

## Human Psittacosis Cured by Penicillin Therapy

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### SUMMARY

*A number of recent reports in the literature have told of cure of psittacosis in man following enormous doses of penicillin in the early stages of the disease. In most of these cases, however, the infection was experimentally induced in laboratory studies. Given late and in inadequate amounts, penicillin apparently has no beneficial effect.*

*With a means of treatment at hand, and effective if started early, careful analysis of all cases of "atypical pneumonia" is indicated with a view to determining if the infecting agent might not be the psittacosis virus. A history of contact with birds or bird droppings should be sought in all cases of "atypical pneumonia."*

*A case is reported in which the patient, because of contact with birds, was suspected early of having psittacosis. No benefit was noted following therapy with 100,000 units of penicillin every three hours for one day, but rapid recovery ensued when the dose was doubled.*

THE high incidence in recent years of so-called "atypical pneumonias" with the implied inability to demonstrate or apply specific therapy for the causative agent in most cases, is accompanied by several unfortunate tendencies. There is the temptation incorrectly to consider all such cases of atypical pneumonia as belonging to a single disease entity; there is not enough concern at failure to demonstrate a causative agent in any given case; the lack of applicable specific therapy is too readily presumed. One must be on guard to avoid confusing with "primary atypical pneumonia of unknown cause" not only the unusual varieties of bacterial pneumonias but also the non-bacterial pneumonias in which the infecting agent is known, for included in these latter two groups are pneumonias in which specific therapy is possible. Psittacotic, or ornithotic pneumonia now appears to be one of these.

The ubiquity of the infective agent of psittacosis, one of the largest of the known viruses, has been established. Human infections have been traced not only to the psittacine birds, parrots and parakeets, but also to canaries, finches, petrels, chickens and pigeons. As stressed by Meyer,<sup>6</sup> who for this reason favors the term ornithosis over the narrower psittacosis, the bird reservoir of infection is large and

diffuse; and Smadel<sup>9</sup> has observed that the incidence of psittacosis in humans having "atypical pneumonia" is greater than is generally recognized.

The diagnosis of psittacosis is seldom made early in the course of the disease because it depends for its confirmation upon procedures carried out in very few laboratories—the isolation of the virus from the sputum or blood of the patient through the inoculation of mice or other suitable animals, or the demonstration of a rising titre in the patient's blood of complement-fixing antibodies for psittacosis antigen. Early diagnosis is therefore presumptive. In all cases of "atypical pneumonia," a history of contact with birds or bird droppings should be sought; onset with severe headache, fever, toxicity, gastro-intestinal symptoms and non-productive cough, the presence of a normal respiratory rate, relatively slow pulse rate, absence of classical signs of pneumonia with evidence of consolidation by x-ray, and a relatively normal leukocyte count, may be suggestive.

The basis for the successful specific therapy of psittacosis is found in the experimental work of Heilman and Herrell,<sup>4</sup> who in 1944 reported that penicillin in enormous dosage given soon after inoculation with the psittacosis virus cured the disease in mice. Bedson and May,<sup>1</sup> in England, similarly demonstrated that psittacosis virus is definitely susceptible to penicillin when in the tissues of the mouse. The amount of penicillin required to keep in check infection with this virus in the mouse to the extent of making the infection subclinical was found, however, to be very great; calculation from mouse to man would approximate 11,000,000 units for a human.

Meyer and Eddie<sup>6</sup> also stress the effectiveness of penicillin therapy early and in large dosage in experimental infections in mice and rice-birds. As to the sulfonamide drugs, although Early and Morgan<sup>2</sup> demonstrated that sulfadiazine therapy was definitely effective, although less so than penicillin, in experimental infections of mice by one strain of psittacosis virus (strain 6 BC), earlier works in animals and in human cases failed to establish sulfonamide drugs as effective agents in this disease. Streptomycin therapy as reported by these same workers was completely ineffective, and the author knows of no evidence contrary to this finding.

Reports of penicillin therapy of cases of psittacosis in man, with a few notable exceptions, are somewhat disappointing. Therapeutic effectiveness of penicillin in humans with psittacosis is reported by Turgasen,<sup>10</sup> by Flippin, Gaydosh and Fittipoldi,<sup>3</sup> by Parker,<sup>7</sup> and by Kirkwood.<sup>5</sup> It might be noted, however, that the penicillin dosage employed in these

cases was very much less than that which would be expected to be effective on the basis of the experimental work to which reference has been made. Moreover, often the penicillin was administered quite late in the course of the disease. Indeed, Parker<sup>7</sup> in his report of two cases of psittacosis in man, concludes in this vein: that not much is to be expected from the dosage of penicillin ordinarily used in reported cases, and that when the temperature falls by lysis in a self-limited disease of two to four weeks' duration, it is difficult to conclude that the penicillin had much to do with the result obtained. Penicillin therapy of humans infected in laboratory with psittacosis virus, as reported by Meyer and Eddie,<sup>6</sup> where the diagnosis and therapy were established early and the dosage of penicillin was relatively large, presents a much more striking picture of the efficacy of such therapy. One such laboratory infection in a man is reported by Rosebury, Ellingson, and Meiklejohn.<sup>8</sup> In that case, penicillin and sulfadiazine in combination were strikingly effective. The infection in that case was known to be caused by the 6 BC strain of psittacosis virus which had previously been demonstrated experimentally by Early and Morgan<sup>2</sup> to be susceptible to sulfadiazine, although in lesser degree than to penicillin.

More closely than in any other reported case of penicillin therapy of non-experimental psittacosis in

a human, the circumstances surrounding treatment in the following case report are believed to approach those prevailing in the treatment of laboratory infections. The diagnosis was made and penicillin therapy begun reasonably early in the course of the disease; the dosage of penicillin was very large and the response appeared dramatic (see Figure 1).

CASE REPORT

The patient, a 27-year-old housewife, complained of recurring chills and high fever accompanied by marked gastric and intestinal flatulence and some nausea. She said that five days previously she had had so severe a headache that she had had to go to bed. She took two laxative tablets and shortly thereafter severe diarrhea developed. That night she had shaking chills and fever. In the morning she felt well enough to go shopping, but had frequent watery bowel movements. That evening chills and fever recurred. The following day, a physician prescribed a bismuth compound, empirin and codeine, and the diarrhea and cramps were brought under control. Shaking chills and fever continued, however, with apparent fall of temperature in the mornings to approximately normal. Very troublesome gastric and intestinal flatulence developed and the patient felt very ill and weak. She admitted only a mild infrequent, non-productive cough. The evening prior to admission to hospital, the temperature was 105.4° F.

Upon physical examination at home it was noted that the patient was obese and appeared to be about the stated age. The skin was warm, moist, and slightly flushed. The patient

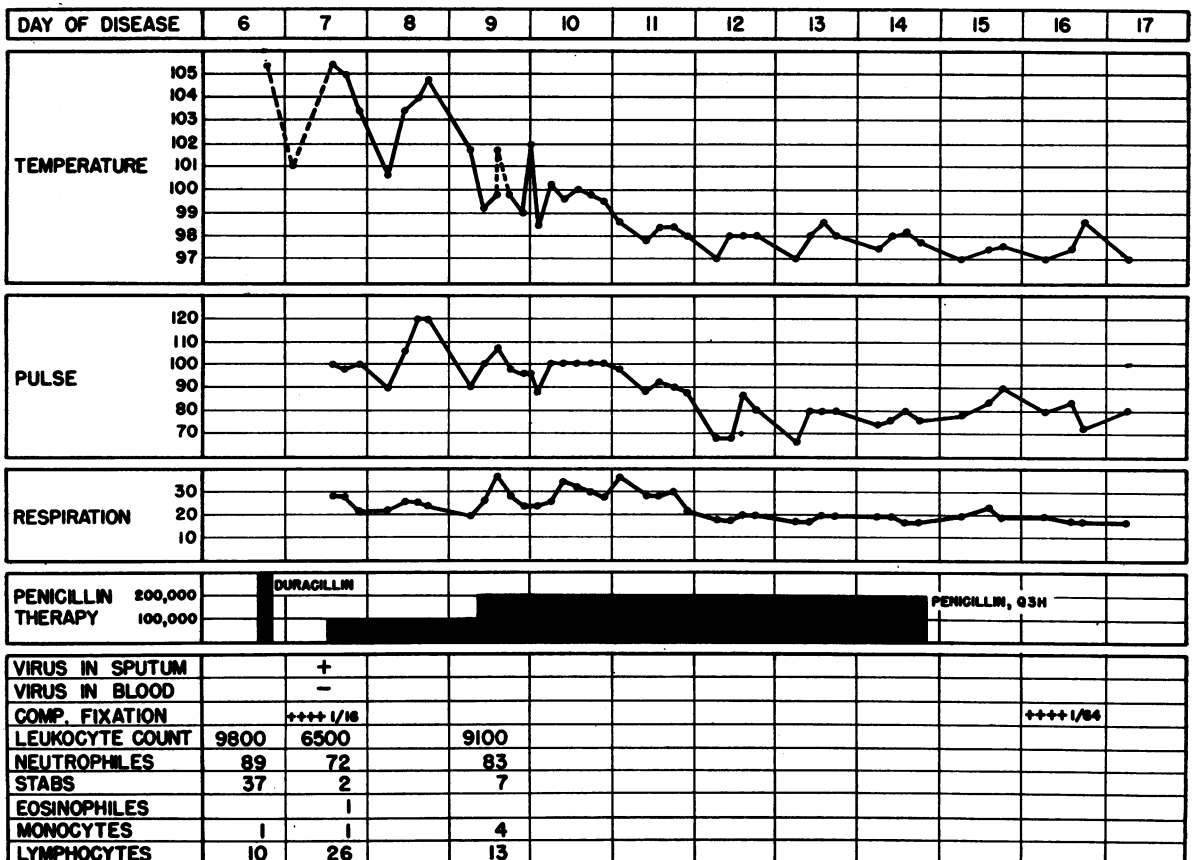


Figure 1.—Graph showing clinical course, pertinent laboratory findings and therapy.

complained of being "choked with gas." There was slight nasal congestion and injection of the fauces. No rigidity of the neck was noted. There were a few crepitant rales at the base of the left lung, but no evidence of consolidation was present. The heart was not demonstrably enlarged, and the pulse was regular at the rate of 100 per minute. Blood pressure was 98 mm. of mercury systolic and 60 diastolic. The abdomen was soft, with slight suprapubic tenderness. There was moderate gaseous distention. The spleen and liver were not palpated. Reflexes were not remarkable; the Kernig sign was negative. The lymph nodes were not remarkable. Leukocytes numbered 9,800.

It was felt that the patient had pneumonia at the left base, but the minimal findings and minimal pneumonic symptoms, the six-day history of distress, the predominance of gastro-intestinal symptoms and a very high remittent fever, were puzzling. In view of the presence of a cage of two canaries in the bedroom, inquiry was made concerning exposure to parrots and other birds. It was found that some two and one-half weeks before, the patient had purchased a canary from a pet shop, where she had played with a parrot. A tentative diagnosis of psittacosis was made and the patient was given 300,000 units of penicillin in oil intramuscularly and was admitted to hospital the following morning.

On the day of admission, the pneumonic findings in the left base were much more definite. The cough was more severe and was becoming productive of thick, glary, treacle-like sputum. Examination of the blood on the day of admission showed hemoglobin value of 13.7 gm. per 100 cc., erythrocytes numbering 4,440,000 and leukocytes 6,500, with neutrophils 72 per cent, including 2 stabs, eosinophils 1 per cent, lymphocytes 26 per cent, monocytes 1 per cent. Specific gravity of the urine was 1.006; it was acid and contained a trace of albumin but no sugar or acetone. The blood sedimentation rate (Wintrobe) was 45 mm. per hour.

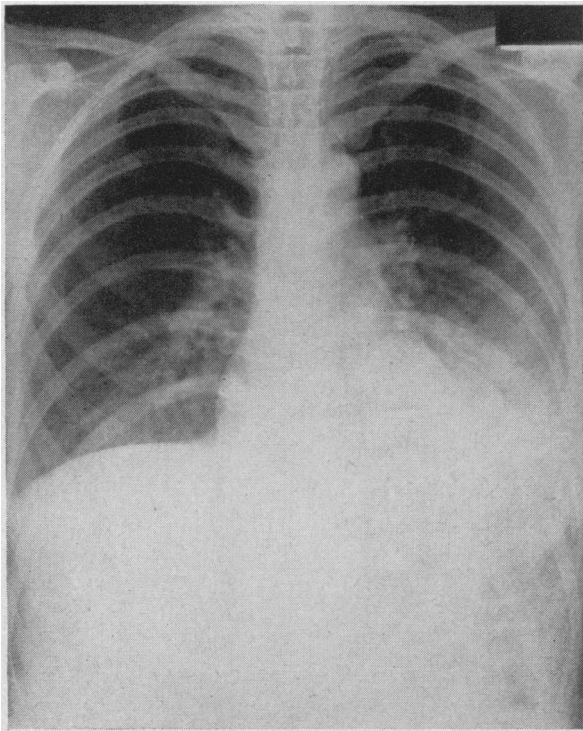


Figure 2.—Roentgenogram of the chest taken on day of admission to hospital, showing pneumonia at left base.

A roentgenogram of the chest showed an irregular area of consolidation at the left lower lobe; the left leaf of the diaphragm was obscured; the lung fields were otherwise clear (see Figure 2). In addition to the usual laboratory studies, blood and sputum were sent to the California State Virus Laboratory for psittacosis studies.

In the hospital, the patient was continued on penicillin therapy, 100,000 units every three hours. The temperature, pulse, respiration and medication are shown in Figure 1. There were sharp rises in temperature in the evening of the first two days to 105° F. and above, with marked toxicity, sometimes feeble pulse and cyanosis of the extremities at the high temperatures. Penicillin dosage was raised to 200,000 units every three hours on the second hospital day. On the third day the patient began to improve rapidly, the cough began to diminish and the sputum became reddish in color, then definitely blood-stained. By the fifth hospital day the temperature returned to normal and remained so, and the signs of consolidation began to clear. On the sixth day, report was received of the growth of psittacosis virus in both mice and cotton rats which had been inoculated with the patient's sputum, and of the presence of a good complement fixation titre for psittacosis in the blood. Another roentgenogram of the chest taken on the eighth day showed only a slight amount of abnormal density remaining in the lung. Blood taken the ninth day showed a rise in complement fixation titre for psittacosis. The patient was discharged on the eleventh hospital day, feeling well, with lungs essentially clear to auscultation.

As soon as the positive laboratory findings became known, the city and state health authorities went into action. The patient's three canaries were sacrificed and examined and although one canary, which had been in the patient's possession for five years, had an enlarged spleen, no psittacosis virus could be isolated from the organs of any of the birds. The pet shop the patient had visited was immediately quarantined. Inquiry disclosed that the patient had been there at least three times during the week in which she had purchased the canary. Blood was taken from the parrot and from five parakeets (a sample of the 14 parakeets in the store). Blood from two of these parakeets showed positive complement fixation titres for psittacosis, but although preparations from the spleens of all five parakeets and the livers of two of them were injected into mice, no virus could be isolated.

In this case, several points appear to be noteworthy. Living psittacosis virus was demonstrated in sputum obtained from the patient almost 24 hours after 300,000 units of penicillin in oil had been given intramuscularly, and six days after the apparent onset of the disease; virus was not demonstrated in the blood obtained at about the same time. Although 300,000 units of penicillin in wax and oil, followed within 18 hours by the institution of a dosage of penicillin of 100,000 units in aqueous solution every three hours, did not appear to produce any marked amelioration in the patient's condition, an increase of dosage to 200,000 units every three hours was closely followed by dramatic improvement. This was many times the dosage previously reported in human cases and approached the dosage used in experimental infections in mice. This high dosage was maintained for perhaps an unnecessarily long

period, but was accompanied by prompt and complete recovery without any indication of relapse of the infection. Epidemiological studies failed to demonstrate conclusively the source of the patient's infection; the evidence would indicate that the patient's canaries could be exonerated and that the source of infection was probably infected droppings present in the pet shop from birds other than those sacrificed and tested by animal inoculation. It is believed that this case furnishes strong evidence that penicillin in very large dosage is curative of psittacosis in man.

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