Medical Staff Conference: Psittacosis

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Medical Staff Conference: Psittacosis

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This article is available in Henry Ford Hospital Medical Journal: https://scholarlycommons.henryford.com/hfhmedjournal/vol3/iss2/10
Dr. Mateer: This conference will deal with the diagnosis, therapy, epidemiology and pathogenesis of psittacosis.

Dr. Quinn: We shall develop three aspects of psittacosis: First, to define the diagnostic features which will make the disease recognizable to the clinician; second to examine critically the experimental and clinically used therapeutic agents in psittacosis; and thirdly, to review the position of the psittacosis agent morphologically and immunologically among the virus agents.

CASE PRESENTATIONS

Dr. McGraw: Case No. 1. Mrs. I. M., H.F.H. No. 233836, is a 52 year old, white female who presented herself at the emergency room on November 21, 1954, with a chief complaint of chills, fever, and headache for one week and of feeling sick all over. Her past history and system review were not contributory to the present illness.

The present illness began approximately one week prior to admission, at which time she noted the onset of severe headache, general malaise, fever and a mild sore throat. She worked for one day with these complaints, but then stayed in bed until seen at the hospital. The fever, chills, severe headache and malaise, along with anorexia, persisted all week without improvement. There was no cough, chest pain, epistaxis, vomiting, jaundice, dark urine or abdominal pain. The patient said she owned parakeets, one of which had died about one month ago.

The physical examination on admission revealed an acutely ill-appearing woman with a temperature of 103.4° F., respirations 28 per minute and pulse 95 per minute. The respirations were not grunting. The nostrils did not flare. The skin was hot and moist. The only other abnormal findings were limited to the chest. Slight dullness to percussion and a few rales were noted over the right mid-anterior chest.

The pertinent laboratory data was as follows: normal urinalysis; white blood count 9,600 per cubic millimeter with a normal differential; negative routine blood culture; negative cold agglutinin titer; unremarkable throat culture; sedimentation rate of 31 millimeter per hour (Winthrop). The complement-fixation test for psittacosis is revealed in Table I.

The hospital course of the patient was benign. She was placed on tetracycline (achromycin), 250 mg. four times daily, 12 hours after admission, and her temperature became and remained normal in 24 hours. Symptomatic improvement was rapid. The physical findings in the chest were normal by the 5th day. The patient was dis-
charged on the 11th hospital day. She received a total of 9 grams of tetracycline.

Three weeks after discharge, she complained only of tiring easily and of the slowness
with which her previous strength was returning.

Dr. Montgomery: Case No. 2. Mrs. B. B., H.F.H. No. 514105, is a 40 year old,
white housewife who was admitted to Henry Ford Hospital on December 7, 1954,
with chief complaint of headache and malaise of five days duration.

The family history was significant in that her sister (Case 1) had been treated at
the Henry Ford Hospital in November, 1954 for psittacosis. This patient had been
repeatedly exposed both to the sister and her sister's sick parakeet.

The present illness began five days prior to admission, at which time she developed
severe occipital headache and general malaise. Three days prior to admission she noticed
chills, fever, night sweats, dry non-productive cough, and a few episodes of mild
epistaxis. These symptoms persisted until the time of admission. There were no
gastrointestinal complaints or chest pains.

The physical examination revealed a normal temperature and respiratory rate. The
pulse was 80 per minute. There was no jaundice, rash or lymphadenopathy. Examina­
tion of the lungs revealed only a few inspiratory fine rales at the right posterior base.

The laboratory data was as follows: The white blood count was 11,500 per cubic
mm. with a normal differential; the sedimentation rate was 40 mm. per hour (Winthrop);
urinalysis, negative; routine blood culture, negative; cephalin-cholesterol test, negative;
cold agglutinin titer, 1:4. The complement fixation for psittacosis is revealed in Table I.

The patient's symptoms were unchanged until she was placed on tetracycline, 250
mg. four times daily, on the 5th hospital day and gradually subsided in the next five
to six days. She received a total of 11 grams of tetracycline.

TABLE NO. I
PSITTACOSIS COMPLEMENT-FIXATION TESTS
(Performed by Dr. E. M. Yagle)

<table>
<thead>
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<th>Case No. 1</th>
<th>11/24/54</th>
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<tr>
<td>12/14/54</td>
<td>1:64+</td>
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</table>

Dr. Eyler: Case No. 1. (Fig. 1.) There are multiple patches of consolidation with
the largest patch at the right base. The consolidation is not very dense, and is interspersed
with areas of aerated lung. In the right upper lobe just beneath the clavicle, overlying
the first interspace and second rib, there is an additional area with aerated lung in
the center, which suggests the possibility of cavitation. No well defined cavity wall
is recognized. On the left side there are multiple strands radiating into the upper
lobe. A differential diagnosis would lie between multiple foci of acute infection and
chronic infection, such as tuberculosis.

(Fig. 2.) Two days later, only a few strands remain on the left and most of the
process has cleared on the right side. There are still, however, strands of density in
both of the areas previously involved.

(Fig. 3) By November 29, 1954, the process had cleared.

SUMMARY Initially, the pattern of densities and distribution raises the question
of chronic infection, such as tuberculosis, as well as being compatible with a patchy
pneumonitis of an acute type. The course establishes it as an acute infection.

The second patient, by comparison with the first, had very minimal changes with
faint, diffuse consolidation in the right lower lung field. The films suggest that it is in
the right middle lobe. There are old scars at the left base.

A progress film at four days shows only a few linear strands of atelectasis remaining in the area of previous consolidation.

**SUMMARY** This, too, is compatible with an acute pneumonitis which has cleared almost completely in four days. The consolidation was relatively diffuse.

*Dr. Bunch:* Historically, the family epidemic type of psittacosis was recognized long before the etiologic agent was identified. It is to be noted that the two patients presented this morning are sisters, that the sister who owns the parakeet was apparently the first one infected and her sister and brother-in-law both developed symptoms later. We have not had an opportunity to perform a complement fixation on Mrs. M's brother-in-law. Interestingly enough, Mrs. M. states that her family dog became ill during this period of time also. As we shall see later, dogs are not usually included as hosts for this disease, but there was one family epidemic that was possibly initiated by the purchase of a sick dog from a bird shop where psittacosis was known to exist.

The onset of psittacosis may be either sudden, or gradual and insidious. It is probably more often sudden with chilly sensations, fever, marked malaise, anorexia, and perhaps even sore throat. The temperature usually ranges from 100. to 102. degrees F. at the onset and gradually rises. It may be present from seven to fourteen days. Cough is almost always present. Epistaxis occurs in one-fourth of the cases, a rare finding in primary atypical pneumonia. Nausea and vomiting are common. Diarrhea or constipation may be present.
One major characteristic of this illness is the discrepancy between x-ray findings and chest symptoms and physical findings. There may be a slight, dry, irritating cough, which in later stages may become mucoid or even mucopurulent, but physical findings in the chest may be limited to a few fine rales or slight dullness in spite of very marked x-ray changes. The x-ray presents patchy areas of pneumonitis which may range from very slight increased densities to marked involvement of both lungs. In the first patient presented this morning, the findings were so extensive that the immediate roentgenologic diagnosis on the first film was moderately advanced tuberculosis with probable cavitation. Ordinarily there is slow resolution on x-ray examination, although physical signs may disappear by the third week. Our first case was characterized by rapid resolution of her extensive lesions.

Ordinarily there is a bradycardia, but severely ill patients may present collapse, tachycardia and tachypnea. The size of the spleen is a controversial issue, some clinicians having reported its enlargement as a characteristic finding of psittacosis, yet the current literature implies that the spleen is palpable in only very few cases. “Rose spot” rashes have been noted, but are usually not part of the picture. Mental symptoms may occur especially in more severely ill patients and include disorientation, mental depression and delirium.

There is usually an absence of a leukocytosis. A definite leukopenia is present in only 25 per cent of the patients.

As regards complications, thrombophlebitis may occur and has been responsible for some deaths. Relapse is quite common and prevention of relapse requires most conservative management during convalescence.

Perhaps the most interesting pathologic characteristic is that the lungs may appear to be completely consolidated and yet microscopic examination shows that these areas are unevenly involved, and alveoli containing air or serum are dispersed throughout the consolidated portions. The liver may exhibit focal necrosis. The spleen may be enlarged and contain relatively small follicles and engorged sinuses filled with microcytic cells. Frequently, involvement of the kidneys occurs. Hemorrhages and capillary thrombi in the adrenals have been reported.

The complement-fixation test has become the most useful laboratory tool in confirming a clinical diagnosis of psittacosis. It is a fairly simple test to do, and the commercial antigen is quite reliable. Interestingly, there is a cross reaction between lymphogranuloma, psittacosis, and some of the other mammalian members of this group so that it is impossible to tell on the basis of the complement fixation test which one of the organisms is affecting the patient. Complement fixation titer begins to rise about ten days after the onset of the illness, but may take as long as 30 days to reach significant titers. Titers up to 1:64 have been reported during the first month of the illness; these are considered to be significant titers. They may actually go much higher than this. There are instances in which an anamnestic type of reaction has been reported producing a positive complement fixation test to psittacosis. It has been noted that if the illness were truly psittacosis, the complement fixation titer remained elevated for a year or more after the acute illness; whereas if it were due to another member of the lymphogranuloma-psittacosis group, or if it were an anamnetic reaction, the complement-fixation titer would fall to low levels after about three months. Continued high level of a positive complement fixation titer to psittacosis after one year implies either continuous exposure, which might be experienced by
bird shop owners, or else a carrier state or chronic recurrent infections, such as reported by Meyer and Eddie. 

In research laboratories, certain organisms of the lymphogranuloma-psittacosis group may be differentiated with neutralization test even though the complement fixation titer to both psittacosis antigen and “lygranum” may be elevated.

The organisms may be identified in biopsy or autopsy material. However, clinically this does not appear to be a practical mode of diagnosing the illness. The isolation of the agent from sputum is possible but not practical because of its extreme hazard to laboratory personnel.

Dr. Quinn: In summary one should think of psittacosis in patients who have symptoms of influenza, of viral pneumonia or of typhoid fever. One should then inquire as to symptoms common in psittacosis, but unusual in other respiratory viral illness, namely, epistaxis, nausea, vomiting, constipation or diarrhea. Next, we should inquire into the possibility of bird contact, including parrots and parakeets, and especially if the bird was recently ill. Another common feature is frequency of family occurrence, particularly in the winter months. Finally, normal routine laboratory findings including negative cold agglutination test, and chest x-ray findings of interstitial pneumonitis should lead the clinician to request paired blood specimens for complement fixation test with the psittacosis antigen. A positive titer of 1:16 or higher is quite suggestive in a single specimen. A three-fold to four-fold titer in paired acute and convalescent specimens is diagnostic of infection by a member of this group of agents.

Let us now examine the available reports and our experience in the treatment of psittacosis.

Dr. Vetne: The effect of penicillin treatment in psittacosis infection has been studied in animal experiments, mainly on mice, and in small series or in scattered cases on humans. It must be kept in mind that psittacosis in humans can vary from a very mild to a very severe infection. It is, therefore, difficult to evaluate the effect of penicillin in the relatively few human cases so far reported.

Eighty mice were inoculated with psittacosis virus by Heilman and Herell. Forty of these had no treatment and showed 88 per cent mortality. In the forty other mice, penicillin treatment was started one to 17 hours after inoculation of psittacosis virus. Treatment was continued for seven days. In this group, there was only five per cent mortality. In another study on 104 mice, there was an eight per cent mortality in the treated group and 100 per cent in the untreated group. In both of these studies, penicillin-treated mice who recovered were sacrificed thirty days later and examined for psittacosis virus. Liver and spleen in most of these animals were found to have inclusion bodies of psittacosis.

Meyer reports three human infections with psittacosis virus, successfully treated with penicillin. Treatment was started on the sixth to eighth day of illness and continued for eight to ten days after the patient had become afebrile, which usually occurred within 48 to 72 hours. Meyer points out the importance of continuing penicillin treatment for a sufficiently long period after the patient become afebrile. Relapse has been reported in cases treated with penicillin for only two or three days after the patient became afebrile.

Wolins reports six patients treated with penicillin of which four recovered promptly with 400,000 units of penicillin daily. Two cases showed no response to penicillin for four or five days and finally they recovered “spontaneously.”
Dr. Lovett: Since chlortetracycline (aureomycin) became available, there have not been sufficient cases of psittacosis available to provide for an extensive clinical trial. However, the results reported so far are very encouraging. In 1948 Wong and Cox at a symposium of the New York Academy of Science, reported that chlortetracycline had an excellent therapeutic effect on experimental psittacosis infection in chick embryos and albino mice. Their work showed that the prolongation of life following the inoculation of chick embryos with psittacosis was directly affected by the size of the protecting dose of chlortetracycline, but that the protective action of the drug was not affected by the size of the inoculating dose of virus. In 1950, Gogolak using chick embryos, showed that chlortetracycline prevented division of the elementary bodies of the virus and significantly inhibited their growth in size.

During 1949 and 1950, Henry Brainerd, Theodore Woodward and Thomas Green separately reported in detail on a total of six cases of psittacosis infection in humans treated with chlortetracycline. Two of these cases had previously failed to respond to treatment with penicillin. The dosages used varied from three to four grams in divided doses daily for a period of seven to ten days. The response to therapy in each of these cases was good and was indicated by a prompt drop in the temperature and by subjective and clinical improvements. The lung lesions as shown by X-ray were found to clear rapidly.

Karl Meyer, reports two deaths in a review of ninety-two cases in man, treated with chlortetracycline prior to 1951, a mortality of 2.5 per cent.

This mortality rate indicates improvement over the previously reported mortality rates of 18 per cent in approximately 600 cases during the 1929-30 psittacosis epidemic, 11 per cent for the cases reported between 1930-1940, and 9.3 per cent of 288 cases treated with penicillin between 1940-46.

In summary, chlortetracycline appears to be the drug of choice in the treatment of psittacosis infection at the present time. It prevents elementary body division and retards growth of the virus. One may expect drop in the patient's fever, and subjective and clinical improvement within 48 to 72 hours after beginning therapy, some clearing of the pneumonitis within four to seven days, may also be expected.

Dr. Quinn: We have treated five cases of psittacosis, three with penicillin and two with tetracycline. All responded favorably, but one of the patients treated with penicillin suffered two relapses. We noted repeatedly from the histories of our patients prior to admission, that short courses of either of these drugs was followed by relapse. Our feeling is that tetracycline is the drug of choice, but more important is the necessity of adequate therapy.

Dr. Bunch, will you review the pertinent points in the epidemiology and pathogenesis of this disease which are important in establishing the clinical feature of relapse and the need for adequate therapy.

Dr. Bunch: This psittacosis organism is characterized by predilection for psittacine birds. A number of other animals and birds have been reported as having had the disease or have been experimentally infected. These include many strains of mice, rabbits, hamsters, squirrels, monkeys, sparrows, domestic fowl and turkeys, doves and pigeons. Of course, man also may be infected.

The most common mode of transmission is probably by droplet infection. Humans have been infected from merely being in a room for as little as five minutes where an autopsy was being performed. Man to man transmission has been reported and is particularly dangerous for nurses and physicians in attendance of psittacosis patient.
The causitive organism is a particularly interesting organism. It is classified in the lymphogranuloma-psittacosis group of viruses. These organisms range in size from 250 millimicrons to 350 millimicrons, thus placing them between the true large viruses such as smallpox, and the rickettsia. Consequently, they can be seen with a light microscope with appropriate stains. Further, because of the ease with which they are seen, their life cycle has been studied.

These organisms may go through their life cycle either in an intracellular or extracellular phase. One or more virus particles may enter a cell. A common matrix is formed about a single virus particle. This single virus particle is known as an elementary body. About 24 hours is required for a particle to enter and form its matrix. After this time, the virus particle within the matrix begins to multiply and as multiplication progresses, particle size decreases as the virus colony enlarges. The particles are always surrounded by common matrix and this plaque of numerous virus particles with its matrix is called an inclusion body. During the second 24 hour period, it may fill the entire cytoplasm of the cell. If the cell is doubly or triply infected, the other inclusion may parallel the initial one. After about 48 hours, the matrix of the inclusion body begins to liquefy and during the third twenty-four hour period, death of the whole cell occurs and rupture follows with the release of elementary bodies which are then infective for other cells. The extracellular multiplication of these organisms follows a similar pattern.

The effects of penicillin and chlortetracycline on the life cycle of the organism has been studied. Penicillin apparently prevents division of the virus particle intracellularly, but there continues an abnormal growth of an irregularly shaped vacuolated plaque which maintains the ability to enter the host cell. With chlortetracycline, the virus particle division is prevented and the virus growth is suppressed to the point that even if small plaques did develop intracellularly, they have little or no effect on the invaded host cell.

There has been insufficient experience with tetracyclines clinically to be certain of any definite answers about their superiority. Regardless of whether penicillin or tetracycline is used, however, there is evidence that there continues to be intracellular organisms for as long as one year after treatment. In fact, one case has been reported by Meyer and Eddie, of a patient who had developed a carrier state from which organisms were isolated as long as eight years after the initial infection. It is this tenacious persistence of the organism which predisposes to the clinical relapse which is common.

BIBLIOGRAPHY