

complete my paper, I think the paper itself would have answered many of the points brought up in the discussion, and I will touch on a few of them. I agree in *toto* with what Dr. Gray and Dr. Friedenwald said. I do not quite agree with Dr. Mills in some of the points brought out by him. In the first place, the danger of rupture of this bag—this bag communicates with the inside of the tube. If any one of these coverings should break, no harm can result. In the second place, the position of the bag. It is put down on a silk thread, which has been swallowed the night before, until it gets in the cardia. A fisherman with experience can tell when he has a certain kind of fish by the feel, and so one can tell when this bag is in the cardia. Dilate a little and draw it up until it firmly engages. If you do not get a steady pull by the part bulging out below the cardia, the cardia is firmly contracting. If you do not get that pull you are not in the right place and you manipulate up or down until you get into the right place. Dr. Mills suggested to me last night repeated shorter dilatations should be made. My patients dread it more and more each time. It is not a pleasant procedure. Fifty per cent. of the cases are cured by one attempt. I have the statistics of a number of cases in which I have used it.

Then we have quite a wide range of position of this bag. If you hit within an inch in any direction, you are still in the cardia, depending on the pull. You can tell by the feel of it.

I do not believe we get the same results with air dilatation that we can with water dilatation. We can distend the bag to the same degree, but the hardness of the bag varies, and since air is more compressible than water you can not stretch with air as much as you can with water. Every case I have stretched with air has later had to be stretched and cured with water treatment.

With reference to the remarks of Dr. Vander-Hoof, I am firmly convinced that medicine has a place in the first and in some of the second-stage cases. In the third-stage cases you are only temporizing by medical treatment. One of these patients died because he was put off; his condition of mild cardiospasm had lasted for thirty years. He got to such a degree that a thread would not go through his cardia. He had a long tortuous esophagus, so that it was impossible to pass anything down. He died in spite of a gastrostomy, which was done to give him food.

In regard to what Dr. Niles has said, I feel one can often start something going and can not stop it. That is what etiological factors do when they start cardiospasm going. When you remove the etiological factor the thing has been started and does not stop.

Dr. Friedenwald is correct when he says that cases with dilatation and cases without dilatation have to be handled differently, and there is no cure with dilatation, as a rule, excepting by the mechanical methods.

COCCIDIOIDAL GRANULOMA, INCLUDING THE FIRST REPORTED CASE EAST OF THE MISSISSIPPI*

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Of interest from several viewpoints is the case of N. D., a colored woman, who was admitted to the tuberculosis ward of the Roper Hospital, Charleston, S. C., on December 10, 1918.

The hospital record furnishes unsatisfactory information of the case for two reasons. First, she was delirious when admitted and remained so until she died; second, the diagnosis of pulmonary tuberculosis appeared so plainly to be correct that, probably on account of the condition of the patient, a thorough investigation of the case was not made.

Her age was given as 45 years and her occupation as household service. At the time of admission her pulse rate was 136 and the pulse was very weak. Her respiration rate was 44. Her temperature normal. Physical examination showed marked emaciation; teeth covered with sordes; rales and areas of consolidation were in the apex of the right lung and a lesion described as a bedsore was on the right buttock. On the second day at 4 p. m. her temperature was 99; pulse 146; and respiration 64. That night her pulse was 128; temperature 97; respirations 52. The next morning her temperature was 100.8; respirations 48; and her pulse was so weak it could not be counted. Death occurred on this day, December 12, and she came to necropsy with the diagnosis of pulmonary tuberculosis. No sputum nor other examinations appear to have been made.

At the necropsy there was some doubt of the correctness of the diagnosis, mainly on account of the character of the pulmonary lesions, but the real nature of the condition was not suspected until the microscopic slides came to me for observation. The gross necropsy findings are recorded as several empty cavities in the apex of the right lung, with complete but delicate encapsulation, and no surrounding tubercle formation, some toughness and emphysema of the lung generally, edema of the lungs, parenchymatous degeneration of the heart, and acute nephritis.

The microscopic slides were brought to me for consultation and on hurried examination I was about to pass the case as one of tuberculosis when I happened to notice a peculiar body within a giant cell. Then, upon thorough detailed examination, I found the widespread invasion of the parasite *coccidioides immitis* with the lesions produced by it, and came to a diagnosis of coccidioidal granuloma.

After discovering the true nature of the case

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an attempt was made to find out something of the previous history of the woman. It was learned that she was born and had lived on one of the sea islands near Charleston, had come to work in Charleston as a household servant several months past, and had never been out of this region. She was taken sick about October 1, 1918, with what was thought to be influenza. The attack was rather severe. She was in bed three weeks, and on getting up was unable to resume her work. After being up for two weeks she returned to bed, where she remained until death, during which time she was treated for kidney trouble by a negro physician. It was learned also that she had a sister living with her who was sick in the same way at the same time, but went back to the islands, and nothing further was known of her.

It has been said that the anatomic changes in coccidioid granuloma resemble those of tuberculosis so closely as to make the diseases indistinguishable save by finding the organism.

Now, while this case would probably have passed as tuberculosis had the organism not been seen, after the nature of the lesion was recognized the anatomic changes furnish certain features which are different at least from the typical case of tuberculosis; and even without finding the organism it should be put down as of doubtful nature. In the first place, the small cavities in the lung did not show a typical tuberculous reaction surrounding them and there was no caseation evident either grossly or microscopically. There was a thin granulation tissue wall which was highly vascular; there were no tubercles; the young connective tissue cells, endothelial cells, leucocytes, lymphocytes and giant cells were not organized about particular foci; the giant cells, which were numerous, were most plentiful near the cavity, were irregular, not hyaline, and contained clumps of nuclei of varying numbers about the center of the cell. The parasite was present within the giant cells as the single round cell with capsule and round central body about 15 microns in diameter; as larger encapsulated bodies within or outside the giant cells, containing varying numbers of minute crescentic, angular, or rounded, daughter bodies; or as larger irregular spaces without definite capsule surrounded by granular detritus—apparently from the destruction of the cell which contained the body—containing varying numbers of the same minute daughter bodies. The destruction of tissue appeared to be individual cellular destruction, disintegration and dissolution, rather than larger areas of multicellular death which would have shown the presence of necrotic material. The cavity was more or less clean of necrotic substance. The vascularity, the lack of focal organization as tubercles, the character of the giant cells, and the lack of multicellular necrosis, particularly of caseation, seemed to furnish differentiation from tuberculosis in this particular lesion of this case.

In other organs the miliary character of the lesions gave rise to a closer resemblance to tuberculosis, but even here the lack of multicellular necrosis and the appearance of the giant cells furnished differentiating features. Miliary le-

sions were widespread in the liver, spleen, and pancreas. In the pancreas the invasion occurred in the acini and also in the islands of Langerhans. The lesions were small and bore little resemblance to tuberculosis. There were individual gland cell destruction, the accumulation of young connective tissue cells and lymphocytes, but no giant cells. The parasites were mainly the large segmenting forms. In the spleen both sinus walls and malpighian bodies were the seat of young lesions. Here single cell invasion and destruction, with the accumulation of segmented parasites in cell remains with no reaction as yet occurring, was seen. Here also were small collections of young connective tissue cells and lymphocytes, with an occasional small giant cell. The foci in the liver were practically limited to the interlobular framework, where were young lesions very similar to those in the spleen, but with more giant cells and resembling miliary tubercles more.

The kidneys exhibited the most extensive involvement, of a linear distribution as a rule, resembling the extension of abscesses of these organs. The glomeruli and intertubular tissues were mainly affected, but the granulosomatous tissue had grown and ruptured into the tubules until even the lumen was extensively invaded. The lumen of many tubules contained pus and some parasites and these were undoubtedly passing out in the urine. There was little of the tubercle-like formation and few giant cells were seen. It was more of a granulation tissue growth, with extensive polynuclear infiltration taking place in parts of glomeruli. It obliterated whole glomeruli, occurred between tubules, bursting into tubules, and in large areas the tubular structure was practically obscured. The parasites were in various stages, prominent in large connective tissue or endothelial-like cells, or extracellular. There was no multicellular necrosis and no caseation, but evidence of single cell destruction and disintegration with liberation of parasites.

I saw no positive evidence of invasion of epithelium or the essential cells of any of these organs, and the pathology of the process appeared to me to be a matter of blood vascular dissemination of the parasite, the phagocytization of the organism by an endothelial cell, possibly of the capillaries, probably also by wandering endothelial leucocytes, the destruction of the phagocyte and liberation of the segmented organism, further phagocytization with progressive cellular destruction, the accumulation of endothelial leucocytes and some lymphocytes, and the formation of foreign body giant cell phagocytes, with thus a gradual growth of the lesion. The absence of polynuclears except in the larger lesions in the kidneys, and here their lack of proximity to the parasite, seemed to signify that polynuclear leucocytosis was not a part of the early reaction and might have been the result of secondary infection.

As to the atrium of infection, the oldest lesion was apparently in the lung, the others seeming to be from hematogenous dissemination. Whether the infection followed influenza, or whether the

sickness was from coccidioides infection in the beginning, the history is also suggestive of primary pulmonary invasion. There were no superficial lesions except the bed sore on the buttock and no sections were taken from it.

The case calls to our attention a disease heretofore unrecognized in this part of the country.

The disease coccidioidal granuloma was first reported in 1891 in a native of the Argentine Republic by Wernicke.¹ The parasite in this case was thought to be a sporozoon. In 1894, Rixford² reported a case from California. The parasite in this case was studied by Rixford and Gilchrist³ and named coccidioides immitis. Later in 1894, the third case, also from California, was reported by Thorne⁴ and Rixford.⁵ The fourth case was reported, in 1900, by Ophuls and Moffitt,⁶ who first recognized that the organism belongs to the molds instead of being a protozoon.

Up to the present there have been forty-four cases reported, this making the forty-fifth. Forty-one were in residents or former residents of California. One originated in Colorado, one in Missouri, the first in the Argentine, and this, the forty-fifth, in South Carolina. The San Joaquin Valley of California has been the source of the majority of reported cases.

A large per cent. of these cases has been in adult males, in fact only one woman and one child are reported in the first twenty-eight cases. This case is, I believe, the second reported in a woman. The disease is not confined to any particular nationality, class or race; Caucasians, Mongolians, American Indians and negroes are represented; a native of the Argentine, a Portuguese, German, American Indian, Mexican, Japanese, Chinese, Greek, and native white and black Americans. All classes of society are included, but the majority have been laborers engaged in irrigation work in lower California.

Considering the widespread development of the disease, it is not improbable that it is present where it has not been recognized and is more prevalent where single cases have been found, and that it passes for tuberculosis.

Those common cases of supposed tuberculosis in which the tubercle bacillus is not demonstrable should be closely investigated for this or similar organisms.

ONSET AND COURSE

In some cases the onset has been sud-

den, very much like the acute febrile diseases, while in others there has been a gradual onset, the patient hardly knowing when the illness began. Many cases have shown remissions, usually for periods of only a few weeks, but occasionally as long as two years. Evidences of systemic infection by the appearance of multiple abscesses have commonly occurred in the course of several weeks. Some cases have gone on to a fatal termination without the appearance of cutaneous abscess formation, and in these cases the lungs have appeared to bear the brunt of the infection; the patient has shown thoracic pain, cough, rapid emaciation, weakness, night sweats, chills and irregular fever which ranged from 99 to 104, but in some remained below 101, and late profuse expectoration, at times blood-tinged. Cases with initial skin lesions have usually progressed more slowly and have developed painless subcutaneous abscesses, very much like glandular tuberculosis. These abscesses have destroyed tissue extensively and bones have been frequently involved, notably the occipital bone, sternum, vertebrae, ribs, femur and humerus.

The abscesses have burrowed deep, but usually have pointed, and discharged quantities of thick pus, frequently containing apparently pure cultures of coccidioides immitis. All of these apparently cutaneous cases which have come to necropsy have shown systemic involvement.

Before death the lungs have usually presented the physical signs of tuberculosis.

The patients have not responded to treatment, but have become progressively weaker, always with some fever, some showing a weak rapid pulse, some having several convulsions, some being delirious for several days before death.

LABORATORY FINDINGS

Blood cultures have been negative save in one case. The sputum has been profuse, mucoid in some cases, purulent in others, and the coccidioides immitis has been found in large numbers.

The urine may show albumin and casts. It probably contained the parasite in this case.

The leucocyte count has been from 9,000 to 20,000 with a normal differential count

save for the presence of 3 or 4 per cent. eosinophiles.

The lesion of the infection has been found in practically every organ and tissue of the body.

TREATMENT AND PROGNOSIS

No successful treatment has been devised and all cases save one have died within from a few weeks to nine years. The only case recovering was one in which the infection was recognized in an extremity and the infected member amputated apparently before dissemination had occurred.

SUMMARY

The first case of *coccidioides immitis* infection in South Carolina and east of the Mississippi is here reported. It is the forty-fifth case known, the second case in a woman, and the fourth that was not in California.

The confusion of the disease with tuberculosis has again occurred, even though a complete investigation of the case would no doubt have revealed its true nature. The parasite should have been found in the sputum and urine. Again we are reminded that even in medicine things are not always what they seem and no diagnosis on circumstantial evidence can be positive. The failure to use methods and means which are at hand for diagnosis, no matter how apparently clear the case may be is inexcusable.

It is highly probable that infection by *coccidioides immitis* is with us where we have not recognized it, and it is desirable that those cases of supposed tuberculosis in which the tubercle bacillus is not demonstrable should be carefully investigated for this or kindred infection.

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DISCUSSION

Dr. J. Heyward Gibbs, Columbia, S. C.—The doctor's report of this case is significant in several respects. In the first place, he calls attention to the fact that this disease exists as an indigenous condition on the South Atlantic seaboard. The probabilities are that we have overlooked this condition. In the second place, his report of his case calls attention to the fact that this relatively rare disease may exist as a widespread systemic infection without the auxiliary skin lesions, and that unless careful searches and investigations be made, we may encounter such a condition and mistake it for a common pulmonary disease, tuberculosis or other types of acute infectious diseases.

It is decidedly unfortunate that Dr. Lynch's report does not incorporate a more complete clinical picture and study of this particular patient. I am in hopes in his closing remarks he will take occasion to point out to us the staining characteristics of the organisms concerned. The organisms of this disease can readily be obtained from the pustular lesions of the skin and the urine, but I do think Dr. Lynch should emphasize the means of identifying the organism in these secretions and excreta.

Dr. Lynch (closing).—In response to Dr. Gibbs' question the parasite or organism is found in the pus from the cutaneous lesion or in pulmonary involvement it may be found in the sputum. It is fairly easy of recognition. It varies in size considerably from 5 to 50 microns. It is a mold. It can be found easily by the addition of potassium hydroxide to the fresh pus. It is a double contoured or encapsulated round cell. It does not show budding, except in old cultures. Its internal segmentation differentiates it from the organisms of blastomycosis. It will stain easily, but it is unnecessary to stain it. The recognition of a mold with internal segmentation, without the formation of external spores, is very suggestive of the presence of the parasite.

A Member—Does it grow in chains?

Dr. Lynch—Not in the body. I do not recall at present the character of the medium which is best suitable for it to grow on. In this case we did not get the parasite before death and did no cultivation. It has been cultivated and transmitted experimentally to a number of the lower animals with the production of the same lesions. I believe Ophuls was the original cultivator.