

fusion with acromegaly, except in congenital cases. Rickets is pre-eminently a disease of impaired bone formation, as manifested by the slow eruption or entire absence of the teeth and by the impaired growth or softening of the bones; while acromegaly, on the other hand, is pre-eminently a disease of increased bone formation.

The ends of the bones, especially the epiphyses of the wrist, unquestionably are enlarged in rickets, while the hands and feet may be flattened and apparently widened, but there is no increase in the thickness of the hands or feet. The bones of the head show no malformation, except flattening and lengthening of the cranium with projection of the occiput and the softened spots. This causes the cranium in rickets to appear too large for the face, while in acromegaly the face appears too large for the cranium.

Also in rickets we find deformities of the pelvis, and if the child creeps, deformities of the arm bones, and if he walks, bending of the leg bones. This is quite different from acromegaly, in which we have widening, hardening, and general growth of the bones. Softening of the ribs causes a sinking in just before the junction with the cartilages, giving the formation of the rachitic rosary, which from another cause we also find in acromegaly. Kyphosis, when it occurs in rachitis, is in the dorsal region, while in acromegaly it is almost invariably in the cervico-dorsal region. It is thus seen that it is hardly possible to confound the one disease with the other.

The diagnosis between the *osteitis deformans* of Paget and acromegaly is generally not difficult.

The following schedule shows some of the marked differences:

<i>Osteitis Deformans.</i>	<i>Acromegaly.</i>
1. Rarely occurs before fifty, never before forty years of age.	1. Very generally begins before forty years of age, almost never after fifty.
2. The long bones are the ones primarily affected; rarely are the hands or feet affected.	2. The hands and feet are enormous; long bones are generally not much affected.
3. The long bones are often curved, giving great deformity.	3. The long bones are normal in shape, possibly thickened at the extremities, but are never curved.
4. Often one limb or one bone is affected long before another limb or bone.	4. The hands, feet, arms, and legs are generally nearly symmetrical.
5. The cranial bones are affected, rarely the facial.	5. The facial bones are affected, rarely the cranial.
6. The lower part of the face is narrow, giving it a triangular appearance.	6. The lower part of the face is broad, giving it an elliptical appearance.

The above gross differences, to say nothing of the more minute ones, will generally render easy the diagnosis of *osteitis deformans* from acromegaly.

*Arthritis deformans*, perhaps, approaches more nearly than any other bone disease to the external conditions found in acromegaly. In *arthritis deformans* decided changes take place in the articular tissues, and are accompanied by pain, with sooner or later great deformity and ankylosis of the joints. Tender nodules may appear in the muscles, while the muscles themselves become atrophied. The disease is apt to attack the same joints on both sides of the body symmetrically, but soon spreads to all of the joints. The hands are thin from the wasting of the fat and muscles, but the ends of the phalanges and metacarpal bones may be enlarged and nodular. The fingers are more or less flexed and turned toward the ulnar side of the arm, while the joints of the hand are all stiff and more or less completely ankylosed. How different is this condition from the acromegalic hand!

Within the joints bony or cartilaginous protuberances are found on the outer surface of the epiphyses in *arthritis deformans*, while in acromegaly we may find osteophytes at the ends of the bones, or bony growths in the joints. Aside from this similarity in the joint lesions these two diseases show no agreement of symptoms or appearances. The hypertrophy of the soft parts of the hands and face, with the enlargement of the bones of the face, with the cervico-dorsal kyphosis, enlarged tongue, changed voice, and signs of pituitary enlargement, will all or any of them render the diagnosis from *arthritis deformans* easy.

Schulz has reported a case of acromegaly associated with arthritis deformans.

The condition known as *pulmonary hypertrophic osteoarthropathy* must be carefully separated from acromegaly, as it simulates the latter disease by causing an enlargement of the hands and feet. This osteoarthropathy is subsequent to, or consequent on, some affection of the lungs, which may be a bronchitis, an emphyema, or perhaps most frequently some new growth located primarily or secondarily somewhere in the respiratory tract.

The hands are enlarged, but principally in the joints and the ends of the fingers, the middle of the hand not being attacked. The elbow, shoulder, and knee joints are all affected, and there is always more or less impaired motion. The wrist joint is large, the hand proper not much enlarged, while the fingers are increased in size, especially the last phalanx, but the soft parts are not hypertrophied. The appearance of the finger nails is also quite characteristic of this disease. They appear too large for the fingers, spreading out at the sides, and even curving over the ends of the fingers, often giving the appearance of the beak of a bird, while the enlarged ends of the fingers have caused them to be likened to "drumsticks." Turning to the acromegalic hand, with its immense thickening of the hand proper, hypertrophy of the soft parts, equally enlarged phalanges, sausage-shaped fingers, small nails, much too small for the fingers, one might make the diagnosis by the hand alone. The bones in pulmonary hypertrophic osteoarthropathy are enlarged, but not the soft parts, while in acromegaly both are enlarged. In the former disease dorso-lumbar kyphosis may be present, while in acromegaly the kyphosis is cervico-dorsal.

The feet and toes in this disease are affected similarly to the hands. The face presents a different appearance from that of acromegaly; it is more rounded, the lower jaw is very rarely enlarged, prognathism does not occur, the face appears small, the soft parts are not hypertrophied, and the lips and tongue are normal in size.

*Local hypertrophies* are not instances of partial acromegaly. These local enlargements of one extremity, or one finger, or one toe are generally congenital, though they may increase in size at the time of puberty. One side of the face may be affected, involving the bones and soft parts, including the tongue, tonsil, and palate on that side, but whatever the enlargement there is no symmetry.

One more disease remains to be diagnosed from acromegaly, viz., *adiposis dolorosa*. This disease is characterized by an enormous deposit of fat, first in the form of nodules, either in one location or in corresponding places on the upper or lower extremities. These deposits soon cause pain, diminished sensibility, and muscular weakness, and the muscles may show the reaction of degeneration. The absence of any marked enlargement of the hands, feet, and face, as well as the absence of increased bone growth, excludes confusion with acromegaly.

**PROGNOSIS.**—The duration of acromegaly is variously estimated from ten to twenty years. The patient may die of some intercurrent disease, or may live for years with but a slow progression of the disease, but no case of complete recovery has yet been reported.

This disease is one of continuous progression, especially in the growth of the bones. Under treatment, or without treatment, periods of apparent quiescence or periods of cessation of symptoms occur, and the soft parts of the hypertrophied portions of the body not only may not enlarge, but may actually appear to be diminished in size. Yet even in such cases the bones apparently continue to grow.

These periods, when the patient may say that he feels well, are sooner or later followed by marked exacerbations of all the symptoms, often coming on suddenly. These symptoms, all of which may be ameliorated by treatment, are severe headache, often dizziness, obstinate constipation, troublesome dyspepsia, aggravated eye or ear symptoms, great temporary loss of strength,

and melancholia, with more or less pain referred to various parts of the body. At this time the soft parts on the hypertrophied portions of the body appear larger, although œdema may not be found.

A more or less complete recovery from these exacerbations, or severe symptoms, generally occurs, but the patient is not quite as well in all respects as he was before. Thus the disease proceeds, with some symptoms more or less constant, until there is hardly a tissue or organ of the body that is not affected in greater or less degree.

Finally, little by little the patient falls into a condition of progressive cachexia, with partial or nearly complete loss of muscular power, due to atrophy of the muscles, so that he may be compelled to remain in bed. This condition may last for several years, and then death occurs unexpectedly and suddenly from syncope.

It is possible that an enlarged pituitary body may cause coma and death. Most cases of acromegaly, however, die of some intercurrent affection, the most frequent of which are cardiac disease, nephritis, or diabetes, all of which are the results of the connective-tissue hyperplasia of the involved organs, viz., heart, kidney, and pancreas respectively.

The headache and cerebral disturbances may become so severe as to cause suicidal tendencies, and temporary insanity may occur, probably caused by pressure from an enlarged pituitary body.

**TREATMENT.**—This disease is incurable, but in any given case we can safely expect to ameliorate many of the nervous symptoms. When there is an exacerbation of symptoms, of all treatment rest is the most important, under which all the phenomena, except those produced by actual lesions, will improve. Pain, the most frequent cause of complaint, has been variously treated by all of the analgesics, but with only temporary and varied success. The bromides are often of service in relieving the headache and the feeling of pressure in the head.

The constipation should be treated, while dyspepsia, when present, can be best helped by a diet that requires but little mastication, as prognathism, which is so frequently present, is one constant cause of the dyspepsia.

Positive impairment of sight or hearing cannot be improved, and if the sight is affected at all the loss of vision will probably increase. Tinnitus aurium, if due to this disease, can probably be but little, if at all, helped.

Any tonic or bracing treatment, combined with rest, will often cause a cessation of the acute symptoms and an apparent pause in the disease, except in the last stages.

If there is atrophy of the muscles and great loss of muscular power, strychnine, given by the mouth or hypodermically, is of value, especially when combined with faradism.

Cardiac insufficiency and renal insufficiency should be treated as though they were primary diseases, without regard to the acromegalic condition.

The treatment of glycosuria should be cautious, i.e., the true diabetic diet should be assumed with care, if at all. If diabetes is present, the patient might be fed on pancreas, as in acromegaly diabetes seems to be generally, if not always, of pancreatic origin.

The specific treatment of acromegaly undoubtedly must bear some relation to the secretion of the pituitary gland. I believe that, like exophthalmic goitre, we may have an increased pituitary secretion, or a diminished secretion, or a perverted secretion. In some cases, or at certain stages, of exophthalmic goitre we have a set of symptoms, such as great nervousness and cerebral irritation, exophthalmos, palpitation, and loss of weight. In these cases or at these times thyroid feeding will aggravate every symptom. In other cases we have dulling of the intellect, mild exophthalmos, cardiac weakness without much palpitation, muscular debility, and a putting on of weight—in other words, some of the symptoms of myxœdema, due to a diminished thyroid secretion, all of which symptoms ameliorate with thyroid feeding.

During the stage of almost imperceptible, gradual, and perhaps symmetrical growth of the bones, pituitary feed-

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would probably be of no benefit, and might even aggravate or precipitate unpleasant symptoms, such as headache. But when a case of acromegaly comes into our hands for treatment the hypophysis disease has progressed far enough to give nervous symptoms and selective enlargements so typical of the disease. At this time we are probably having a diminished amount of normal secretion or a wholly or partially perverted secretion from the hypophysis, causing terrible headaches, irregular nerve and muscle pains, vasomotor disturbances, muscular weakness, cardiac weakness, and perhaps severe cerebral irritation. For this condition and at this time pituitary substance will, I believe, often, if not always, be found of marked benefit.

In a case of acromegaly that I am now treating I have obtained good results from pituitary tablets, the dose varying from six to twelve grains a day. In this case the headache, which had been continuous for two years, is now but rarely present. While under the treatment the appetite improves, the muscular weakness disappears, the nervous restlessness is gone, and the patient is able to do her usual work, which she was not able to do before the use of the pituitary substance. Also, the hypertrophy of the soft parts of the face, hands, and feet greatly diminishes. On stopping the treatment, the headaches and muscular weakness again develop, and the face and hands very noticeably again increase in size.

It is probable that in the cases in which the thyroid gland is pathologically so changed that it cannot furnish its normal secretion, as denoted by mild myxœdematous symptoms, the feeding of thyroid extract might be of some benefit.

I do not believe that any treatment other than the above, and general tonic and hygienic treatment, is of any avail in this disease.

Oliver T. Osborne.

**ACTINOMYCOSIS.**—This disease is a combination of abscess formation and new growth of connective tissue. In most cases the disease has the character of a subacute or chronic suppurative process, but in some cases the new growth of connective tissue may be so marked a feature of the process that it may present the character of a tumor or neoplasm. The disease affects man and certain domestic animals, particularly cattle, in which it is probably best known. It has a wide geographical distribution.

In cattle it most commonly affects the jaw bones, where it may take origin in the medulla or the periosteum, and may lead to the tumor-like conditions which have been long known as medullary sarcoma or osteosarcoma of the jaw, or as "lump jaw," etc. The external soft parts about the jaws and face, the tongue, the peripharyngeal tissue, the stomach, the skin, and the subcutaneous tissues in various places, may also be the seat of the disease. Anatomically, the lesions consist in general of an overgrowth of granulation and connective tissues, throughout which are distributed, more or less numerously, small, yellowish, soft suppurative areas or abscesses. If the seat of the lesions be the jaw, there is usually more or less new growth of bone as well.

In swine the mammae, the peripharyngeal tissues, the vertebrae, and the spleen have been observed to be the seat of the disease. In horses the disease may occur in the spermatic cord after castration, as well as in the jaw bones and in the bones of the extremities. A few cases of the disease have been observed in dogs.

In man the disease is probably more common than is generally supposed. It most frequently affects the tissues in and about the oral cavity, the pharynx, and the neck. It also frequently affects the lungs, the bones of the thorax, and the intestinal tract. Almost any organ or part of the body may become the seat of the disease. Anatomically, the disease in man is essentially a destructive suppurative process accompanied by a new growth of connective tissue which in general is not as abundantly developed as in the disease in cattle, so that in man the tumor-like lesions are less frequent.

The disease is due to the action of a vegetable parasite

upon tissues which are suitably susceptible. This parasite is an organism closely allied to the bacteria, but belonging to a higher class. It occurs in the lesions, and in the discharges from them, as small aggregations or

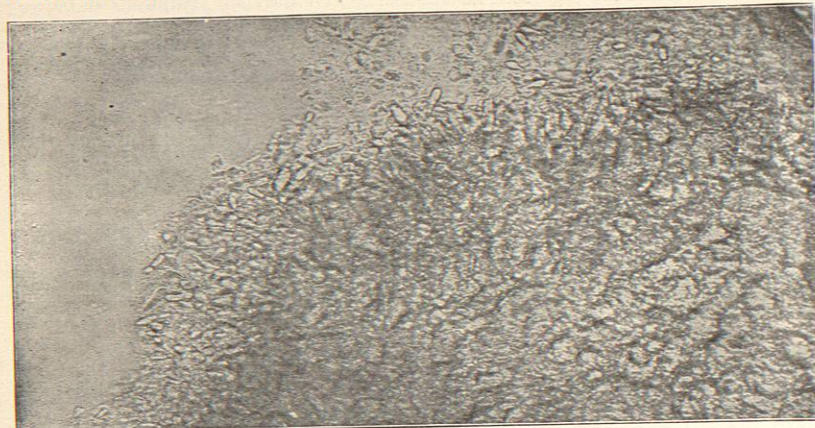


FIG. 28.—Portion of the Margin of an Actinomycotic Granule, crushed under a cover glass, as it appeared under a moderately high magnifying power. Various forms and appearances of the "clubs" are shown.

colonies, of variable size, which in most cases are visible to the naked eye as grayish or yellowish granules or lobulated bodies, less than 1 mm. in diameter. The presence of the peculiar granules in the lesion or in the pus is characteristic and diagnostic of the disease. As a rule they are soft, and when placed on a slide and covered with a cover glass, they are flattened or crushed by the weight of the latter. In some instances, especially in cases in cattle, they may be more or less calcified. Under a low magnifying power a granule crushed beneath a cover glass will appear as an aggregation of lobulated hyaline masses, with rounded, finely serrated borders which may have a slightly brownish tint. In some instances a fine radial striation may be made out at the margins. As a rule masses of pus cells will be found surrounding the hyaline masses and making up a portion of the bulk of the granules. Under a higher magnifying power the hyaline material in places will have the appearance of being made up of a dense feltwork of delicate filaments having the diameter of bacilli of moderate size and closely packed together. At the margins these filaments usually have a radial arrangement, and some of them project beyond the limits of the hyaline mass. In the case of some granules, the margin of the hyaline mass may be formed of a row of closely set, elongated, finger-shaped, or club-shaped, or bulb-shaped bodies, composed of a hyaline substance and arranged radially (Figs. 28 and 29). These bodies constitute the so-called "clubs" or "rays" on account of which the name "ray fungus" has been applied to the parasite. They are of variable size and width, often being three or four times the width of the filaments. In stained preparations a stained filament may often be seen in the median portions of the "clubs" or "rays," which for this and

other reasons are regarded as modifications of the marginal filaments (Fig. 29). In fact, it seems very probable that these bodies are nothing more than the results of degeneration of the marginal filaments, as has been pointed out by Boström ("Beitrag zur path. Anat. u. allgem. Path.," Ziegler, bd. ix., 1890). The "clubs" are much more frequently found in the granules from lesions in animals than in those from man. If one of the granules be broken up on a cover glass and suitably stained there will be seen on microscopical examination, besides long filaments which branch, short rod-like or bacillus-like or coccus-like forms (Fig. 30). At the present time it is considered that the bacillus- and coccus-like forms are the result of degeneration and of breaking up of the filaments. Some writers seem to think that the presence of the "clubs" or "rays" is a constant and necessary feature of the granules of genuine actinomycosis, and so they call those cases pseudo-actinomycosis in which granules are found which have little more

to distinguish them from true actinomycosis than the absence of these bodies. In view of the fact that in one and the same case granules, both with and without "clubs," may be found, it seems probable that the so-called pseudo-actinomycosis is really not distinct from the true disease.

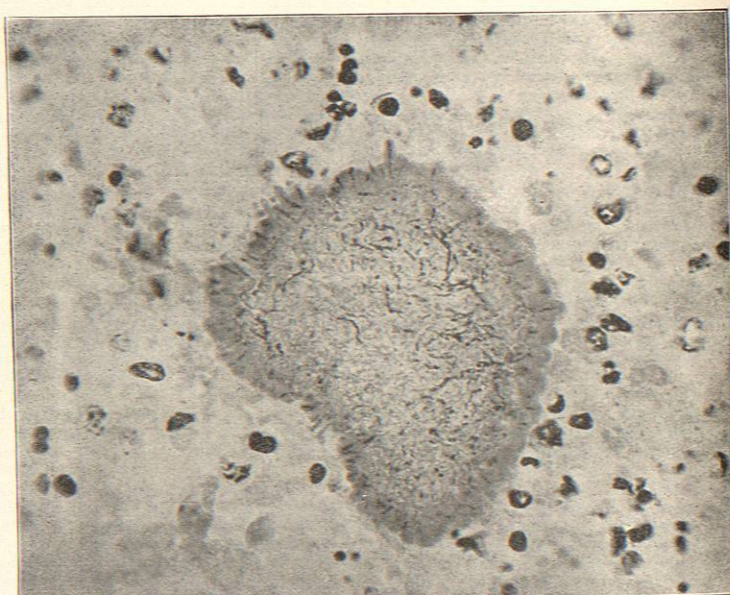


FIG. 29.—A Granule or Colony of Actinomyces, in a section about two micromillimetres thick, showing the "clubs" with central filaments at the margin. The general structure of the colony is shown also. From an abscess in the heart in a human case.  $\times 750$ .

Microscopically, the lesions consist of larger or smaller abscesses, each containing one or two of the granules or colonies, and bounded by connective tissue, in all grades of development (Fig. 31). In the latter, giant cells may

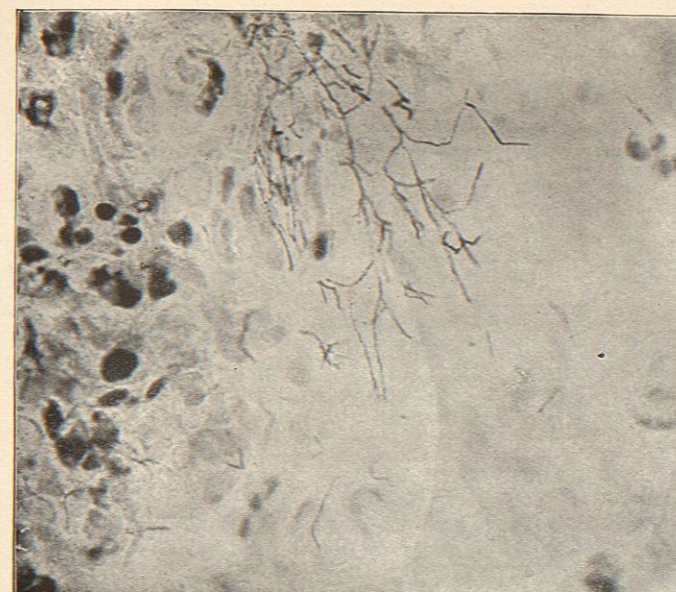


FIG. 30.—A Cover-Glass Preparation Made from a Granule. Some rods and branching filaments in association with pus cells are shown.  $\times 1,000$ .

be present. A granule in a section stained by Gram's method appears as a mass of filaments embedded in a hyaline material and showing at the margin more or less radially arranged filaments, or the "clubs" or "rays" previously described (Figs. 29 and 32). The hyaline material seems to be composed in many instances of non-staining degenerated filaments. In other instances the nature of this hyaline material is not clear, but it is very probably the result of degenerative processes in the colony. It is not uncommon to see bacillus-like fragments of the organism in or among the pus cells surrounding the colony. The pathological significance of the granules in the lesions of the disease was first clearly shown by Bollinger in 1877, although their presence had been noted previously by several observers whose work was incomplete and did not receive general recognition. Bollinger regarded the granules as growths of a fungus and as the essential cause of the disease. Harz, a botanist, confirmed Bollinger's ideas of their fungous nature and called the organism "actinomyces bovis," a

name that has clung to it ever since. The disease in man was first recognized and identified as due to the same cause as that found in the disease in cattle by Ponfick a short time after Bollinger's publication. The granules, however, had been seen in a suppurative process in the neighborhood of the vertebrae in man by Langenbeck in 1845, and had been described and figured by Lebert in his "Atlas of Pathological Anatomy," published in 1856.

Many untrustworthy observations have been published concerning the cultural peculiarities of "Actinomyces bovis." It is commonly stated in text-books that culture methods have shown that various pathogenic species of this parasite are known, but the writer considers that the observations upon which these statements are based are open to serious question.

According to Wolff and Israel (*Archiv f. path. Anat.*, Virchow, 1891, Bd. 126), the organism grows on agar practically only in the absence of oxygen. Cultures made by breaking up the granules and spreading the fragments over the surface of the agar begin to show the growth of colonies after about three days. Some days later the colonies may have attained the diameter of 2 or 3 mm. They are grayish white in color, rounded in outline, with wavy margins in some instances, and often have an elevated nodule in the centre.

In bouillon, growth may be obtained without the exclusion of oxygen. Granules planted in this medium become larger in the course of a few days. The growth then appears as a sediment at the bottom of the culture tube, composed of opaque, whitish, irregular granules, usually less than

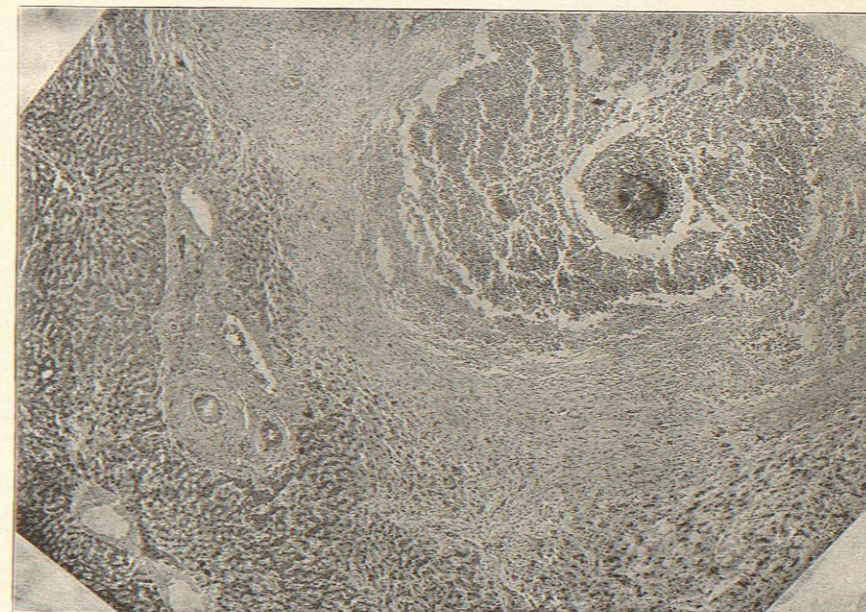


FIG. 31.—Section of a Portion of an Actinomycotic Lesion in the Liver of the Same Case as That Mentioned in Fig. 29. The abscess, containing a "colony" or "granule," and the surrounding connective-tissue growth extending into the liver substance, are shown. The "colony" appears as a rounded, dark mass in the right upper quadrant of the figure. Low magnifying power.

1 mm. in diameter. The granules are often conglomerated into irregular masses. The bouillon is never clouded if the growth is not contaminated.

Microscopical examination of the growth in the culture shows longer and shorter rods and threads, the last mentioned sometimes branching. The organism stains irregularly, and often shows rounded or club-shaped swelling or other irregularities in shape, especially at its extremities. It does not altogether preserve its filamentous character in the cover-glass preparations from the cultures. This is probably due to the fact that the filaments are broken up in the manipulation. An additional peculiarity of this organism is the presence of deeply staining rounded or oval bodies in the rods and threads. These are of about the same diameter as the rod, and are frequently

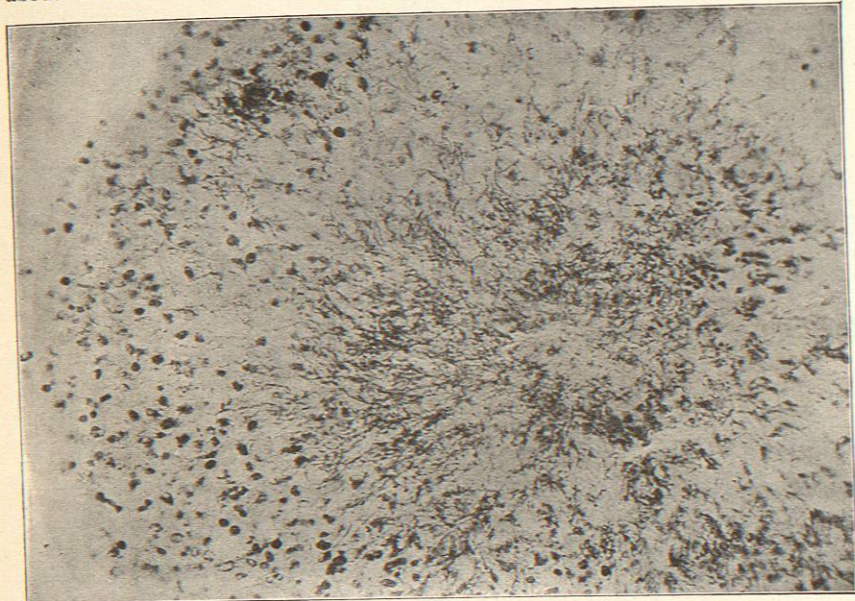


FIG. 32.—A Colony of Actinomyces in a Section of the Same Lesion as in Fig. 29. This is a colony composed of filaments and hyaline substance. There are no "clubs." X 500.

distributed along the length of the rod or filament at variable intervals. Their nature and function are not understood.

Animal inoculations with actinomyces at the hands of various investigators have not led to conclusive results. Max Wolff and James Israel (*loc. cit.*) in 1891 published the most interesting work that has ever been done on this subject, but their results lack confirmation.

The exact position of the organism in the botanical world is still a matter of discussion, as is also the name of the group of micro-organisms to which it belongs. On account of its branching it is to be regarded as belonging to a more highly developed group than the bacteria, while it is not so highly developed as to be classed with the moulds or hyphomycetes. The tendency at the present time is to call it and similar branching organisms "streptothrices." Of such organisms a small number have been more or less satisfactorily described, some of which have been met with in inflammatory processes. The precise relationship of these to actinomyces bovis is not very clear at the present time.

The most frequent seat of primary actinomycosis in man is the tissues about the buccal cavity and the neck. Primary actinomycosis of these parts forms more than half of all the recorded cases. Next in frequency is primary actinomycosis of the digestive tract and of the lungs.

Primary actinomycosis of the outer skin, exclusive of the skin of the face and neck, is less frequent. Ruhrah (*Annals of Surgery*, October, November, December, 1899, vol. xxx., Nos. 4, 5, 6), who has collected all the reported cases that he could find in the literature, gives the following figures: Total number of cases, 1,094, including certain cases probably counted more than once. In these cases the disease affected the head and neck in 56 per cent., the digestive tract in 20 per cent., the lungs in 15 per cent., and the skin in 2 per cent; 6 per cent. are classified as doubtful. Various cases have also been recorded of actinomycosis of various organs, including the brain, without any demonstrable primary lesion in the situations above mentioned.

The infecting organism is probably frequently carried into the tissues along with foreign bodies, especially such as occur in food material in the case of cattle. The not infrequent finding of such foreign bodies in or near the lesions of the disease, and the observations of the increase of the disease in herds of cattle when a change has been made in their food, as also the very frequent localization in the neighborhood of the mouth, pharynx, etc., support this idea. No one, however, has satisfactorily demonstrated the parasite outside of the lesions, and we know nothing definite concerning its habitat in the outer world. There is evidence that the infection may be transmitted from animals to man or from one individual to another.

Actinomycosis in man is distinguished from the disease in cattle not only by a less extensive new formation of connective tissue, but also by its greater tendency to the formation of fistulae and sinuses, by which the disease may extend widely from one organ to another. Such sinuses may extend from the tissues about the mouth or pharyngeal cavities deeply into the thorax and along the spinal column (prevertebral phlegmon). In actinomycosis of the lungs fistulae may perforate the chest wall or go through the diaphragm into the abdominal cavity. In actinomycosis of the intestines fistulae may form which usually perforate the anterior abdominal wall; they may, however, extend through the lumbar region or into the rectum or bladder. The disease may also extend metastatically through invasion of the blood stream by the organism, and in this way various organs at a distance, such as the heart, brain, kidneys, etc., may become the seat of the disease. Only rarely does it spread by the way of the lymphatics. Secondary infections with pyogenic cocci may occur.

The clinical course and prognosis of the disease depend upon its extent and localization, and upon the occurrence of secondary infections with the pyogenic cocci. The last mentioned is an unfavorable complication. In extensive involvement of internal organs there may be fever and marked disturbance of nutrition. In localizations about the buccal cavity and neck there is good evidence that many of these cases will heal by the simplest surgical treatment or even spontaneously. Probably many such cases go unrecognized. The bones of the jaw are rarely affected in man. The occurrence, in the soft parts

of the neck or cheek near the jaw, of hard swellings which have arisen painlessly and present a fluctuating or suppurating focus, should excite suspicion of actinomycosis.

Actinomycosis of the lungs in general resembles chronic pulmonary tuberculosis. The affection may last for months or years. It is characterized by cough, by much sputum, which is often fetid or bloody, and by marked pains in the breast and back. There are also irregular fever and progressive emaciation. Fistulae perforating the chest wall and involving the sternum or ribs are not infrequent. In this the disease differs radically from tuberculosis of the lungs. The prognosis is generally bad. Remissions with appearances of healing occur. The process may be localized in any part of the lungs. It usually appears as small abscesses or broncho-pneumonic patches, from which cavities may be formed accompanied by new growth of connective tissue.

Actinomycosis of the intestines is characterized by extensive induration due to a marked development of peritoneal adhesions and to the extension of the process to the abdominal wall and neighboring organs. As before mentioned, the tendency to the formation of the fistulae is marked. Metastatic involvement of the liver is not unusual. The prognosis must be regarded as unfavorable in general.

Actinomycosis of the skin, according to Leser (*Archiv f. klin. Chir.*, 1899, xxxix.), may appear as a circumscribed ulcerated lesion or as a nodular formation with central cicatrizations. The subcutaneous tissue may also be affected and a chronic phlegmonous condition be produced.

One of the forms of the disease known as "Madura foot" is very probably actinomycosis of the part. This is the so-called "white" or "ochroid" variety, in which the characteristic granules in the lesions are of this color. The "black" or "melanoid" variety of "Madura foot" is due to an altogether different vegetable parasite, which is a hyphomycete (Wright: Transactions of the Association of American Physicians, 1898, *Journal of Experimental Medicine*, vol. iii., 1898).

The diagnosis of actinomycosis is made by finding the characteristic granules or colonies of the organism in the lesions or in the discharges from the same. These in some instances may be so obscure as to escape observation with the naked eye. Microscopic examination is necessary to distinguish the colonies or granules from small pieces of necrotic tissue and masses of pus cells. The pus or suspected material should be spread on a piece of glass. In this way the granules will be more easily seen. In actinomycosis of the lungs the organism may be found in the sputa and in the discharges from fistulae in the wall of the thorax. In the sputum the parasite is to be distinguished from the common leptothrix of the mouth by the fact that the filaments of the latter are larger, straighter, and thicker and do not branch as do the filaments of actinomycosis. The leptothrix filaments are also frequently adherent to epithelial cells.

The treatment of actinomycosis should be operative if the extent of the disease admits of it.

In internal treatment good results are said to have been obtained from the use of potassium iodide.

The photographs which accompany this article were made by Mr. L. S. Brown and the writer, in the Clinico-Pathological Laboratory of the Massachusetts General Hospital.

James H. Wright.

**ACTIVE CONSTITUENTS OF PLANTS. CLASSIFICATION OF.**—If this term were strictly interpreted, we should omit from consideration all but those constituents which produce positive physiological effects, other than nutritive, upon the animal system. As this treatment would exclude some substances having important medical and pharmaceutical relations, especially the latter, it is deemed better to consider briefly all plant constituents which affect the properties or uses of drugs or medicines.

Of the nutrients proper, the albuminoids may be dismissed as of neither medicinal nor pharmaceutical importance in the department of materia medica. The sugars,

inulin, starch, and cellulose, as well as the more important plant acids, are considered in their respective alphabetical order. The other principles of interest to us may be conveniently divided into the inorganic and the organic. The inorganics from this source are not treated as of importance in the modern materia medica. The vegetable compounds of iron, being readily assimilated, are probably worthy of much more study and rational employment than has been the case heretofore. Sea weeds have long been a well-known source of iodine, and some vegetable drugs apparently owe their properties largely to this element. For the rest, the value of the inorganics in drugs depends chiefly upon the presence, especially in such fruits as prunes and tamarinds, of the well-known laxative salts, the properties of which do not differ from those of inorganic origin. It is possible to obtain important cutaneous stimulant effects from the use of many vegetable substances rich in needles of calcium oxalate, although the fact has never been duly appreciated.

The organic constituents which here require attention are the vegetable acids, gums, fixed oils, resins, volatile oils, amaroids, glucosides, alkaloids, and enzymes, together with such mixtures as oleoresins, gum-resins, and balsams.

**Vegetable Acids.**—The number of vegetable acids which have been extracted from plants is very great, though only a few are found widely distributed among different plants. In the plant they serve a variety of useful purposes. Some of them, at least, act as reserve foods, being manufactured during darkness and consumed in the light, while the reverse is true of starch. They combine with organic and inorganic bases, which are thus rendered soluble and transportable. They render many fruits more palatable, thus influencing dissemination, and, on the other hand and in other cases, by their irritating or antiseptic properties they protect the plant against its enemies. Those which are of a resinous nature are thus particularly useful in preventing fermentation and decay (see Resins). Another class form an essential element in the composition of fats and are known as fatty acids (see Fixed Oils). Some of the vegetable acids, as tannic, citric, benzoic, and hydrocyanic, are of direct use as medicinal agents, while others are of pharmaceutical interest, as influencing the extraction of the associated substances. It has been claimed in numerous instances that a basic organic substance is more efficient when administered in combination with its natural acid. Many of the natural compounds of these acids are with the inorganic constituents, and it is these salts which chiefly render some fruits and vegetables laxative. The antiseptic properties which render many acids of value to the plant are made to render a similar service to man.

The acid properties of the vegetable acids are much weaker than those of the inorganic acids, so that they yield up their bases to the latter. They are also less corrosive and irritating than the latter, and they cannot perform the same service in digestion. Taken continuously or in excess, they can impair digestion or cause gastritis, and they are supposed to favor a rheumatic diathesis. Their salts are commonly more soluble than those of the inorganic acids. Their incompatibilities are in general the same as those of the latter.

**Gums** are supposed to exist as waste substances in the plant. They usually form in successive layers upon the inside of the cell wall—the process known to botanists as "mucilaginous degeneration." While these statements are true of those gums which are collected as such for medical and pharmaceutical uses, another class, occurring in such drugs as althaea, apparently act as reserve foods. These are of interest as affecting pharmaceutically the preparations of drugs. The gums are insipid, insoluble in alcohol or ether, but soluble in water to form a mucilage or an adhesive jelly. They differ in their precipitation tests, but are mostly precipitated by lead acetate and by alcohol. Their presence in an alkaloidal solution will very often prevent the precipitation of the latter by tannin and by weak solutions of metallic salts. Chemically, the gums are compounds of special acids with