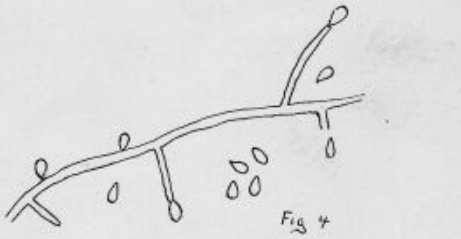


Fig 4

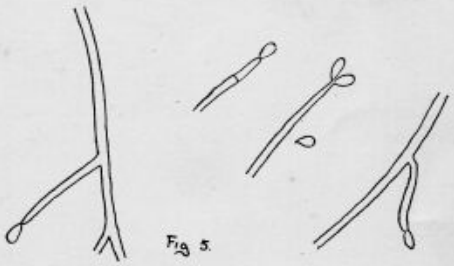


Fig 5.

Fig 7

PLATE I.—To face p. 220.

FIG. 1.

FIG. 2.

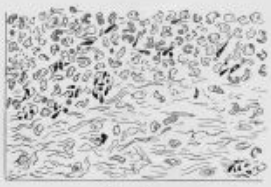


FIG. 3.

Sections from local lesion.—Dog.

FIG. 4.

Peribronchial lymph glands.—Mouse.