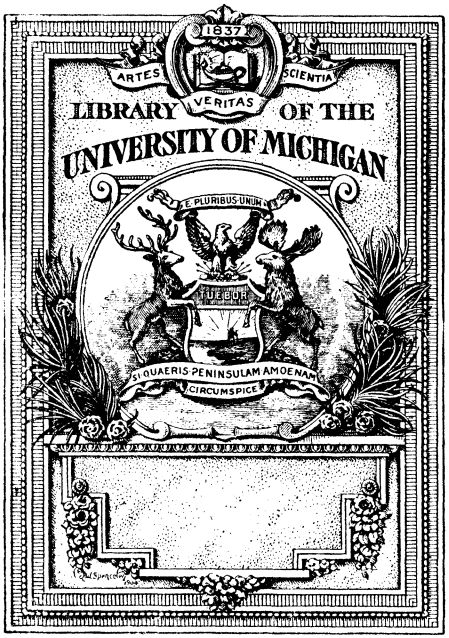
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From Professor Paul C. Freer

Philippines - Laboratories Bureau

1902.—No. 1.

DEPARTMENT OF THE INTERIOR.

BUREAU OF GOVERNMENT LABORATORIES.

BIOLOGICAL LABORATORY.

Preliminary Report of the Appearance in the Philippine Islands of a Disease Clinically Resembling Glanders.

BY R. P. STRONG, M. D.

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LETTER OF TRANSMITTAL.

DEPARTMENT OF THE INTERIOR,
BUREAU OF GOVERNMENT LABORATORIES,
OFFICE OF THE SUPERINTENDENT OF LABORATORIES,
MANILA, P. I., *July 19, 1902.*

SIR: I have the honor to transmit herewith a preliminary report of the appearance in the Philippine Islands of a disease clinically resembling glanders, by Richard P. Strong, M. D., Director of the Biological Laboratory.

I am, very respectfully,

PAUL C. FREER,
Superintendent Government Laboratories.

Hon. DEAN C. WORCESTER,
Secretary of the Interior, Manila, P. I.

PRELIMINARY REPORT OF THE APPEARANCE IN THE PHILIPPINE ISLANDS OF A DISEASE CLINICALLY RESEMBLING GLANDERS.

By R. P. Strong, M. D.

Veterinarians and owners of horses are advised that an infectious disease which may clinically at times closely simulate farcy (the nodular, cutaneous form of glanders) has been found to exist in the Philippine Islands. My attention was first called to this malady by Dr. J. G. Slee, veterinarian of the Board of Health, Manila, who sought aid from the Laboratory in the diagnosis of the disease with which several horses were afflicted, and requested an examination of these animals for glanders. That this malady sometimes closely resembles the cutaneous form of glanders may be evidenced from the fact that in the first case encountered a diagnosis of farcy had already been made by three veterinarians. Upon a microscopical study of material removed from the pseudo-farcinous buds, however, it has been possible to show that the disease under discussion is of an entirely different origin from glanders. Indeed, while farcy is an affection which owes its origin to one of the schizomycetes or fission fungi (bacillus Mallei) the malady under consideration, it seems, is not due to bacterial infection at all, but to a parasite of an entirely different group, namely, one of the budding or yeast fungi (a blastomyces).

CLINICAL MANIFESTATIONS.

The disease starts as a small nodule situated in the cutis and frequently in the neighborhood of some slight abrasion. The primary node usually appears upon one of the extremities or in the cervical or abdominal region, but may be situated on the shoulders or chest. From the first nodule the infection spreads, apparently along the course of the lymphatics, and eventually many buds form. Frequently the adjacent lymphatics become swollen and arranged in a row presenting somewhat the appearance of beads on a rosary. The nodules vary in size from about 5 mm. to 3 cm. in diameter.

The hair is preserved over the younger tumors, which at first are hard, but usually soften later and form larger abscesses. If left to themselves, they generally finally open and leave ulcers with margins which are usually irregular. When the abscesses are incised in their early stages they are found to contain a bloody, purulent, tenacious material. The contents of the older tumors is yellowish white, gelatinous, and very tenacious. When the cervical region is affected, the submaxillary glands are not uncommonly swollen, and the lymphatic glands near the other parts involved are usually enlarged, soft and freely movable. The disease extends gradually, and in neglected cases may spread over almost any part of the body and even invade the nasal mucosa. A mucous discharge from the nose then appears, and the picture now more closely resembles glanders. We, however, have not yet seen the primary nodule situated in the nares. In the cases observed there seems to be no tendency for the process to invade the scrotum, testicles, or penis. Indeed, though there have been nodes very near these organs, there has so far been no involvement of them. In the fairly severe cases there may be some general disturbances, such as slight fever and loss of appetite. In the severe ones anemia and cachexia appear in addition. The mild cases may run an almost afebrile course.

While glandular metastases occur, metastases in the internal organs have not as yet been observed. Occasionally sinuses form in the subcutaneous and deeper muscular tissues. The disease runs a chronic course and may last for months, but the prognosis is usually favorable and a very large majority of the animals eventually recover. Cattle are sometimes affected with this malady, but it is not so common in these animals as in horses.

ETIOLOGY.

As has been referred to above, upon microscopical examination it was very soon seen that the disease had an entirely different origin from glanders. Cover slip preparations and cultures made from many early and late nodules showed no bacteria. In a few instances micrococci were found present, but it seemed likely that these organisms had invaded the lesions secondarily from the skin, as it was particularly in the older and more superficial abscesses that they were encountered. In no case have bacilli been met with either in cover slip preparations or on the

various culture media employed. In fresh microscopic preparations made from material of the nodes, while the absence of bacteria is noticeable, what is still more striking is the presence of numerous oval glistening bodies measuring from about 4 to 5 μ long by about $3\frac{1}{3}$ μ wide, and presenting a double contour. These bodies are found lying both free and inside the cells. In specimens of the pus stained with Ehrlich's triacid solution, the cells which contain the parasites are seen to be generally of two varieties, namely, large endothelial phagocytes and polymorphonuclear neutrophiles. Inside the cells these oval bodies generally appear in the hardened specimens as clear, glistening spots somewhat resembling vacuoles. Often from three to five may be seen in one cell. Frequently they do not stain with the aniline dyes. Even after prolonged treatment with carbol-fuchsin, most of them remain clear, though some show a deeply staining point which is usually placed eccentrically, or others inclose several deeply stained granules. Occasionally there is some staining at the periphery of the body while the central part remains clear. A smaller number may, however, uniformly color a fairly deep red or assume a pinkish tinge. In specimens of the pus carefully hardened at a low temperature, treated with carbol-fuchsin and mounted in water, while one still finds a large number of clear ovals, many others are stained a deep red and some of an eosin color. It can not be said that the age of the blastomyces is the only factor which determines this affinity for the dye, as many young cells stain poorly, while occasionally older cells color intensely. From these preparations, however, it is easy to see that the glistening, oval bodies observed in specimens, hardened in alcohol and ether or hardened without certain precautions, are the empty capsules of the blastomyces from which the protoplasm has in some way escaped. In the specimens mounted in water it is very common to find one or several deeply colored staining granules situated inside of the clear capsule and endowed with very active Brownian movement. We have not been successful in staining the empty capsules with the methods employed in coloring the capsules of bacteria, nor have we been able to obtain any apparent reaction with the iodine stains. Frequently there is the appearance surrounding the oval bodies of a ragged envelope which stains faintly. The capsules may be made very distinct by treating them with dilute acid or alkaline solutions.

The exudate from the nodules is very rich in cells and consists

chiefly of large phagocytic cells and polymorphonuclear neutrophiles. In addition to red blood corpuscles, there are a fair number of small round mononuclear cells, some eosinophiles, and a few plasma cells. A few of the neutrophiles show iodophilia with Ehrlich's stain. The exudate also contains a large amount of fibrin.

CULTURAL PROPERTIES OF THE BLASTOMYCES.

The organism does not grow well on bacteriological media, such as plain agar, glucose, maltose, saccharose, and beer-wort agar or bouillon and potato. After from seven to ten days, on glucose or wort agar, sometimes a very delicate growth may be observed along the track of the needle on the surface of the media. Cover slips show that the organism is living and slowly reproducing itself. Small portions of the material removed from the nodule and mixed with a small quantity of bouillon or agar in a hanging drop show numerous budding forms after from forty-eight to sixty hours in a moist chamber. After a still longer time jointed hyphæ may be noted, and later formations of lateral and terminal conidia. In the protoplasm of the cells may be frequently seen vacuoles and bodies resembling oil drops. No fermentation of any of the sugars has as yet been observed.

We have been successful in producing small nodules in one monkey by subcutaneous injection of material containing the blastomyces.

DIFFERENTIAL DIAGNOSIS.

The disease briefly reviewed above is not to be confused with that termed *"Bursattee"* in India, as described by F. Smith as being due to a "mould fungus," or with that known as *"farcin du boeuf,"* an affection of cattle which exists in the West Indian Islands, especially Guadeloupe, and which owes its origin, according to Nocard, to a streptothrix, or more correctly, to an actinomyces. It is, however, probably very closely related to the variety of lymphangitis epizootica studied particularly by Fermi and Aruch and to a similar infection described by Tokishige in Japan. Rivolta had previously noticed certain highly refractive bodies constantly present in the pus from nodules of cases of lymphangitis epizootica, which he termed *cryptococcus farcinimosus.* By other observers these bodies have been considered as coccidia or as sporozoa. In the Japanese variety the scrotum, penis, and testicles are particularly liable to

infection, and metastases of the lungs may occur and even changes in the periosteum of the bones and cartilages. Tokishige considered a saccharomyces which he named *saccharomyces farcinimosus* to be the true etiological factor in this disease. Nevertheless it appears that his organism was rather to be classed as an oïdium. The organism described by Fermi and Aruch differs considerably, however, from that regarded by Tokishige as the causative agent. The former observers obtained colonies on potato cultures after three days. The cells were rounded or oval, and buds formed at the ends. Hyphæ were not mentioned. Tokishige's saccharomyces required from thirty to fifty days for development on artificial media, and in time the surface then became folded like coils of the intestine. Microscopically, hyphæ and yeast cells occured together.

As our organism as yet shows no tendency to ferment sugars we prefer to consider it for the present, at least, as a blastomyces. The disease is still under study in the laboratory, and a more complete report will appear at a later date.

The diagnosis can usually be suspected and in many cases made in the following manner: A small amount of material from a freshly opened nodule should be transferred, preferably by an oese, to a glass slide and covered with a cover glass which is gently pressed down. On examination with a moderately high power (Zeiss DD, Oc. 4) numerous glistening ovoid bodies with a double contour as described above may be seen in the field of vision. The diagnosis should be confirmed by cultures.

TREATMENT.

On the appearance of the first node the hair should be shaved for a considerable distance around it, the nodule opened early, curetted, cauterized, and thoroughly cleansed with some antiseptic solution, such as benzoyl acetyl peroxide,[1] bichloride of mercury, or creoline. Applications of formalin have also given good results. A 1 to 1,000 solution of benzoyl acetyl peroxide should be injected subcutaneously completely around the early tumor with the hope of limiting the extent of the disease. As each new node appears, it may be treated in like manner. The skin in the neighborhood of the tumors should be kept perfectly clean. It is advisable to thoroughly irrigate the open ulcers at least twice a day. In the interval some ointment such as iodoform or sulphur should be applied.

[1] Generally termed "Benzozone" or "Acetozone."

Veterinarians and owners of horses are advised before destroying animals suffering from supposed farcy to have microscopical examinations made from the nodules of the infected animals at the Government Biological Laboratory. It seems probable that a number of horses suffering with this disease have already been destroyed. As has been stated above, a large majority of the cases eventually recover, although the disease may persist for months.

JUNE 26, 1902.

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