

## HUMAN BOTRYOMYCOSIS OF THE LIVER \*

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The disease of horses subsequently known as botryomycosis was first described by Bollinger<sup>1</sup> in 1870. He found multiple grayish-white fibrous nodules in the lung of a horse. Areas of softening occurred within the nodules and in the pus were yellow white granules which were just visible and resembled the yellow granules of actinomycosis. Examined under the microscope these granules do not exhibit the characteristic appearance of the "ray fungus," but are composed of coccus-like bodies surrounded by a homogeneous medium, which, regarded as a capsule, collects the microorganism into a zooglea mass. On the surface of the granule are rounded projections which give it a mulberry-like form. A disease characterized by the presence of this microorganism is not uncommon in horses and in some countries, particularly in the tropics, affects the human skin. The disease in man has not been described in this country and in none of the instances observed elsewhere has it attacked an internal organ.

Botryomycosis is described in text-books of veterinary medicine.<sup>2</sup> It occurs occasionally in cattle and swine. Several writers make the statement that actinomycosis is not uncommon in cattle and infrequent in the horse, whereas, the similar lesion of botryomycosis is frequent in the horse and uncommon in cattle. Firm nodules are formed in the skin, particularly in regions where it is subjected to continued rubbing of the harness; for example, below the collar, and after the skin has broken and pus is discharged, infection is transferred to other parts of the skin exposed to like friction, the microorganism being, presumably, rubbed into the ducts of cutaneous glands. Infection of wounds occurs and the development of a slowly growing fibrous tumor or botryomycoma has been repeatedly observed in geldings at the site of the cut end of the spermatic cord. Botryomycosis occurs in organs not obviously exposed to infection, for example, the udder.

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1. Bollinger: *Mycosis der Lunge beim Pferde*. Virchows Arch. f. path. Anat., 1870, xlix, 583.

2. Hutya and Marek: *Pathology and Therapeutics of the Diseases of Domestic Animals* (Translation). Chicago, 1912; Kitt: *Lehrbuch der pathologischen Anatomie der Haustiere*. Stuttgart, 1906-1910.

The newly-formed mass of fibrous tissue is usually situated in the subcutaneous tissue, but may extend into the muscles. Tumor-like masses, weighing from 30 to 60 pounds, are described. The lesion arising at the cut end of the spermatic cord may extend along the inguinal canal to the peritoneum. The swelling consists, in large part, of dense fibrous tissue, but all the elements of an infectious granuloma, including epithelioid and giant cells, are represented. Formation of pus occurs particularly about the colonies of microorganisms, and fistulous suppurating canals often penetrate the lesion and open on its surface. Numerous nodules may be formed in the skin near the primary lesion. Regional lymphatic nodes may enlarge and form foci of suppuration, but more frequently the lymphatics and lymphatic nodes are unaffected.

Botryomycosis of the horse occasionally occurs in the internal organs and is usually secondary to infection of the skin or of a wound. Primary botryomycosis of internal organs has been observed rarely. Secondary nodules have been found in the kidneys, liver and spleen, in bones and in other organs usually in association with infection of the spermatic cord. Simultaneous development of the lesion in a number of organs has been observed in several instances.

Peculiar to botryomycosis are the minute yellowish-white lobulated or mulberry-like granules composed of cocci held together by a homogeneous material which is often conspicuous as a clear layer at the periphery of the body, the whole having the appearance of a colony of micrococci. W. Ernst<sup>3</sup> points out that the smallest masses of cocci are not surrounded by the encapsulating material which stains with acid dyes such as eosin or picric acid, but form this material at a later stage. The rounded projections on the surface of these bodies giving them their mulberry-like form are produced by multiplication of cocci within the capsule, distending and rupturing it at certain points, for in favorable sections he found bacteria uncovered by the homogeneous material projecting through this otherwise intact medium.

To the peculiar colony-like structure which has been described, Bollinger, finding it in the lung, gave the name *Zooglea pulmonis equi*. Rivolta<sup>4</sup> subsequently rediscovered the same microorganism in a tumor from the cut spermatic cord of a horse, and considering it analogous to *Actinomyces*, gave it the name *Discomyces equi*. Johne<sup>5</sup> found the microorganism in a fungoid growth from the spermatic cord of a horse and in nodules of the skin, and recognizing its coccus form, called it *Micrococcus ascoformans*. In 1886, Rabe<sup>6</sup> first described cultures and inoculation

3. Ernst, W.: Centralbl. f. Bakteriolog., 1908, xlv, Part 1, 121.

4. Rivolta: Giorn. di anat. e fisiolog., 1884, x, 10. Quoted by Baumgarten.

5. Johne: Ber. über d. Vet. in Königh. Sachsen für 1884; Dresden u. f. 1886 and 1887. Quoted by Galli-Valerio.

6. Rabe. Deutsch. Ztschr. f. Tiermed., 1886, xii, 137. Quoted by Galli-Valerio.

experiments made with material obtained from the lesions of the horse. The micrococcus which he obtained formed silvery gray colonies, and these later assumed a yellow tint; an opaque yellow layer developed on potato. Stabbed into gelatin what was regarded as a characteristic change occurred; about the line of inoculation there was feeble liquefaction, a cup-like cavity shaped like a tulip being formed near the surface. All cultures had an odor recalling that of strawberries. No capsule resembling that seen in the tissues was formed in cultures. Inoculation into small animals caused immediate death or formation of an abscess. In the horse, however, a tumor similar to that which occurred spontaneously was produced at the site of inoculation and contained the characteristic capsulated masses of micrococci. Rabe named the microorganism *Micrococcus botryogenes*. Similarly successful inoculation experiments have been performed by Kitt,<sup>7</sup> de Jong<sup>8</sup> and others, but the distinctive cultural characters described by Rabe have not been confirmed.

Kitt regards the organism as a variety of *Staphylococcus pyogenes aureus*. Galli-Valerio,<sup>9</sup> who has studied the cultural characters of an organism obtained from a typical human lesion of the skin containing characteristic masses of cocci, has found no distinctive cultural peculiarities and agrees with the view of Kitt. Poncet and Dor<sup>10</sup> first isolated the organism from a human lesion of the skin and produced on the udder of a she-ass a pedunculated growth which was not examined microscopically; they regard the microorganism as a distinct species. Baumgarten<sup>11</sup> expresses the view that the microorganism is undoubtedly a distinct species belonging to the same group as *Staphylococcus pyogenes aureus*, but regards as distinctive its capacity to form within the tissues a gelatinous membrane about colonies of cocci. This view being accepted, the term botryomyces is not applicable to the microorganism. The name botryocycosis applied to the disease is, like actinomycosis, firmly established in the literature of the subject.

The following case is described because, in the first place, doubt has been expressed concerning the occurrence of botryomycosis in man (see section on pseudobotryomycosis). The case, moreover, is apparently the first recorded instance in which the disease in man has attacked an internal organ, in this instance the liver. Since the disease, it appears, has not been observed in this country, the case may direct attention to

7. Kitt: Centralbl. f. Bakteriöl., 1888, iii, 177. Monatsch. f. prakt. Tierheilk.

8. De Jong: Diss. Giessen, 1899. Quoted by Baumgarten 1890, i, 148.

9. Galli-Valerio: Centralbl. f. Bakteriöl., 1902, xxxi, Part 1, p. 508.

10. Poncet and Dor: XI congr. français de chirurgie, Paris, 1897; Lyon méd., 1897, No. 43, p. 213 and 1898, No. 5, p. 145; Arch. gen. de méd., 1900, iii, 129, 274. Quoted by Galli-Valerio.

11. Baumgarten: Lehrbuch der pathogenen Mikroorganismen, Leipzig, 1911.

other instances of the same condition. There is no complete record of the autopsy performed on the patient. Unfortunately no cultures were made at the time of autopsy.

#### CASE REPORT

The patient, a girl aged 11 years, from Sabula, Mo., was admitted to the St. Louis Children's Hospital Aug. 27, 1910, in the service of Dr. George M. Tuttle, who has kindly permitted me to make use of the accompanying history.

*History.*—The mother of the child is said to have died of tuberculous pneumonia. She has a father and one sister in good health.

In the spring over one year before her admission the patient had scarlet fever and has not been well since that time. She has been losing weight and strength since last November, when she is thought to have had malaria. Her appetite has been poor and at times she has had fever. She has had severe pain in the abdomen and there has been pain at times in the right side, at times in the left.

No horses in the vicinity are known to have been diseased. The patient received milk from a neighboring farm; one cow of the herd showed signs of sickness during the fall and died the following spring "with a wasting disease that affected her water."

*Examination.*—On admission the patient was a well developed girl but weak and emaciated, having the appearance of a child much older than her real age. The skin was jaundiced and dry and the superficial veins were everywhere much congested. Over the body there was desquamation of the epidermis, and scattered, numerous small ulcers about the size of a pin's head.

The entire epigastric region was distended by what appeared to be a hard, irregular mass continuous with the liver and extending into the left hypochondriac region. The edge of the liver was thin, extended a half finger's breadth below the costal margin in the mammary line and approached to within about a centimeter of the crest of the ilium in the axillary line. There was marked rigidity and tenderness over the entire abdomen, most severe in the epigastric region and in the neighborhood of the left kidney where the pain was so severe that palpation was impossible.

Respiration was rapid, 40 to the minute, and very shallow. With deep respiration there was pain referred to the swelling in the epigastrium. The intercostal spaces, the depressions above and below the clavicle, and the supra-sternal notch were much depressed. There was well-marked bulging of both sides of the chest at its base, more marked on the right side. Auscultation and percussion gave no noteworthy information. The apex beat of the heart was displaced to the left and was found just outside the nipple line.

While in the hospital the patient gradually became weaker. Her appetite was fairly good. She passed copious soft white or yellow stools. A stool examined August 31 was grayish-white and contained fat crystals in abundance; there were no bile pigments.

The temperature was invariably between 97 and 98.8 C. save on the second and third days after admission (100) and on the third day before death (100).

The blood examined on August 29 contained 3,272,000 red blood corpuscles, 60 per cent. hemoglobin and 28,400 leukocytes.

The urine while the patient was in the hospital has the following characters: Specific gravity, 1.008 to 1.015; albumin, present; bile pigments, present; sugar, absent; there were granular casts and a few leukocytes.

The patient became unconscious on the morning of September 8, and died with slow, gasping respiration three hours later.

*Necropsy.*—A necropsy was performed by a hospital intern. A note stated that more than half of the liver substance was involved by a tumor-like lesion which was firm and contained cyst-like cavities filled with pus. Similar abscesses were found elsewhere. There was hydrops of the gall-bladder. Only the liver, which was put in Kaiserling's solution, was preserved.

Liver: On the upper surface of the liver near the posterior border below and on either side of the falciform ligament is a large, irregular, puckered area approximately 10 cm. across, where the tissue has a deep yellow color broken by grayish depressed spots. At the margin of this area surrounding it are low rounded

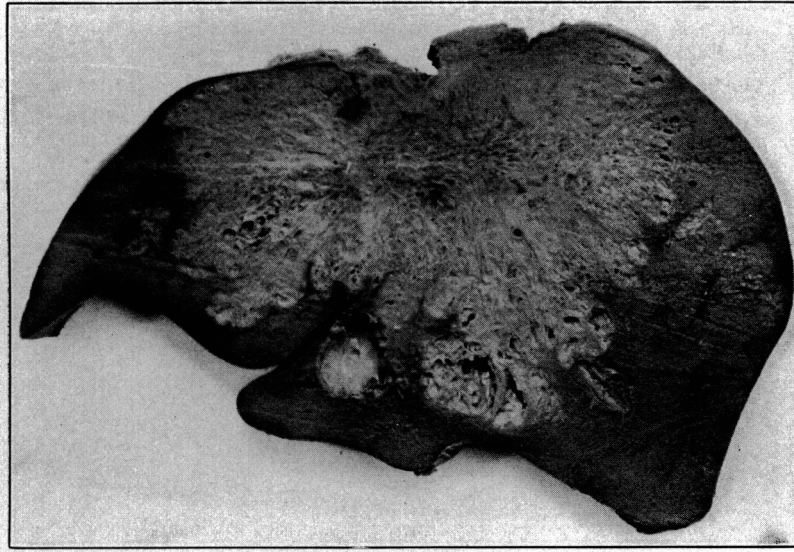


Fig. 1.—Photograph of the cut surface of the liver with botryomycosis. The center of the lesion consists of fibrous tissue; in the periphery are abscess cavities.

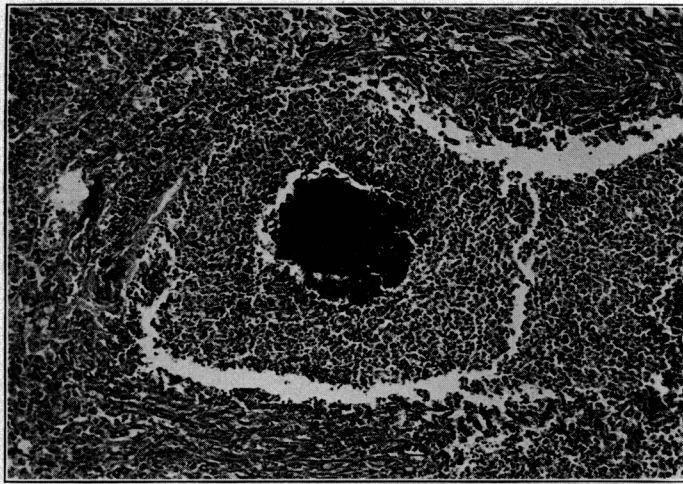


Fig. 2.—Microphotograph showing a botryomycotic granule surrounded by pus and within a cavity the wall of which is formed by newly-formed fibrous tissue.

confluent elevations of the liver substance often 2 or 3 cm. across. The centers of these elevations are soft, have a yellowish tint and correspond to abscess cavities in the underlying tissue. The surface of the liver near these abscesses shows in places bluish-red discoloration. Remains of adhesions are attached to

the surface of the liver at the site of the lesion. Section made transversely through the liver (Fig. 1) shows that an immense tumor-like mass has replaced the greater part of the substance of the organ. The cut surface of the lesion has an irregularly semicircular form with its base corresponding to the upper surface of the liver. Bands of fibrous tissue radiate from the central part of the base which is represented by the irregular puckered area seen on the upper surface of the organ. The tissue composing the lesion varies in different parts. Immediately below the puckered superficial area just mentioned there is a narrow,

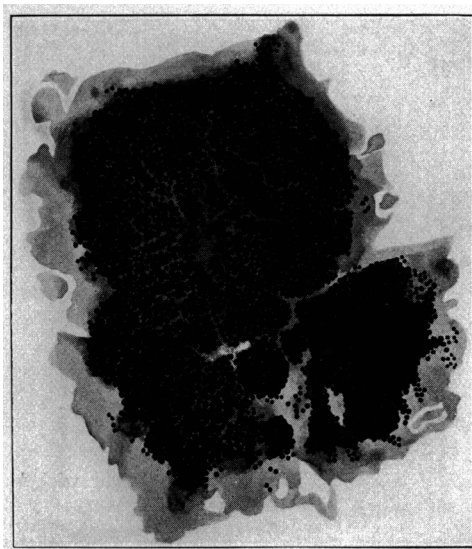


Fig. 3.—Drawing showing a botryomycotic granule composed of coccus-like bodies held together by a homogeneous substance which forms a capsule.

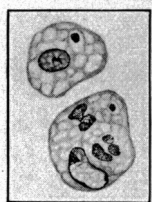


Fig. 4.

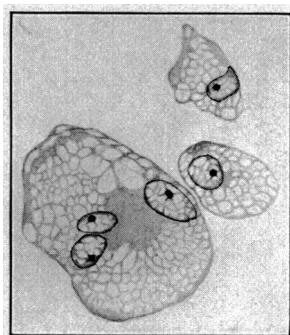


Fig. 5.

Fig. 4.—Drawing showing phagocytic cells containing droplets of fat.

Fig. 5.—Drawing showing large fat-containing cells which occur in large number within the newly-formed fibrous tissue.

irregular zone of tough, fibrous tissue. The tissue below occupying the center of the lesion is firm and consists of opaque yellow material broken by numerous fibrous bands which in general radiate toward the periphery of the lesion. Further outward the tissue is less dense and there are numerous small cavities filled with soft purulent material. In some places the cavities form irregular, elongated,

communicating channels or sinuses separated by dense fibrous tissue. At its periphery the lesion has a honey-combed appearance and in places there are large abscess cavities. The largest of these cavities is 2 cm. across; it is filled with soft yellowish pus and is lined by yellowish membrane about 0.5 mm. in thickness. On section not more than one-third of the area is represented by normal liver tissue. In this liver tissue lobulation is obscure and there is a greenish tint as if due to jaundice. In the right lobe of the liver outside of the main mass of the lesion are two large portal spaces within which is an elongated channel with opaque yellow wall containing purulent material. Scattered in the remainder of the lobe are minute abscesses collected together in several groups.

The gall-bladder was found at autopsy to be distended, but otherwise showed nothing noteworthy.

*Microscopical Examination of Liver.*—The liver substance is replaced by masses of dense fibrous tissue in which are cavities containing polynuclear leukocytes and other cells surrounding conspicuous masses of coccus-like bodies (Fig. 2). The fibrous tissue varies considerably, being in places dense and poor in cells, elsewhere loose in texture and richly infiltrated with cells. In this connective tissue occur masses of large cells distended with fat and so abundant that they give to the tissue the yellow color mentioned above. The size of the abscesses and sinuses which contain the colonies of microorganisms varies greatly, and in the older parts of the lesion there are wide channels containing leukocytes and surrounded by fibrous walls rich in cells. There is no abrupt line separating the lesion from the liver tissue which persists. Liver cells at the margin of the lesion are compressed, atrophic and often contain abundant brown yellow pigment. Thickened strands of fibrous tissue separate these cells and in the adjacent relatively normal liver substance fibrous tissue of the portal spaces is considerably thickened.

Botryomycotic granules vary in abundance and size in different parts of the lesion. Three masses, each visible to the naked eye in the stained specimen, the largest being approximately 1 mm. in length, are grouped together in one field of the low power (Obj. 3, Oc. 1). These masses are composed of bodies resembling staphylococci (Fig. 3) which stain deeply with either hematoxylin or methylene-blue. At the edge are the irregular rounded projections which give a mulberry-like form to the entire mass when examined in fresh pus. In some instances the larger bodies in section appear to be separated into several isolated masses. Micrococci appear to be less densely packed together at the center of the mass, which stains less deeply than the outer part. Between the cocci is what appears as a homogeneous background which stains with eosin or picric acid (van Gieson's stain). In many instances particularly about the larger bodies, this homogeneous material is conspicuous at the edge forming a kind of capsule separating the cocci from the leukocytes about. The distinctness with which this clear zone can be made out varies much; in places it may be wholly lacking. The cocci exhibit some variation in size and particularly at the margin of the colony minute microorganisms are found.

Immediately about the botryomycotic granules polynuclear leukocytes occur in large number (Fig. 2). Adherent to the surface of the mass red blood corpuscles are frequently seen. In most instances it is obvious that the botryomycotic granule lies in a small abscess cavity surrounded by pus, for in its immediate neighborhood tissue has disappeared and the purulent exudate (in the hardened tissue) has occasionally retracted from the surrounding wall of fibrous tissue. Leukocytes are usually well preserved, but in places a moderate number have lost their nuclei and are in process of disintegration. Polynuclear leukocytes which have ingested coccus-like bodies similar to those which form the colonies are not infrequent. Scattered cocci are occasionally found outside of cells, but in such instances the leukocytes in the immediate neighborhood are in part necrotic.

The wall of the abscess is formed by fibrous tissue containing numerous cells. In contact with the cavity are large cells with large oval or slightly irregular vesicular nuclei and abundant protoplasm. These cells (macrophages) are phagocytic and contain within their substance red blood corpuscles, nuclear fragments and remains of cells, still recognizable as polynuclear leukocytes (Fig. 4). They occasionally contain cocci similar to those which form the colonies. The regularity and thickness of this zone of mononuclear cells varies greatly. The loose fibrous tissue in the wall of some large abscess cavities is thickly infiltrated over a wide area with cells having the characters just described. Many of these cells are of very large size, four or five times the diameter of a polynuclear leukocyte and distended with the remains of many ingested cells, some of which are still recognizable as polynuclear leukocytes. Similar cells are, in places, vacuolated, vacuoles being formed by fat recognizable by the usual reactions.

In places the connective tissue, perhaps in contact with the zone of phagocytic cells surrounding an abscess, is closely packed with very large cells, whose protoplasm is replaced by vacuoles. These vacuolated cells occurring in the meshes of loose fibrous tissue give it some resemblance to adipose tissue. The nuclei of these cells (Fig. 5) are oval or slightly irregular in outline and situated near the center of the cell. The protoplasm stains faintly, being almost entirely replaced by vacuoles which may be so small that they give the protoplasm a finely granular appearance, or so large that they distend the cell. Occasionally these vacuolated cells are unusually large and have several nuclei, from two to as many as six, collected near the center of the cell. In tissue containing these large vacuolated cells plasma-cells occur scattered in considerable number among them. Sections of the dense yellow tissue (see description of gross appearance) containing masses of the vacuolated cells which have been described, exhibit when stained with Searlach R. or Sudan III, large red areas occupying a considerable proportion of the tissue. Microscopic examination shows that the cells which by usual methods are vacuolated are filled with fat in large or small droplets; in osmic acid preparations these globules are black. Areas in which the fat-containing cells occur in great abundance are usually in contact with zones containing recognizable macrophages and surrounding foci of suppuration. Transitions from macrophage to vacuolated cells are readily found. The latter appear to be macrophages which have persisted in the meshes of the newly formed fibrous tissue and have undergone advanced fatty degeneration.

In some spots botryomycotic granules are in process of destruction and the surrounding suppuration is in process of disappearance or has completely disappeared. The central coccus-like body may be relatively small; the surrounding tissue may contain no nuclei and appear hyaline. If a cavity persists about the mass of microorganisms polynuclear leukocytes are scant and mononuclear cells have increased at their expense. At a later stage both types of cells have in large part disappeared, the surrounding cavity is absent, and the fixed tissue has approached to the immediate neighborhood of the colony. In contact with the mass of coccus-like bodies is a tissue composed of a fibrillated ground-work and elongated spindle-shaped cells with oval vesicular nuclei. These cells have the characters of so-called epithelioid cells of the tubercle, and in general, directed with their long axes pointing to the central mass, form a zone surrounding the colony. In this zone may occur one or more multinucleated giant cells with many nuclei scattered throughout the cell. Outside of this zone is white fibrous tissue in whose meshes are plasma cells in immense number together with a few lymphoid cells. In some instances a focus or nodule similar to that which has just been described contains no mass of microorganisms in its center and closely reproduces the structure of a tubercle. In the center are one or two large giant cells which have the characters of those seen in tubercles: the nuclei are arranged at the margin of the cell and surround an almost homogeneous area. About the giant cells is a narrow zone formed by a fibrillated



ground-work containing a few cells of epithelioid type. This fibrillated stroma may stain deeply with eosin and exhibit a hyaline appearance. Further outward epithelioid cells are mingled with numerous plasma-cells. Giant cells containing micrococci have been found.

Collections of coccus-like bodies forming large lobulated colonies occur in abundance throughout the lesion. This microorganism acting as an irritant has caused a series of changes in the liver. There is destruction and disappearance of tissue in the immediate neighborhood of the colony and accumulation of polynuclear leukocytes; a cavity containing purulent exudate is formed about the microorganisms. White fibrous connective tissue is formed in abundance in the wall of the abscess. At the margin of the abscess cavity mononuclear cells make their appearance, and acting as phagocytes (macrophages), ingest polynuclear leukocytes, red blood corpuscles and other cells and attain a size many times that of a polynuclear leukocyte. The fibrous tissue nearby is at first rich in cells, containing plasma-cells in immense number. The process of phagocytosis of polynuclear leukocytes and other cells at the margin of the abscess cavity represents an early stage in the process of healing and tends to bring about the disappearance of pus about the parasite. As pus is absorbed the surrounding fixed tissue grows into contact with the mass of microorganisms which are now perhaps killed but not yet dissolved. Cells of epithelioid type and giant cells similar to those of the tubercle come into contact with the persisting microorganism. A lesion resembling, but not identical with, the tubercle is formed. The colony of cocci finally disappears. In the newly formed fibrous tissue between the abscesses there are areas in which large vacuolated cells are so abundant that they form a conspicuous element of the tissue. These cells appear to be mononuclear phagocytes (macrophages) which have persisted in the wall of the abscess and undergone fatty degeneration. They are in places so abundant that they give to the tissue a deep yellow color. Large abscess cavities occur at the advancing margin of the lesion whereas its center is formed by dense fibrous tissue.

#### HUMAN BOTRYOMYCOSIS

Botryomycosis in man was first described by Poncet and Dor.<sup>10</sup> On the hand of a woman near the digito-palmar fold of the little finger an indolent red spot ulcerated and gave place to a pedunculated tumor the size of a small nut. In sections of the tumor they found the masses of coccus-like bodies to which Bollinger gave the name *Botryomyces*, and by personal observation convinced themselves of the identity of the bodies they observed with those found in the fungus-like growths from the spermatic cord of geldings. Poncet and Dor have perhaps diminished for subsequent observers, the value of these bodies as criteria for the identification of botryomycosis by the interpretation which they have offered. They have maintained the untenable view, wholly unsupported

by the bacteriologists who have studied botryomycosis, that the peculiar bodies are not microorganisms, but products of the degeneration of tissue cells. They regard the coccus-like bodies as pyknotic nuclei. From the lesion Poncet and Dor isolated a staphylococcus, which inoculated into the udder of an ass, produced a small pedunculated growth. No examination of the nodule was made. Poncet and Dor have described as botryomycosis three small pedunculated growths, two being on the hand and one on the most prominent point of the stump formed by amputation of the arm at the shoulder.

Faber and Ten Siethoff<sup>12</sup> have described a group of little nodules on the border of the eyelid occurring at the site of a styne in a boy who had tended a horse suffering with a fungoid growth from the cut spermatic cord. In the viscid pus squeezed from the lesion were mulberry-like masses with the structure of those which occur in the horse. Pedunculated tumors containing similar bodies have been observed in France by Sabrazes and Laubie<sup>13</sup> (in one case on the auricle, in a second on the palm of the hand), and by Delore and Gauthier<sup>14</sup> (in one case above the eyebrow, in a second on the finger). Similar observations have been made in Switzerland; Reverdin and Gulliard<sup>15</sup> have described a pedunculated tumor the size of a pea on the palm of the hand, and Galli-Valerio<sup>9</sup> has seen a nodule of similar size and shape on the anterior surface of the fore-arm.

The disease is apparently much more common in northern Africa than in Europe, and French physicians living in Algeria have described in considerable number instances of a similar but much more severe disease. Brault<sup>16</sup> has described two cases in which small pedunculated tumors containing the characteristically-grouped microorganism have occurred on the fingers of women in Algeria. Legrain<sup>17</sup> has described a considerable number of cases of botryomycosis. Attached to the dorsal surface of the right hand of a Berber woman he found a tumor the size of her fist; it consisted of five masses each pedunculated and the whole attached by a narrow base. A tumor in another Berber woman made its appearance on the stump of a finger accidentally amputated and attained the size of a large mandarin. It was removed, but reappeared, forming a mass larger than before; the growth did not invade the underlying muscles or tendons.

12. Faber and Ten Siethoff: *Nederlandsche oogheelkundige bijdragen*, 1897. Quoted by Bodin.

13. Sabrazes and Laubie: *Arch. gèn. de méd.*, November, 1899; *Arch. de parasit.*, 1898, i, 410.

14. Delore and Gauthier: *Gaz. d. hôp.*, Nov. 8, 1900.

15. Reverdin and Gulliard: *Rev. méd. de la Suisse romande*, 1900, No. 11, p. 500.

16. Brault: *Arch. de parasitol.*, 1901, iv, 308.

17. Legrain: *Arch. de parasitol.*, 1898, i, 148.

In a subsequent publication, Legrain<sup>18</sup> described other growths on exposed surfaces the largest of which was the size of a child's head. Somewhat similar observations have been made by Archibald<sup>19</sup> on material sent to him from various parts of the Sudan; seven growths removed from the scalp, breast, arm, hand, foot or cheek of natives contained agglomerations of coccus-like microorganisms identical with those peculiar to botryomycosis. The same bodies had been previously observed by a member of the laboratory staff in a growth removed from a camel. In one instance the lesion occurred in a native woman, 45 years of age, who had suffered with a swelling of the breast since childhood; it implicated the entire breast, resembled a fungoid cancer and exuded grayish-white pus from numerous sinuses. In another case a tumor of the scalp implicated the underlying bone and from sinuses on the surface thin pus-containing yellow granules escaped.

Butler and Welsh,<sup>20</sup> in New South Wales, found a swelling outside of the left orbit causing softening of the temporal bone in a child 4 years of age. The scant viscid pus contained numerous yellow granules which consisted of masses of cocci. In a Japanese Kayser and Gryns<sup>21</sup> found the right foot swollen and riddled with sinuses from which escaped exudate containing botryomycotic granules.

#### PSEUDO-BOTRYOMYCOSIS

Poncet and Dor identified with botryomycosis of the horse the pedunculated fleshy growths in which they found the mulberry-like bodies described by Bollinger. Subsequent writers have given the same name to similar pedunculated nodules, even though they have failed to demonstrate the presence of these readily recognizable bodies. Such growths having the structure of redundant granulation tissue have been described as botryomycosis by Bodin<sup>22</sup> (two cases), Spourgitis<sup>23</sup> (two cases), Gehinet<sup>24</sup> (six cases), Alglave<sup>25</sup> (two cases), Thévenot and Alamartine<sup>26</sup> (five cases), Lenormant<sup>27</sup> (five cases), and others. In none of these cases have botryomycotic colonies been found. To the same growths, Küttner<sup>28</sup> (four cases), who found none of the mulberry-like encapsulated groups of cocci, gave the name *Granuloma telangiectoides*. Two

18. Legrain: Quoted by Gehinet.

19. Archibald: Brit. Med. Jour., 1910, ii, 971.

20. Butler and Welsh: Edinburgh Med. Jour., 1910, iv, 115.

21. Kayser and Gryns: Geneesk. Tijdschr. voor Nederl. Indie., 1907, xiii. Ref. Bull. d. l'inst. Pasteur, 1908, vi, 863.

22. Bodin: Ann. de derm. et de Syph., 1902, iii, 289.

23. Spourgitis: Paris Thesis, 1900. Quoted by Gehinet.

24. Gehinet: Paris Thesis, 1902.

25. Alglave: Bull. Soc. anat. de Paris, 1906, lxxxi, 524, 535.

26. Thévenot and Alamartine: Lyon Chirurg., 1909, ii, 154.

27. Lenormant: Ann. de derm. et de syph., 1910, xi, 193.

28. Küttner: Beitr. z. klin. Chir., 1905, xlvii, 1; Bennecke, München. med. Wehnschr., 1906, 1553.

German writers, Reitmann<sup>29</sup> (one case) and Kreibich<sup>30</sup> (three cases), have adopted the same name for similar growths. Jacquet and Barré,<sup>31</sup> who, like the writers just named, found in their tumors no structures having the characters of so-called botryomyces, think that the use of the name botryomycosis should be discontinued, and the growth they describe should be designated benign hypertrophic granuloma or pseudo-botryomycosis.

Hartzell,<sup>32</sup> describing the same lesion observed in this country (Philadelphia), has suggested *granuloma pyogenicum* to replace botryomycosis of French authors, and this name has been adopted by Sutton,<sup>33</sup> who has described a case which occurred in Liberty, Mo. Wile<sup>34</sup> has described as granuloma pyogenicum two instances of small pedunculated nodules observed in New York City, one on the cheek of a child 8 years of age, the other hanging from the navel of an infant 2 months old. The nodules had the histological structure of granulation tissue, in the first instance richly supplied with blood-vessels. No masses of encapsulated cocci were found within the nodules, but scattered cocci were found at the periphery. Wile describes as typical instances of the same lesion the cases of Hartzell, Küttner, Reitmann, Kreibich and Jacquet and Barré, in none of which were found the characteristic botryomyces of Bollinger, and reaches the conclusion that botryomycosis does not occur in man; he doubts, indeed, the occurrence of a disease, botryomycosis, in the horse, but does not discuss the subject at length.

It is apparent that the diagnosis of botryomycosis has repeatedly been made from the clinical characters of the lesion. A growth makes its appearance usually at the site of an injury on an exposed skin surface, in most instances on the hands or face, and grows rapidly, attaining the size of a small pea or nut. With excessive growth in all directions the mass assumes a mushroom-like or pedunculated form. It is reddish and fleshy in appearance; superficial ulceration occurs frequently and bleeding is readily induced. After partial removal rapid growth occurs. Histological examination shows the usual structure of granulation tissue; young connective tissue is infiltrated with leukocytes and mononuclear cells, and in some instances with plasma cells. In some instances dilated blood-vessels are abundant, but in other instances blood-vessels are not more conspicuous than those in granulation tissue. It is undoubtedly inappropriate to designate this lesion botryomycosis solely because it is fleshy in appearance and pedunculated. In the absence of demon-

29. Reitmann: Arch. f. Derm. u. Syph., 1908, xci, 185.

30. Kreibich: Arch. f. Derm. u. Syph., 1909, xciv, 121.

31. Jacquet and Barré: Ann. de derm. et de syph., 1909, x, 574.

32. Hartzell: Jour. Cutan. Dis., 1904, xxii, 520.

33. Sutton: Am. Jour. Med. Sc., 1911, cxlii, 69.

34. Wile: Jour. Cutan. Dis., 1910, xxviii, 663.

stration of the yellow granules which are peculiar to botryomycosis, the diagnosis is no more possible than the diagnosis of actinomycosis in the absence of the ray fungus. Schridde<sup>35</sup> has recently described protozoa-like bodies within large mononuclear phagocytes found in a pedunculated growth similar to those which have been described. These intracellular bodies are round, oval, semilunar or pear-shape and present some resemblance to the bodies found with kala-azar and oriental sore. No botryomycotic granules were noted in the nodule in which these bodies were found, and he regards the growth as an example of the lesion to which Küttner gave the name *granuloma telangiectoides*.

#### BOTRYOMYCOSIS OF HORSES IN THE UNITED STATES

I have been able to obtain no literature on the occurrence and distribution of botryomycosis of horses in the United States. Through the kindness of several veterinary physicians I have received information concerning its occurrence. Dr. V. A. Moore, at the New York State Veterinary College, Ithaca, New York, has seen no instance of the disease. Dr. J. R. Mohler, Chief of the Division of Pathology, United States Bureau of Animal Industry, Washington, has written me as follows: In looking through our card-index catalogue we have failed to find any references to literature on the subject of the occurrence of this disease in this country. Our records of pathological specimens show that Dr. Leon A. Reek of Melbourne, Fla., submitted some tissues from a horse on Nov. 4, 1909, Record No. 3,418, which showed the presence of botryomycosis. This disease in all probability exists in this country, but the cases are not reported.

Dr. Maximilian Herzog has seen several cases in the hospital of the Chicago Veterinary College, but believes that the disease is infrequent in Illinois. Dr. A. T. Kinsley of the Kansas City Veterinary College, writes as follows:

I have found three cases in horses in Kansas City, two of them involving the spermatic cord, as the sequel of castration. The other involved the point of the shoulder and apparently resulted from infection from a bruise caused by the collar. I have had specimens sent to our laboratory from North and South Dakota, two cases from Nebraska, several from Kansas and one from Iowa in the last five years. In my opinion these cases are not at all rare although I do not know that they are diagnosed commonly, usually being passed over as cases of infection without specific diagnosis.

During four years in Colorado, Dr. B. F. Kaupp saw one instance of botryomycosis, the disease occurring in a mule.

The foregoing data indicate that botryomycosis in horses is uncommon in the states of the Atlantic coast, whereas in the central portion of the United States it is more common. A considerable number of instances have been observed in Kansas City, Mo., a part being from Missouri, a part from neighboring states.

35. Schridde: *Deutsch. med. Wchnschr.*, 1912, xxxviii, 218.

The unusual nature of the lesion which has been described suggests some unusual mode of infection. Botryomycosis of the human skin is not uncommon in certain tropical countries, yet no record has been found of botryomycosis of an internal organ. In the present case the lesion appears to have been primary in the liver and its occurrence here suggests that infection may have occurred by way of the gastro-intestinal tract. There is no evidence in favor of this view save the statement that one cow from which the child received milk at the time of her infection was affected with a fatal wasting disease. Botryomycosis of cattle has been observed, but is uncommon; the disease occasionally attacks the udder.

#### SUMMARY

Bacteriological examinations indicate that the disease of horses, cattle and swine known as botryomycosis is caused by a microorganism resembling *Staphylococcus pyogenes aureus*, but characterized by the formation of compact colonies held together by a homogeneous material which forms a kind of capsule. About these colonies or granules which are formed only in the tissues there is suppuration and tissue formation producing a lesion which has all the characters of the infectious granulomata.

Human botryomycosis has been observed most frequently in tropical or subtropical countries such as Algeria, the Sudan, Australia and Java. It has been observed in France and Switzerland, but heretofore has not been observed in the United States.

The disease in man affects exposed surfaces such as the hands or face, and has repeatedly followed injuries of infected parts. Pedunculated masses of considerable size may be formed. They consist of newly-formed fibrous tissue in which are foci of suppuration and sinuses opening on the surface. The peculiar botryomycotic granules are always present.

Small pedunculated growths having the structure of exuberant granulation tissue have frequently been described as botryomycosis, although the microorganism peculiar to the disease has not been discovered in the lesion. There is no demonstrable relation between these growths, which have been designated granuloma pyogenicum, telangiectatic granuloma or pseudo-botryomycosis, and botryomycosis as it occurs in man and lower animals.

The case which has been described represents, as far as I have been able to determine, the first instance of the disease described in this country, and is, it seems, the first instance in which it has affected an internal organ. The disease has attacked a child 11 years of age. A massive lesion replaces almost the entire liver and consists of fibrous tissue and foci of suppuration within which occur botryomycotic granules

in large number. It is not improbable that some peculiar mode of infection explains the unusual situation of the lesion. The child received milk from several cows, one of which died with a wasting disease, but no more definite history can be obtained. Botryomycosis has been observed in domestic animals in Missouri where the human instance of the disease occurred.

For the photographs I am indebted to the kindness of Dr. R. H. McBaine. The drawings have been made by Mr. C. D. Jarrett.  
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