about in every department of milk production and vending every local board of health should require efficient pasteurization, a few hours before delivery to the consumer, of all milk which it finds unsafe for consumption as raw milk. All such milk must be put in sterile containers, and properly marked with the time and date of pasteurization and the degree and duration of temperature to which it was subjected.

In conclusion it is only fair to say that interest in the question of tubercle bacilli in milk has not in my mind minimized the gravity of the annual death rate from milk-induced gastroenteritis of children, or from milk-borne epidemics of scarlet fever, diphtheria, and typhoid. With these diseases we have an immediate evidence of the mischief done, but the entrance of tubercle bacilli into any of the glands, organs, or tissues may be unattended with any symptoms, or at least with any that are appreciable to the family or physician of the little victim. And it may be months or years later that the child so infected becomes crippled, or shows evidence of tubercular disease that may partially maim him, or end his life. It is the knowledge that practically one-seventh of us are carried off by tuberculosis, together with the uncertainty of just what percentage of the whole number so dying are infected during childhood through milk, that makes the freeing of our milk from tuberculosis so crying a necessity.

181 Park Avenue.

ACUTE GLANDERS.

REPORT OF A CASE, WITH A REVIEW OF RECENT LITERATURE, AND A COMPLETE BACTERIOLOGIC REPORT.*

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CLINICAL REPORT BY DR. MEYER.

Acute human glanders, though not uncommon in Russia, is an extremely rare disease in New York, but nine cases having been reported to the New York Board of Health during the past two years. Such a case, therefore, should be of sufficient interest to warrant publication; hence the following detailed report of a case admitted to the First Surgical Division of Mount Sinai Hospital (service of Dr. Gerster¹), Aug. 28, 1907. Because of a suspicion that he might be a sufferer from glanders or some similar contagious disease the patient was transferred from the general to the isolation service.

A smear taken from the pus on admission showed bacilli resembling those of glanders (see below) and a tentative diagnosis of acute glanders was made. In view of the diagnosis, the New York Board of Health was notified, but the diagnostician who saw the case refused to consider it one of glanders, nor was this diagnosis ever officially admitted by the board, in spite of the suspicious character of the lesions and the conclusive bacteriologic findings. The horses in the stable over

which the patient lived were thoroughly examined by them without finding any evidence of disease.²

History.—The patient, a Russian, 38 years old, a presser by occupation, four months in the United States, was semi-stuporous on admission, the history being obtained from friends. The most important part of the history, from the standpoint of diagnosis (viz., his residence over a stable), was not obtained until the death certificate was being signed, and then only after the most careful questioning. The history as obtained was, that the patient became suddenly ill a week before admission, with chilly sensations, general malaise, and high temperature; he soon became delirious. Two days later a painful tender swelling (not reddened) was noticed on the inner side of the left leg. The following day it was incised, but the wound showed no tendency to heal. The patient became rapidly worse, until on admission, August 28, his condition was one of extreme sepsis.

Examination.—The physical examination at this time showed: Small pustules on uvula and pillars of fauces. Joints tender and swollen. Glands, inguinal, very much enlarged. Lungs, a few râles over both chests, but no signs of consolidation. Skin: (a) Numerous small acne-form pustules surrounded by reddened areas; (b) larger pustules having flattened centers; (c) numerous shot-like swellings, freely movable under normal skin; (d) reddened indurated swellings with soft centers involving the muscles; the majority had red unbroken skin over them; on inner aspect of left leg was one that had been incised, showing a necrotic ulcer extending into muscle; there was a scanty discharge. Penis: Two large hemorrhagic bullae on corona; left testicle enlarged and tender.

Two days before death, a dusky red area, with bluish center, appeared on the sole of the left foot (this was the first lesion on the soles of the feet). The day preceding death, the eruption became very profuse, involving every portion of the body, a great number of nodular swellings becoming soft and fluctuating (but not rupturing). A nasal discharge first appeared about this time.

A blood culture taken on the day of admission (August 28), showed *Bacillus mallei*; a culture taken two days later was also positive. Inoculation experiments gave typical results (see bacteriologic report).

Treatment.—The patient's condition on admission was such that it was apparent that no treatment would be of any avail. He was, however, put on the usual supportive and stimulating treatment; the pustular lesions were treated with Lugol's solution. An attempt was made to obtain some bullock's serum for injection, it being held that as cows are immune to glanders, their serum may contain something inimical to the growth of the *B. mallei*. Since a supply of the serum could not be obtained in time, this method of treatment could not be employed. Wherever possible, it should, however, be used, as it affords the best hope in this terrible malady.

In reviewing the literature,³ one is struck by the failure of making even a tentative diagnosis of glanders in the early stage of the disease. The diagnoses most frequently made are pneumonia or pleurisy, acute articular rheumatism, or typhoid fever; among other early diagnoses made were cellulitis, erysipelas, influenza, impetigo contagiosum, and tertiary lues.

The main reason (aside from the comparative rarity of the disease) for failure to make a diagnosis, espe-

2. It is worth noting that 530 horses were condemned and destroyed by the New York Board of Health during 1906, and 470 during the first nine months of 1907. During the same periods there were, respectively, six and three cases of human glanders.

3. The following literature may be referred to: Hoke: *Prager med. Wehnschr.*, xxxii, p. 353. *Presbyterian Hosp. Rep.*, 1904. Silkman: *Med. Rec.*, Oct. 5, 1907. *Boston City Hosp. Rep.*, 1905. Pest, A.: *Bost. Med. and Surg. Jour.*, Nov. 23, 1905. Beattie, D. W.: *West. Med. Review*, i, p. 46. Woodcock, L. A.: *Lancet*, Lond., Feb. 3, 1906. Anderson: *Glasgow Med. Jour.*, 1905, lxiv, p. 281. Stephenson: *Trans. Royal Academy, Dublin*, xxiii, p. 313. Cheney: *California State Jour. Med.*, 1905, iii, p. 220. Wherry: *Glanders in Manila*, Bureau Public Printing, 1904. Form 24. Spencer: *Lancet*, Lond., 1905, i, p. 997. Ames, J. L.: *Boston Med. and Surg. Jour.*, 1905, clii, p. 42. McFadyean, J.: *Jour. Comp. Path. and Ther.*, 1904, p. 295. Robins, G. D.: *Canada*, 1906. *THE JOURNAL A. M. A.*, 1889. Goodall: *Lancet*, Lond., 1905, ii, p. 589.

*Read in abstract at the meeting of the Harlem Medical Association, December, 1907.

1. To whom we are indebted for permission to publish this case.

cially in the early stages, is due to the fact that the eruption does not usually appear until the disease has lasted some time. In the majority of the cases the diagnosis has been suspected only a few days before death, when a suggestive eruption appeared in the course of a disease not developing along the lines of the original diagnosis.

The case reported differed from the majority of the cases recorded in literature in that it did not markedly simulate any other disease; it resembled them in that the diagnosis could not possibly have been even suspected during the first three or four days, as the only symptoms present (according to the history) were those of sepsis. Just when the skin and joint lesions first became manifest could not be ascertained. They were not present the first two days, although they were well marked on admission, one week after the onset. While typhoid might have been suspected before the skin lesions made their appearance, the onset was not at all characteristic of this disease.

A further item of interest gleaned from a cursory review of the literature of the last three or four years is that of the number of cases reported in the United States. Out of a total of 32 cases of acute glanders reported, 18 were in the United States (4 of these in New York City,⁴) 13 in Europe and 1 in Manila. Of course, many cases are not reported in the literature.

In a typical case, with a good history, the diagnosis should not be difficult, provided one has the disease in mind. Acute glanders in man, however, is seen so seldom that it is usually not even thought of, especially when there is little in the way of skin lesions. A bad coryza, which may be the most marked local sign of glanders, is, of course, often present in grip or pneumonia. Many of the cases recorded in the literature, in which mistaken diagnoses were made, showed neither coryza nor skin lesions at the onset, this being often characterized by chill, followed by typical symptoms of pneumonia or grip or by joint symptoms simulating rheumatism. Only after a variable time had elapsed did there appear nasal symptoms or a skin eruption which suggested the possibility of glanders in any case. When, however, with a more or less septic condition, there appear on the skin indurated painful reddened areas with soft centers, with less tendency to rupture than ordinary abscesses, and which, when opened, discharge a thin serosanguinous material, the resulting ulcer having a necrotic base, usually involving muscle, and with no tendency to heal, glanders should be thought of, and all the means at our disposal should be made use of in aiding us to reach a correct diagnosis.

The injection of mallein, which is employed in diagnosing incipient or latent glanders in horses, is of no service in an attack of suspected acute glanders in man, as a positive diagnosis depends mainly on a rise of temperature (in addition to a local reaction), and this is already present. We have heretofore depended on finding the *B. mallei* in the cultures, and in the typical results obtained by inoculation. These means will, in practically all cases, enable us to reach a diagnosis, but they are time consuming, requiring from one to three days to furnish results.

Recently a new method⁵ of arriving at a diagnosis has been devised, one based on the phenomenon of agglutination and precipitation, and, therefore, similar to

the Widal test in typhoid.⁶ This method, according to the report, is used officially in the diagnosis of glanders in horses, in Austria and Prussia, and is considered fairly accurate.

It may not be out of place here to quote from Councilman's⁷ article on the diagnosis of glanders: "Taken in its entirety, the clinical history of the disease is almost characteristic, but at a given period, and, indeed, for a long time, it may be impossible to make the diagnosis." Quoting further: "The skin lesions which are so prominent in the horse appear in man only in the later stages of the disease, and abscesses in the muscles (which are very rare in the horse) are common in man and often constitute the first evidence of the disease. The acute disease begins in man with chills and high fever, which sometimes takes a typhoid form. There is often intense pain in the joints and muscles, with general weakness and malaise. This condition is followed by the development in the muscles or subcutaneous tissue of hard swellings, which rupture and discharge a thick mucoid pus mixed with streaks of blood. In some cases there is a diffuse erysipelatos inflammation of the skin, preceding the formation of pustules; or large ulcers may be formed by necrosis of the skin. Nasal discharge is not so marked as in the horse, but examination rarely fails to show nodules and ulcers; muscle abscesses are usually present. The pustules are most common toward the termination of the disease, and often appear only just before death. The acute form is almost invariably fatal, usually between the sixth and thirtieth days of the disease."

With the exception of one case of laboratory glanders, all cases we have found reported in the literature were fatal. The only treatment employed in this case (in which there was a six-day incubation period with symptoms resembling typhoid) was the ordinary surgical treatment of an abscess. The patient was ill about three months, with several relapses of three to four days' duration.

BACTERIOLOGIC FINDINGS BY DR. CROHN.

The bacteriologic findings in this case are noteworthy, particularly on account of the demonstration of the value of blood cultures in the early diagnosis of these conditions. The results obtained were as follows:

As was previously mentioned, the patient was admitted with a diagnosis of a general staphylococemia, but did not answer, in many respects, to the typical picture corresponding to a bacteremia of this type. At this point, the diagnosis of a general infection with the glanders bacilli was suggested, and steps were immediately taken to confirm the clinical diagnosis by laboratory means. This consisted first of smears and cultures from the pustules; second, emulsions of pustular contents for animal inoculation; third, blood cultures. The first blood culture was taken three hours after admission, and 15 c.c. of blood were withdrawn from the median cephalic vein. At the end of 48 hours, all the media showed a culture of glanders bacilli.

The smears which were taken from a number of the pustules over the body, presented the following: Gram stains of the smears showed rather indefinitely staining Gram-negative organisms. On utilizing, however, dilute carbol fuchsin or methylene blue there were seen long, slender bacilli, colored rather faintly, and having an unevenly tinted cell body, with numerous darker staining areas. The general configuration of these bacilli was suggestive of the *B. mallei*.

At the end of forty-eight hours, the cultures from the pustules showed a slight, grayish, confluent growth along the line of inoculation on all the media. Emulsions were made of some of the contents of the pustules, and four male guinea-pigs were inoculated intraperitoneally with small doses of the mixture. On the same day that the cultures from the skin lesions showed growth, the guinea-pigs which had been inoculated with material from the pustules began to react. The animals appeared sick, showed increased temperature, refused food, and evinced considerable tenderness on handling the lower part of the body. The scrotum showed considerable swelling, was distended, reddened and hot. The testicles were enlarged and painful. (This last effect of the intraperitoneal injection of glanders bacilli into male guinea-pigs is called the "Straus reaction," and is regarded as pathognomonic for this organism.) Within the next three days all of the animals had died with the picture of a general infection.

4. The New York City Board of Health reported six cases in 1906.

5. Jour. Infec. Dis., May, 1907.

6. Parke Davis & Co. furnish an agglutination outfit for this test, with full directions.

7. Wood's Handbook.

At autopsy the animals showed multiple foci, consisting of small localized caseous areas in the parenchymatous tissue of many of the organs (spleen, liver, lungs). The tunica vaginalis of the scrotum was enormously distended, and contained purulent, greenish-yellow pus. Each testicle was enlarged from the normal size, that of a pea, to that of a rather large flat grape (1.2 to 2 cm. in diameter) and consisted of a diffuse, caseous, broken down mass of semi-necrotic material. The inguinal lymphnodes were enlarged. Microscopic sections showed the *B. mallei* in all the organs examined.

On the third day after admission, another blood culture was taken. This culture at the end of forty-eight hours, showed a positive growth of the glanders bacillus, similar to the first blood culture. The results of these two cultures may be summarized as follows: The first culture was taken on the day of admission while the patient's temperature was 103 F. The earliest colonies were seen on the plates containing serum. The average number of colonies in the first blood culture was 0.9 bacilli per c.c. of blood. The second blood culture, taken two days later, while the patient's temperature was about 102 degrees, averaged 11 bacilli to the c.c., showing a rapid increase in the severity of the infection as the powers of resistance of the individual diminished. The guinea-pigs, inoculated with cultures of the bacilli recovered from the blood, reacted similarly to those inoculated with material from the pustules, that is, showed the characteristics of a Straus reaction.

The clinical diagnosis of this case was thus corroborated in the laboratory by: First, smears from the pustules showing morphologically characteristic bacilli; second, cultures from the pustules giving characteristic growth on media; third, two positive blood cultures; fourth, inoculation of organisms recovered, into guinea-pigs, with typical Straus reaction and death. (Unfortunately, the family refused permission for autopsy on the deceased).

The interest in this case lies particularly in the fact that we were able to confirm the clinical diagnosis by two positive blood cultures. This is important since it should be remembered that the organisms are difficult to demonstrate and isolate from the pustules of the skin. Gram stain alone may be unsuccessful, dilute carbol-fuchsin or Loeffler's methylene blue are more satisfactory. A search through the literature reveals the fact that in many of the undoubted cases of acute and chronic glanders, considerable difficulty was found in staining and recognizing the organisms in the skin pustules. In such a case, and where animal inoculation is impossible or unsatisfactory, a blood culture will, in a very large proportion of cases, make the diagnosis.

In our case the blood cultures were taken early in the course of the disease (first day of observation); positive growth was seen within forty-eight hours after the culture was taken, and the organism was identified with facility on the media and later by animal inoculation. The value of a positive culture early in the course is readily apparent from the fact that many cases of acute glanders simulate clinically the picture of typhoid fever and are often differentiated from it with difficulty. Not only in differentiating from typhoid fever, but also, when the case is seen early, from pneumonia, from acute articular rheumatism, from staphylococcosis, etc., the blood culture is a desideratum and presents a rapid and practical diagnostic value. In acute glanders, in about 50 per cent. of the cases, positive blood cultures, where attempted, were obtained early in the disease. Pappenheimer,⁸ Coleman and Ewing, Lewis and Duval, and Pilcher⁹ have recently reported success in similar cases.

THE OCCURRENCE OF GLANDERS IN MAN.*

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CLINICAL REPORT BY DR. BEVAN.

During October, 1907, I was called to Milwaukee to see three cases which had puzzled the attending physicians and which presented interesting and difficult problems. There were three brothers, farmers, who lived near each other in central Wisconsin, and the son of one of the men involved in the case. One of the brothers, a man of about 35 or 40 years of age, had traded for a horse, which had been brought down from the northern part of the state. This horse had at the time, or soon after his purchase, developed a swelling under the jaw. The new owner lanced this swelling, and soon after he developed an infected hand. The hand infection was followed by general systemic infection, multiple abscesses and death within a few weeks.

The other horses on the farm were taken ill, and some horses were borrowed from a brother, who lived six miles away on another farm. The borrowed horses also devel-

oped the same illness and were then returned to their owner. The owner, the second brother, was shortly afterward taken ill with an acute illness resembling somewhat acute articular rheumatism. In the meantime a son of the man who had died was seized with similar symptoms, and another brother, who had had some trouble with a knee-joint for some time, suddenly, after a slight injury, developed an enormous, acute, painful swelling of the knee, with temperature, but without any severe, general symptoms.

By this time the families of the patients were in a panic; no one seemed to know what ailed them, and the three individuals were sent to St. Joseph's Hospital, in Milwaukee, and I was called as I had had some experience with lumpy jaw and blastomycosis, and these lesions were considered as possible causes of the small epidemic. I took with me one of the house staff at the Presbyterian Hospital, Dr. W. W. Hamburger, who had done some creditable laboratory work in both actinomycosis and blastomycosis.

On examination I found the following facts:

CASE 1.—*History*.—A man, aged about 40, had had trouble with his knee before the other cases occurred, but who rather suddenly developed an enormous swelling after a trifling injury about the time the other patients were taken ill.

Examination showed a man in fair health, somewhat anemic and below normal weight, with a great swelling of one knee looking somewhat like an enormous Charcot joint. There was no syphilitic history or ear marks of syphilis, only the history of slight swelling and then after slight injury the sensation of something giving way, and the great pain and swelling pointed clearly to a pathologic fracture, due, probably, to sarcoma. Later, the limb was amputated and sarcoma was found. This case was shown to be entirely independent of the other cases and simply a coincidence. It was, however, for a short time, somewhat confusing, as the belief was general that it was due to the same disease from which the others suffered.

CASE 2.—*History*.—This man was a few years younger than his brother, in Case 1. A short time after the return of his horses from his brother's farm, they were taken ill. Shortly after, he himself was taken ill, without any apparent cause. He had no scratch or visible point of infection. He was seized with a high fever, which varied from 100 to 104 F., and which still continued when I saw him about four weeks after the onset. He had a slight cough and a very offensive breath. He had had severe pains and swelling about his joints, especially his wrists. These swellings seemed to be about rather than in the joint proper. He was conscious and had had no delirium. He had developed a number of subcutaneous and muscular abscesses; these had been opened and packed with iodoform gauze. One of the abscesses near the right sternoclavicular articulation had, after being incised, left an ulcer covered with gray, unhealthy granulation which showed little tendency to heal. The man was weak, had lost weight, and presented a fairly typical picture of pyemia.

CASE 3.—*History*.—This boy, aged 14, was the son of the man who had lanced the lump under the horse's jaw, and who had died in a few weeks. He had been ill several weeks, had the same high, irregular, pyemic temperature as the patient in Case 2, varying from 100 to 104 F. He had no visible point of infection. He had had pains and swellings about his joints, and a single abscess in the triceps muscle of the left arm. The attending physician had that morning incised the abscess and found several ounces of pus, some of which he had saved for us.

We made smears of the pus from Case 2 from the ulcer near the right sternoclavicular articulation and found it negative. We made smears from the pus from the abscess in the boy's arm and found a few bacilli, consistent with being the bacilli of glanders, and what was suggestive was that there were no other micro-organisms.

8. Pappenheimer: Proc. N. Y. Path. Soc., p. 173.

9. Pilcher: Am. Surg., 1907, xlv, p. 444.

* Read before the Chicago Medical Society Jan. 8, 1908.

[†] From the laboratory for clinical research of the Presbyterian Hospital.