AVIAN TUBERCULOSIS IN HUMAN INFECTIONS

by

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Approved by:

[Signature]

[Date: Oct. 1/29]
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AVIAN TUBERCULOSIS IN HUMAN INFECTIONS.

Recent publication by L'Esperance in which she reported the finding of the avian tubercle bacillus in glands taken from two cases of Hodgkin's disease at post mortem, thereby intimating that this organism is the etiological factor in Hodgkin's, has been the means of renewing interest in the avian tubercle bacillus.

The writer, in reviewing the literature on avian tuberculosis in human beings, was prompted to inquire as to its incidence or possible existence among those admitted to our modern tuberculosis sanitarium. No data could be found available which tended to present satisfactory answers to the following questions:

1. Does avian tuberculosis exist unrecognized among those suffering from the various forms of tuberculosis in a modern institution for treatment of tuberculosis, and if so, what is its incidence?

2. How does the normal individual react to avian tuberculin?

3. How does a tuberculous individual react to avian tuberculin?

4. What would be the appearance of the avian tuberculin test in persons suffering from Hodgkin's disease?
In attempting to answer these questions, the following methods of experimentation were undertaken:

I

Culturing tuberculous discharges from persons suffering with the various forms of the disease with the hope of ascertaining the number of individuals having avian tuberculosis by identifying the organism found in the discharge as the avian tubercle bacillus; and

II

Making observations of results of skin tests with avian tuberculin on:

1. Normal children under twelve years of age.
2. Individuals suffering from active tuberculosis.

At the present time, we are cognizant of the existence of four fairly distinct types of tubercle bacilli: the piscine or reptilian, the human, bovine and avian. Disregarding the early researches tending to prove that these various forms are rapidly transformed one into the other, our newer conceptions gained largely from the studies of the British Royal Commission show quite conclusively that there is a broad distinction between the human and bovine types; and that there is still more distinction between them and the avian type.

The human type of bacillus was found (2) to have a marked virulence in a restricted number of animals. It is
less virulent for small and large herbivora, rarely infects carnivora, and yet more rarely, reptiles. It has a full virulence for man, the guinea pig and parrot; a conditional virulence for dogs and a very slight virulence for rabbits, but apparently none is shown at all for cattle, sheep, goats, cats or barnyard fowls. This form of tubercle bacillus (28) increases the acidity of culture broth considerably, and its well known morphology needs no description here.

The bovine strain was noted (2) for its marked virulence for a greater number of species than any of the others. It was observed from results of animal inoculations that it caused a generalized, progressive, fatal tuberculosis in guinea pigs, rabbits, cattle, swine, goats and parrots; that it had moderate virulence for man, the horse, cat, dog, and possibly sheep, and that it was avirulent for the barnyard fowl.

In cultures (28), the growth is slower, though not particularly different in appearance from the human, and produces an alkaline reaction in the culture broth. Morphologically, the bovine type of bacillus when compared with the longer, thinner, human type, appears often as an oval or plump rod with blunt ends and a more irregular outline. While vacuolation is not so much in evidence, the staining seems much less uniform.

The avian bacillus - the bacillus of chicken tuberculosis - is similar to the bacillus of human tuberculosis in
general appearance (30), though much more frequently given to pleomorphism. It is a long rod, growing rapidly on glycerine agar from 40° to 45°C, and is distinguished by a moist, creamy consistence rarely seen in any of the others. It produces an alkaline reaction in broth cultures and thrives at a much higher temperature (43°C). Besides producing a fatal tuberculosis among barnyard fowls and rabbits, it is moderately virulent for parrots, pigeons and carnivorous birds as well as swine and horses, yet with little or no virulence for guinea pigs. It has become so prevalent among barnyard fowls within the last fifteen or twenty years that the situation is really acute in certain sections of the country and is calling forth every effort of veterinary science to control it.

Here we may see the proper host relations of the various types of the tubercle bacillus found in warm blooded animals. Newer developments, however, have given the tuberculosis problem a more complex turn than is first supposed upon examination of the protocol showing virulence (Table I).
TABLE I.

The Various Host Relationships of Each of the Three Common Tubercle Bacilli:

<table>
<thead>
<tr>
<th>Host Species</th>
<th>Type Bovine</th>
<th>Type Human</th>
<th>Type Avian</th>
</tr>
</thead>
<tbody>
<tr>
<td>Man</td>
<td>++</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>Cattle</td>
<td>+++</td>
<td>0*</td>
<td>++</td>
</tr>
<tr>
<td>Swine</td>
<td>+++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Horse</td>
<td>++</td>
<td>?</td>
<td>++</td>
</tr>
<tr>
<td>Sheep</td>
<td>++</td>
<td>0*</td>
<td>?</td>
</tr>
<tr>
<td>Goat</td>
<td>+++</td>
<td>0*</td>
<td>0*</td>
</tr>
<tr>
<td>Cat</td>
<td>++</td>
<td>0*</td>
<td>++</td>
</tr>
<tr>
<td>Dog</td>
<td>++</td>
<td>++</td>
<td>0*</td>
</tr>
<tr>
<td>Guinea Pig</td>
<td>+++</td>
<td>+++</td>
<td>0</td>
</tr>
<tr>
<td>Rabbit</td>
<td>+++</td>
<td>*</td>
<td>+++</td>
</tr>
<tr>
<td>Chicken</td>
<td>0</td>
<td>0</td>
<td>+++</td>
</tr>
<tr>
<td>Parrot</td>
<td>+++</td>
<td>+++</td>
<td>++</td>
</tr>
</tbody>
</table>

+++ Virulence
++ Moderate or Conditional Virulence
+ Slight Virulence
0 Avirulence
? Unknown
# Data Insufficient for Definite Conclusion
Bané and M. Christiansen (1), about twenty years ago, reported finding avian tuberculosis in hogs. Monkeys, mice and rats were found infected by DeJong and Rabinowitch (42), and a horse by Watson and Heath (31). Recently, the bacillus was isolated from tuberculous abortions in cattle by N. Plum (23).

It is not within the scope of this paper to present the many interesting observations to be met with among mammals other than man, but it is of interest to note here that the avian bacillus must be reckoned with in animals other than birds, and that it gives rise to the Yersin type of tuberculosis (30), a tuberculosis septicemia in which large numbers of bacilli are found in many tissues without giving the characteristic well known tubercular lesions. In investigating the cause of the increasing number of retentions of hogs at slaughter houses, the Nebraska Experiment Station (30) found on posting them that out of a total of 229 animals, 88.5% of them had avian tuberculosis; 6.2% were of mixed tuberculous infection and 5.2% of the infections were due to the mammalian (presumably bovine) bacillus. It was once thought that all swine infections were due to the mammalian bacillus. Likewise, out of 25 tuberculous cattle, two were found infected with the avian bacillus. Thus we may note that avian tuberculosis is greatly on the increase among our domesticated animals.

In the classical work of Park and Krumwiede (23) with whose survey of the types of tuberculosis in man, every student
of tuberculosis is familiar, we find no data available for the avian tubercle bacillus.

Striking indeed are the results of the above mentioned survey with reference to the incidence of infections due to the bovine type of organism. Our attention is first arrested when it is shown that children under sixteen years of age seem more susceptible, and next when it is noted that the most prominent type of infection among these children is glandular. Another prominent type is abdominal.

In our text-books (32) it is pointed out that the avian tubercle bacillus does not develop in mammals; giving as the probable reason, the fact that it has become adapted to growth at 40 - 45 °C., the normal temperature of birds. Its pathogenicity for rabbits has already been noted. Logical as our author's conclusion might appear, we are faced with a number of cases of human infections due to this organism.

Lederer (12) has reported cases in which avian tuberculosis is associated with polycythemia, and leukemia. Jousset (6), Lipschutz (15), Moore (21) and Fox (21) have also reported interesting findings. Outstanding among the number of cases recording the finding of the avian tubercle bacillus in human infections are those of Lowenstein (16)(17)(18)(19). A brief sketch of one of them follows:

A woman fifty-seven years of age, who had no family history of tuberculosis other than that a sister had had lung
trouble, was presented to Lowenstein. At fifteen, she had had a swelling of the glands of the right axilla. These were extirpated at twenty-eight, but the swelling returned at forty-five, following by laryngitis which caused her to be hoarse ever since. For a number of years she experienced a bad cough (lungen spitzen katarrh) but no bacilli were demonstrable in the sputum. In 1924, she noticed a spontaneous pain in the region of the kidneys, tensamus and pain upon urination. The same developments had already occurred once before. An examination of the patient showed a throbbing over the left kidney, a pressure in the left inguinal region, and swollen glands in the right axilla. The latter were again taken out, the pathological finding showing tuberculosis.

Cultures made from the urine sediment developed typical colonies of the avian tubercle bacillus, which proved true to type upon animal inoculation. The patient experienced an uneventful convalescence after removal of the offending kidney.

Deutsch (5) in his discussion of the clinical picture of these cases says, "Clinically, these cases are characteristic throughout, in that they run a temperature for years. Often during the course there is a mild infection (sepsis) with lower morning and higher evening temperatures, and night sweats to remember. This fever is unusually difficult to influence therapeutically. The general condition of the patient appears so well considering the long, stubborn fever that one's attention
is directed toward it. In the lung there is not great characteristic change. A spot of singular predilection for this type of bacillus is the kidney and the bone marrow. The diseased kidney does not make itself extraordinarily perceptible throughout in respects other than the renal hemorrhage, but the discharge (Sediment) is relatively trifling. However, many times it contains unbelievable spots (Masses) of tubercle bacilli.

"Lowenstein in his last report recorded that the bone marrow likewise became rifled in joint suffering with unusually large numbers of this type of bacillus. Tubercle bacilli were found in the bone marrow in two cases of myelogenous leukemia, and in two cases of polycythemia (rubia) (Lederer-Sternberg, Rennen-Liebermeister). In spite of it, no other tuberculous picture was found. Lowenstein has already pointed out through the work of CRETEIN, that in the spontaneous infection of birds by the avian tubercle bacillus, the bone marrow is regularly infected."

Deutsch (5) then concludes that we should not be content with the information gleaned by staining reactions, but should resort to culturing and animal inoculations with the anticipation of showing up new cases, and the hope of clearing up different courses of tuberculosis with dissimilar strains of the bacillus. He also points out that the finding of tubercle bacilli in severe diseases of the bone marrow (Leukemie, Polyzythamie) should - through post mortem examination and
clinical analysis - attract attention, for he believes that there is a possibility that these cases in part fall on the borderline of Lowenstein's pictures of avian tuberculosis.

In contrast with this picture, Mayo & Hendricks (20) describe two cases of supposed avian tuberculosis which have come to their notice. In both, the disease was only demonstrated surgically, and pathologically after splenectomy. Neither case was running an elevation in temperature, but at operation, the liver was found in both cases to be studded with small, yellow, smooth areas exactly as is seen in chickens with tuberculosis.

The pathologist's report (20) of one case follows:

"The external surface of the spleen presented numerous nodules varying from 1 mm. to 2 cm. in diameter. These nodules (conglomerate tubercles) bear a close resemblance to the cortical abscesses of acute purulent nephritis. On section, the nodules or tubercles stand out in relief, giving the surface a "pebble dash" effect. Foreign body giant cells are present in some areas. A number of the tubercles contain a waxy substance instead of the caseous material that is often found in tubercles in cases of tuberculosis in man. In many tubercles there is no caseation, the center being composed of large epitheloid cells in great numbers, which give a characteristic appearance to the avian lesion, in contrast to that of human and bovine tuberculosis. Lymphocytes are relatively less numerous than in the lesions in man."
There is no record in either of these cases of typing of the organism by animal inoculation.

Great diversity of opinion prevailed as to the value of tuberculin for a long time after Koch (9) delivered his famous address at the Berlin International Medical Congress where he had made known the application of the chemical substance which was prepared in his laboratory for the treatment and diagnosis of tuberculosis. He claimed that reaction only occurred in tuberculous patients by the specific action of his "lymph" on tuberculous tissue, and that the absence of increase of temperature after the subcutaneous dose, decided the non-tuberculous nature of the affection.

Contrary to his contention, Leyden (27), Quincke (27), Ebstein (27), Weber and Biermer (27) early maintained that the absence or presence of reaction after the use of tuberculin must not be regarded as absolute proof of the existence or non-existence of tuberculous disease in all cases.

The medical world went to the opposite extreme in caution after Virchow (34) issued his warning as to the indiscriminate use of tuberculin, and it was used little or not at all by the better informed until the more recent researches found a more definite place for it among the therapeutic and diagnostic agencies. It has recently been purified and isolated (35) and the outlook for its increased use appears much brighter than it did a few years ago.
"Tuberculin" is a more or less flexible term used to describe any of the products of the tubercle bacillus which when injected into a tuberculous animal elicit a reaction that may be described as general, focal or local. The general reaction is characterized by a febrile condition due probably to the existence of hypersensitivity of the individual tested to tuberculin. Such a reaction obtains after subcutaneous administration of the tuberculin. The focal reaction follows the destructive effect of the tuberculin on the granulation tissue breaking down the walls surrounding the infected area and bringing the region of the focus of the infection to increased activity. The local reaction, a phenomenon owing its existence to the hypersensitivity of the skin to tuberculous material is manifested by several modifications. Chief of these are the Von Pirquet, Moro and the Mantoux tests.

The most commonly used, and the modification which probably gives the greatest amount of information is the intracutaneous test devised by Mantoux (36) and others. The technique for carrying out this test is exactly the same as that employed by Schick in making antitoxin determinations for diphtheria toxin susceptibility. Two-tenths (0.2) mg. (0.05 cc.) of tuberculin (human) are injected between the layers of the skin with a 27 gauge needle in such a position that a small blister or bleb is formed on the surface, care being taken to remove immediately any of the tuberculin which might have leaked accidentally from the syringe onto the skin.
"Koch's Old Tuberculin" (O.T.) is prepared by allowing the tubercle bacilli to proliferate on glycerine broth over a long period of time, after which it is filtered free of the organisms, concentrated and standardized by injection into tuberculous guinea pigs.

Zinsser (33), in his study of the local skin reactions in anaphylaxis, divides them into two types, - the first being due to antigens such as horse serum, in which the reaction appears in a few minutes, and again disappears in a few hours. The second type of reaction such as follows the administration of such antigens as bacterial products, (tuberculin) causes no immediate effect, but in about ten hours a notable swelling is apparent, followed in about twenty-four hours by a swollen edematous area varying in size and intensity. It often contains a central necrotic spot which may also vary in size. While some reactions are slow in making their appearance, the vast majority appear in twenty-four hours and reach their height in forty-eight, at which time definite inflammation is noted with some distinct signs of cell necrosis. So that by the end of seventy-two or ninety-six hours, one may observe a small, red lump or nodule varying in size from one to two centimeters in diameter, often having a yellowish colored central spot and being in all quite discrete. The swelling gradually disappears and in some cases desquamation takes place so that by the end of a few weeks, all that can be seen
of the positive test is a small, rather slightly pigmented area at the site of the inoculation.

The negative reaction is readily differentiated from the positive. Generally, at the end of twenty-four hours, there is nothing to be noted but the needle mark of the previous day's inoculation, but frequently one may observe a slight red spot not larger than two or three mm. in diameter. This always disappears by the forty-eighth hour when nothing but the mark of the needle is seen.

Such is our information relative to the reaction of the human being to the human type of tuberculin.

It has been demonstrated quite conclusively by Stubbs(29), Van Es(30), and others that the bovine tuberculin which is used for diagnosing tuberculosis in cattle is worthless as an indicator for culling the tuberculous fowls out of a flock. The high degree of specificity for avian tuberculin is shown in birds by the injection of the same quantity of avian and bovine tuberculin into each of the two waddles respectively. From twenty-four to forty-eight hours after injection into a tuberculous fowl, the waddle which received the avian tuberculin becomes swollen and considerable inflammation is observed, while the opposite waddle, the one which received the bovine tuberculin, remains normal.

Plum (24) records that the cattle he observed which were infected with the avian type of bacillus did not react to bovine tuberculin, but did react to the avian type.
Thus we may note the high degree of specificity in mammalia as well as in fowls.

Reference was made above to the work of L’Esperance(13) in isolating the avian tubercle bacillus from glands taken from two cases of Hodgkin's disease. Her investigations received their inspiration from the fact that the pathology in glandular tuberculosis and Hodgkin's disease is markedly similar, and she based her researches on the presumption introduced long ago in the papers of Sternberg (41), - that there is a relationship between Hodgkin's disease and the tubercle bacillus - her contention being that Hodgkin's is caused by an atypical tubercle bacillus such as the avian type. The general consensus of opinion among our bacteriologists and pathologists seems to be against the infectious nature of that malady.

A number of bacteriological studies have been made on Hodgkin's disease, the earlier of which for the most part are entirely contradictory. More recently, however, considerable attention has been paid to the observations of Negri and Mieremet (37), Bunting and Yates (4), and Rosenow and Billings (26), the latter of whom isolated a gram positive diphtheroid in pure culture from three cases of Hodgkin's disease, and the same organism mixed with a staphylococcus in nine others out of a total of twelve cultured. Negri and Mieremet (37), and independently, Bunting and Yates (4) have found the same organism. Much and Faenkal (38) isolated a gram positive granular bacillus from affected glands, and Knsunchki (11) has
seen the same bacilli in material treated with antiformin as well as in sections from sixteen cases. Many attempts to transmit the disease to guinea pigs, rabbits, dogs, and monkeys have been quite unsuccessful, except for the attempts of Bunting and Yates (3), who produced a local enlargement of lymph nodes, and a histological appearance of the pathological picture of the disease in human beings after injection of pure cultures of their organism into monkeys. In this connection, the work of L'Esperance (14) is also significant in that she also was able to reproduce a histological picture resembling Hodgkin's disease after injection of the avian tubercle bacillus with killed cultures of the bovine bacillus into rabbits.

Rosenow and Billings (26) report great improvement in eleven patients suffering with Hodgkin's disease after treatment with autogenous vaccines prepared from the diphtheroid bacillus and the staphylococcus they found in the glands.

To complicate the matter further, tuberculosis has been frequently found in undoubted cases of Hodgkin's disease.

Thus we find two groups of observers differing widely as to their opinions. While one group follows Sternberg and holds that Hodgkin's disease is in reality a modified form of tuberculosis, and is due to the tubercle bacillus, the other maintains that tuberculosis is in no way the cause but occurs only as a secondary infection.
EXPERIMENTAL WORK
CULTURE OF TUBERCULOUS MATERIAL

EXPERIMENTAL METHOD

Material and Treatment:

Fresh tuberculous material consisting of discharges from 142 cases of pulmonary, 7 cases of renal, 6 cases of intestinal, 2 cases of bone and 1 case of glandular tuberculosis was collected from two local sanitaria and was treated by either the Petroff, Antiformin or Korper methods for concentrating the bacilli. Smears were made simultaneously with the inoculation of four tubes of culture media for each specimen. Four additional tubes were inoculated from one specimen of each of the eight lots that were treated; these were used as media and concentration reagent controls.

The media used was Petroff's Gentian Violet Egg Media, and Korper's Glycerine Violet Potatoes.

The smears were stained by the Ziehl-Neelson Method (cold) and were examined for acid-fast bacilli with the 1.8 mm. oil immersion objective under the microscope.
Incubation:

Taking advantage of the fact that the avian tubercle bacillus grows readily at temperatures ranging from 40 - 45 °C, and the human type of organism is inhibited above 40 °C, the cultures were incubated at a temperature of 41 °C. This was done with the intention of typing by animal inoculation only those tubes which showed growth when incubated at that temperature.

The tubes serving as controls of culture and concentrating reagents were placed in the 37 °C thermostat.

The tubes were all corked and sealed, being opened for two days of each week during the first three weeks of incubation after which they were not opened due to the tremendous loss to molds. At the expiration of the three weeks time, the surface of each tube was streaked with the inoculating needle to mix about any microscopic colonies which might have formed. They were subsequently examined for growth by means of a hand lens at weekly intervals until they had been incubated for a total of ten weeks, when they were discarded.

RESULT

Controls:

Out of the thirty-two tubes placed in the 37 °C thermostat as media and concentration reagent controls, ten were lost to molds or other contaminants, seven developed
no growth and fifteen different tubes representing six specimens developed acid-fast organisms typical of the tubercle bacillus. One set of these control tubes which showed no growth, showed no acid-fast bacilli on the smear made from the inoculum.

TABLE II

Showing Outcome of Control Tubes

<table>
<thead>
<tr>
<th>Lot No.</th>
<th>Smear</th>
<th>Tube 1</th>
<th>Tube 2</th>
<th>Tube 3</th>
<th>Tube 4</th>
<th>Total</th>
<th>Showing</th>
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<tbody>
<tr>
<td>1</td>
<td></td>
<td>Growth</td>
<td>0</td>
<td>Lost</td>
<td>0</td>
<td>1</td>
<td>Growth</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>-</td>
<td>Lost</td>
<td>Lost</td>
<td>Lost</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>Growth</td>
<td>Growth</td>
<td>Growth</td>
<td>Growth</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>-</td>
<td>Growth</td>
<td>Growth</td>
<td>Growth</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td></td>
<td>Growth</td>
<td>Lost</td>
<td>Lost</td>
<td>Growth</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td></td>
<td>-</td>
<td>0</td>
<td>Growth</td>
<td>Growth</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td></td>
<td>-</td>
<td>0</td>
<td>0</td>
<td>Lost</td>
<td>0</td>
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<tr>
<td>8</td>
<td></td>
<td>Growth</td>
<td>Lost</td>
<td>0</td>
<td>Lost</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

+ Acid-Fast Bacilli
- No Acid-Fast Bacilli
0 No Growth
Growth Growth of Acid-Fast Bacilli
Lost Tube Discarded because Contaminated
Smears:

Examination of the smears made at the time the tubes were inoculated, proved the presence of acid-fast bacilli having morphology of the tubercle bacillus in the inoculum of 120 of the 158 specimens examined. Of these smears, 114 were from the 142 cases previously mentioned as having a diagnosis of pulmonary tuberculosis; 2 from 7 cases diagnosed as renal; 3 from 6 cases called intestinal; none from the case of glandular and 1 from the 2 bone cases.

Cultures incubated at 41 ° C.

Thirty-five of the culture tubes incubated at 41 ° C were lost to molds or other contaminators. In only three cases, however, were all four culture tubes from each specimen lost. After thorough examination, not one tube that was left revealed growth. (Table III)

DISCUSSION:

While the material presented is not great, it will show at least to a degree the relative rare incidence of the avian infection in this section.

The thirty-five of the 158 tubes lost to molds and contaminators represent 22.4% of the total number inoculated; an average loss of less than one tube out of each set of four for each specimen. This loss would not invalidate the result.

From Table III it may be seen that out of 7 cases of renal, 6 cases of intestinal, 1 case of glandular, 2 cases
TABLE III

Showing Result of Cultures Incubated at 41°C.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No. of Cases</th>
<th>No. Showing A.F. Bacilli on Smear</th>
<th>Single Tubes Lost to Contamination</th>
<th>Cultures Lost Completely</th>
<th>Growth</th>
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<tr>
<td>Renal T. B.</td>
<td>7</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<td>(Cath. Spec.)</td>
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<td></td>
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<tr>
<td>Intestinal T.B.</td>
<td>6</td>
<td>3</td>
<td>6</td>
<td>0</td>
<td>0</td>
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<tr>
<td>T. B.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glandular T.B.</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>T. B. of Bone</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Pulmonary T.B.</td>
<td>142</td>
<td>114</td>
<td>29</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>158</td>
<td>120</td>
<td>35</td>
<td>3</td>
<td>0</td>
</tr>
</tbody>
</table>
of bone infection and 142 cases of pulmonary tuberculosis, not
a single organism capable of growth at 41 C. was brought to
attention. This would seem to indicate that the acid-fast
organisms seen in the smears made from the material with which
the culture tubes were inoculated were not avian tubercle bacilli.

Attention was above called to the fact that the most
prominent types of infection due to the bovine bacillus were
abdominal and glandular in nature. The reason for this predom-
inating type of infection seems to be indicated by the virulence
of the organism and the portal of entry.

Since we are not permitted to assume any particular
tissue predilection for the bovine bacillus, we must assume
that it is rarely able to progress beyond the lymph nodes be-
cause of its lack of virulence, - that it is only conditionally
virulent in man compared with the human type which has a full
virulence. In view of these observations, we may be justified
in expecting to find such a condition prevailing with reference
to the avian bacillus.

It has been noticed by clinicians that the number of
cases of bone and glandular tuberculosis has greatly dropped
off since the campaigns of anti-tuberculosis societies have
been ridding domesticated animals of tuberculosis. The number
of cases which no longer appear were evidently due to the bo-
vine type of bacillus. Since one rarely finds primary intesti-
tional or renal tuberculosis, and the percentage of glandular
and bone cases due to the avian tubercle bacillus must be increasing because of the decreasing number caused by the bovine type, the observation made by Deutsch (5) is well taken, and we can easily afford to include fowls for inoculation when diagnosis is being made.

Are these bacilli which produce such infections particularly virulent atypical strains of what we call the avian tubercle bacillus, or is it a case of adjustment of an organism to a new type of host after being present in the body for a long period of time? We dare not attempt at this stage of our knowledge to do other than speculate as to the answer.

It may be noticed that by far the larger number of cases of avian tuberculosis are reported from Europe, where as is well known, the incidence of tuberculosis is much greater. It may also be noted that a much higher percentage of the more unusual forms of tuberculosis exists there. Under these conditions, one may expect a higher incidence of infection due to atypical bacilli in Europe than in America.
AVIAN TUBERCULIN TESTS

DETERMINATION OF TUBERCULIN DOSAGE:

The tuberculin (human) used in the following tests was a standardized solution of Koch's Old Tuberculin (O.T.) human (H.K. Mulford Co.), containing 4.0 mg. of tuberculin per cc. of the solution, or 0.2 mg. per dose intradermally (.05 cc.).

The tuberculin (avian) which was kindly contributed by Jensen-Salsbery, Kansas City, Mo., had a strength 125 times that of the human, - 500 mg. per cc., or 25 mg. per dose intradermally (.05 cc.). Van Es, in his tests on poultry used tuberculin in this concentration, getting better results with the more potent solution.

The writer not having any information as to what the proper dosage of avian tuberculin should be for an intracutaneous test, made preliminary tests on the forearms of two individuals who already had shown a moderate reaction to human type of tuberculin.

Procedure:

Two normal adults who gave no history of tuberculosis, or tuberculosis contact, but who had previously given moderate reactions to intracutaneous tests with human type tuberculin were given a series of tests employing one inoculation of a standard 0.2 mg. dose of human tuberculin, and varying concentration of avian tuberculin from that of the human tuberculin upward.
Each of these persons received in all five tests, three on one forearm, and two on the other. One test was with human type tuberculin, and the four others embodied avian, representing the following quantities in 0.05 cc.:

<table>
<thead>
<tr>
<th>Test 1</th>
<th>Test 2</th>
<th>Test 3</th>
<th>Test 4</th>
<th>Test 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human Type Tuberculin</td>
<td>.2 mg.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Avian Type Tuberculin</td>
<td>.2 mg.</td>
<td>.4 mg.</td>
<td>1.0 mg.</td>
<td>25. mg.</td>
</tr>
</tbody>
</table>

Results:
Test 1- The human type tuberculin test as was anticipated proved moderately positive in each case according to descriptions heretofore made in this paper.

Test 2- The test made with the smallest amount of avian tuberculin equal in concentration to the human type proved slightly pink around the needle mark at the twelfth to fifteenth hour, fading so rapidly that nothing was visible by the twenty-fourth hour except the needle mark. No delayed reaction appeared.

Test 3- The test made with the 0.4 mg. of avian tuberculin showed a distinct, diffuse pink area about 1 cm. in diameter at the end of twenty-four hours. No swelling was apparent. At forty-eight hours this reaction had faded to a pale pink, and by seventy-two hours, had disappeared, leaving the area which had been involved with its normal color, while the human reaction was localizing to a definite discrete nodule or lump about 1 cm. in diameter.
Test 4— The 1.0 mg dose brought about a reaction similar to that of the 0.4 mg. dose but of much greater intensity as to redness and area involved. There was also slight swelling rising to the point of inoculation in forty-eight hours, and the redness involved an irregular spot covering an area equal to a circle 1½ cm. in diameter. However, this disappeared in the course of four days in the one case and in five days in the other individual. When contrasted with the human type reaction—a definite lump by then—all that was left was the slightly pigmented point of inoculation.

Test 5— The reaction to the 25.0 mg. dose of avian tuberculin rose rapidly. At twenty-four hours it could not be differentiated from the human type reaction. Slight swelling arose to a peak about the site of injection, and the deep red color gradually diffused out over an area equal to 2 cm. in diameter. Reaching its height between forty-eight and seventy-two hours, the swelling gradually disappeared, and the color more gradually faded to a light pink. On the sixth day when the small lump which was formed by the human tuberculin was beginning to disappear, the flat, pink, diffusing, irregular area due to the avian tuberculin was still visible. No lump or nodule was ever formed, but two weeks after injection, an irregular slightly pigmented area about the site of injection of the avian tuberculin was noted in each case, while the human reaction on the same area had a definite, dark, desquamating, pigmented area, circular in shape.
Discussion and Conclusion:

The above described avian tuberculin reactions seem to take place with intensity which varies with the concentration of the reagent. The 25 mg. dose gives rise to a rather severe inflammation, which due to its diffuse nature and its apparent inability to cause necrosis is not at all similar to the human type reaction after several days, yet its true nature is confusing even after the forty-eight hour period. Much less indecision was apparent in differentiating the natures of the two reactions when the 1.0 mg. dose test was examined, though at forty-eight hours, the spreading redness and slight swelling rising to a small point at the inoculation site also were somewhat perplexing.

The smallest amount of avian tuberculin used would probably be the most logical dose for avian tuberculin tests if we but knew the facts. However, it was suspected in making the tests which are to follow that a quantity of avian tuberculin as small as 0.2 mg. would not bring about a reaction in avian tuberculous individuals which simulated the human type reaction as we know it.

With this in mind, the 0.4 mg. dose was decided upon as the most valuable amount for inoculation in making the skin tests which are to follow, because as was apparent, it was slightly in excess, thus giving a factor of safety which in the presence of a specific substance in the individual
tested would cause a true avian reaction to present itself in the same characteristic manner in which the human type test is involved.

INTRACUTANEOUS SKIN TESTS:

The skin tests which are described below fall into three groups which may be divided as follows:

1. Tests on children not giving reactions to human tuberculin.

2. Tests on individuals suffering with active tuberculosis; children who were contacts, and others reacting to human tuberculin.

3. Tests on three suspected cases of Hodgkin's disease.

1. Tests on children not giving reaction to human type tuberculin:

Twenty-four children between the ages of five and twelve who gave no history of contact with tuberculosis were tested simultaneously with both the human and avian types of tuberculin (intracutaneously) on the forearm. Each was given 0.05 cc. of tuberculin human and avian respectively through two different syringes. The doses given represented 0.2 mg. tuberculin human and 0.4 mg. tuberculin avian.
2. Tests on individuals suffering with active tuberculosis, children who were contacts, and others:

Another group of tests was made on 18 adult persons suffering from active tuberculosis, four children from 8 to 12 years of age, who gave histories of contact, and three adults who gave neither history of contact nor history of tuberculosis. Each of these cases received the same treatment as that described above, - they were given 0.2 mg. (.05 cc.) of tuberculin human, and 0.4 mg. (.05 cc.) tuberculin avian intracutaneously in the forearm (simultaneously).

RESULTS:

1. None of the twenty-four children tested gave a reaction to either test, and no change appeared at the sites of inoculation after twenty-four and forty-eight hours. (Fig. 1 shows a typical result of one of these tests at twenty-four hours.)

2. In all the cases of the second group, there was a marked reaction to the human type of tuberculin, varying in intensity from moderate to severe. In each individual the typical tuberculin (human) reaction appeared as is here- tofore described.

In each instance, the avian reaction in these individuals who give the positive test to the human type of tuberculin is characterized by a more or less large spreading reddened area which is diffuse and which shows no central necrotic spot. It varies in size and in intensity of color
with the severity of the human reaction. In some cases, a slight swelling rising to a small peak at the site of inoculation is noted, but in no instance does the swelling have a definite, discrete circumference at which it begins encircling the injection point. This swelling when it occurs, disappears more rapidly than does the swelling in the human reaction, so that when the latter reaches the stage of a discrete reddish yellow nodule or lump, the avian test has degenerated to a more diffuse, slightly red or pink area, much smaller than the area involved by the human test.

DISCUSSION:

The result of the twenty-four avian tests on the children who did not react to the human tuberculin appeared exactly as the result of the negative human reaction. With this in mind, we may well say that none of the twenty-four gave a positive reaction to either test; but on the other hand, the sites of inoculation of all these tests appeared exactly the same after twenty-four and forty-eight hours, so that one who did not know could not tell which were avian and which were human tests.

This series of tests shows that a reaction to avian tuberculin is not aggravated in normal non-tuberculous persons due to:

(a) A chemical substance in the testing fluid other than tuberculin; or
(b) The avian tuberculin per se. In other words, it allows us to safely state that "non-tuberculous" individuals do not give a positive avian tuberculin test.

From results of tests cited in chickens (29), cattle (24), and swine (29), wherein it was found that the avian tuberculin brought about a specific reaction to avian tuberculosis in these birds and mammalia, one may expect a great deal of specificity to be shown in man. It will be noted that the avian reaction in the above cases resembles greatly the pseudo-reactions seen in Schick tests. They might well be called pseudo reactions, since frequently on examination in twenty-four hours, a spot of more striking intensity of color may be seen within the large spreading reddened area (Fig. 2), which may lead one to believe he is encountering a positive reaction, but on the following day, such reactions have faded to such an extent that all that is visible is the enlarged diffused pink spot due to the avian tuberculin.

A more appropriate term for this type of diffuse, rapidly disappearing reaction which is not at all typical of the tuberculin reaction would be "cross-reaction", intimating that the two tuberculin substances produced by the avian and human types of bacilli respectively are very closely related; or have a common constituent between them.

In view of the fact that it has been shown above that avian tuberculin does not bring about a well defined, discrete,
or specific tuberculin reaction in individuals giving a reaction to the human type of tuberculin, and that no reaction at all is shown in individuals who are not tuberculosis contacts, the elicitation in a person of a reaction due to the avian tuberculin having the exact appearance of a positive human type test would cause one to suspect the presence in that person of a specific substance capable of bringing about such a reaction. If this proves to be the case, avian tuberculin should have a definite place among our diagnostic agencies, and should be used as an aid in the diagnosis of suspected tuberculous conditions in glands and bones, as well as primary tuberculosis of intestines and kidneys.

3. Tests on three suspected cases of Hodgkin's disease:

A brief sketch of the histories of the three supposed cases of Hodgkin's disease, which were all referred to free tuberculosis clinics as glandular tuberculosis are recorded as follows: Each was inoculated in the same manner with the same quantity of avian and human tuberculin that was given previously to the individuals whose reactions are heretofore described:

Case 1. A white man aged thirty-nine, who gave a history of tuberculosis in families of both parents, was traveling about over the country in search of diagnosis and health; had onset four years ago following severe attack of
influenza, and relapse which caused him to remain in bed
two weeks longer. Unable to go to work for several weeks.
Developed cough and lost weight. Developed cervical glandular involvement and went to nationally known clinic for tonsillectomy and section of gland. Diagnosis of Hodgkin's disease made and glands treated with X-Ray. Glands receded though were still hard and palpable. Was also told of pulmonary tuberculosis at that time.

Observation showed productive cough, and sputum showed tubercle bacilli intermittently. X-Ray of chest revealed bilateral involvement with infiltration and consolidation in both upper. Cervical glands were considerably enlarged, hard and palpable; not very painful to touch. Glands show marked improvement to treatment with X-Ray.

Case 2. A Mexican woman thirty years of age first noticed a lump making its appearance in her neck three years ago. She gave it no attention until it began to become larger and spread to the other side. An oval tumor of great size could be felt and moved about above the clavicle on the left side. It was not painful to touch and was firm and hard. A small, hard mass was also noted on the right side. No indication of a focus of tuberculous infection; blood picture normal; no fever noticed and health generally good. This involvement of the cervical lymph glands responded greatly to treatment with lights. Hodgkin's disease suspected, and the patient is still receiving treatment.
Case 5. A young woman, twenty-five, developed cough and general malaise four years ago. Diagnosis of pulmonary tuberculosis made. Later noticed slight swelling in neck which gradually became larger; spread to other side of neck. Physician's diagnosis: Hodgkin's disease. Examination shows cervical lymph glands on both sides greatly swollen; axillary glands swollen, hard and palpable; not painful; easily moved about. Diagnosis of Hodgkin's disease pending tissue section.

RESULT

3. Case 1.

At twenty-four hours, (Fig. 3) the reactions brought about by both human and avian tuberculins were strikingly similar. Both showed a definite area of involvement, the same amount of swelling and the same amount of redness. Both were slightly painful to touch. At forty-eight hours (Fig. 4) while the reaction was at its height, though swelling, area of involvement and redness were greatly increased, and a definite, yellowish, central necrotic spot was visible. With seventy-two hours, the reactions had greatly receded (Fig. 5) leaving only a reddish yellow swollen area surrounded by a pale pink halo in each case; the one due to avian tuberculin being slightly larger than the one due to the human type. So that by ninety-six hours, or four days after injection, a discrete nodule or lump one cm. in diameter in the case of
the human test, and 1\(\frac{1}{2}\) cm. in diameter in the avian, could be seen and felt at the sites of injection of the tuberculin; and aside from size, the one could not be differentiated from the other.

Twenty-four hours after injection of the 25 mg. dose of avian tuberculin, a large area of inflammation was present. The reaction to the human type was as described above. In forty-eight hours, the involved area covered a circular space with a diameter of seven cm; this circle had become darker red at seventy-two hours, and did not begin to recede until the fourth day; while the human type reaction to the usual 0.2 mg. dose of human type tuberculin had localized to a small lump 1\(\frac{1}{2}\) cm. in diameter. For a radius of 1 cm. around the site of inoculation, a slightly swollen area of more intense color was discernable. The fifth day brought a definitely elevated whitish appearing necrotic spot 1 cm. in diameter. The latter gradually became harder and thicker and in a few days, a wrinkled indusium was noted covering it. When the latter dropped away, it left a darkly pigmented, smooth excavation.

**Case 2:**

A reaction of moderate intensity was elicited by the human type tuberculin in Case 2. At the end of four days, a definite little lump showing some signs of cell necrosis had formed. The reaction brought upon by the avian tuberculin
was characterized by an irregular area of darker color in twenty-four and forty-eight hours with no swelling. At seventy-two hours, this area was definitely smaller and fainter in color, and when observed on the fourth day, was quite gone, leaving only the dark point where the needle had been inserted between the layers of the skin.

Case 3:

This young woman was very fair having an extremely white skin which was exceedingly hypersensitive to the human type tuberculin. On observation at twenty-four hours after inoculation, a circular edematous area three centimeters in diameter was noted about the point where the human type tuberculin had been injected. The reaction to the avian type tuberculin was irregular in shape, and covered about two square centimeters. At forty-eight hours, the area involved by the human type test had reached a diameter of four centimeters, and had a blanched necrotic appearing spot within the red one which measured two centimeters in diameter. The edges of this white necrotic appearing spot were discrete, having the appearance of being beveled. The zone affected by the avian type of tuberculin was now slightly larger, having diffused more in the longitudinal direction of the arm. No signs of cell necrosis were visible, though a slight amount of swelling could be discerned irregularly surrounding the site of inoculation, and the color of this inner zone was
markedly more intense. However, it had no definite boundary, gradually falling off into the surrounding area diffusing out into the normal skin.

Upon examination on the third day, the outer zone of the human type test was smaller and paler in color. The white inner area had maintained its appearance of the previous observation. The more intensely red appearing area surrounding the point where the avian type tuberculin was injected had faded noticeably in color, though there was still some slight swelling apparent.

At ninety-six hours, the inflammation about the human type test had disappeared except for the slight pink tint showing about the edges of the white necrotic appearing zone. The avian type tuberculin test had lost all its swelling and was now reduced to a mere longitudinal, irregular, slightly pink area, one and one-half centimeters in length and one centimeter in width diffusing out into the normal skin.

The appearance of the human type test on the fifth day had not changed appreciably, but the pink zone due to the avian type tuberculin had quite disappeared, leaving only a small brown point where the needle had been inserted.

Discussion

Before a legitimate discussion of the foregoing observations is permissible, one of the primary factors influencing the conclusions should be considered. The question to be asked is, "Are these three cases, Hodgkin's disease?"
If there is any doubt on this subject, it should be borne in mind as the results are reviewed.

If there is any absolute pathognomonic agency which can be utilized in differentiating the diagnosis between Hodgkin's disease and certain cases of glandular tuberculosis as well as some cases of lymphosarcoma, it has not received the attention one should expect it to receive from the medical world. Many cases of Hodgkin's disease have gone unrecognized until necropsy. Pathological section when resorted to as an aid to diagnosis gives results upon which considerable reliance can be placed. However, it is well known that results of such examination are governed largely by the personal factor, and what one man may determine Hodgkin's disease, another may determine a malignancy or tuberculosis, upon examination of material taken from the same lymph node. It should also be noted in this connection, that the microscopic picture of tissue taken from tuberculous fowls markedly resembles that of Hodgkin's disease owing to the presence of cells greatly simulating the so called Dorothy Reed cells in sections taken from the former, as well as occasional large granulocytes.

In Case 1, such a method of diagnosis was followed and the patient was classified and treated as a case of Hodgkin's disease in the hands of one physician, while to another his ailment is described as tuberculous edenitis, and the affection - whatever it may be - is responding to treatment
with light. It is further complicated with pulmonary tuberculosis so the real nature of the situation is quite perplexing. He gives a moderately severe reaction to human type tuberculin.

From results noted relative to the reaction to avian tuberculin in this case, one must admit that it is the only reaction of its peculiar character recorded in this paper. It has all the fundamental characteristics of the positive human type reaction, — swelling, cell necrosis, a definite lump at the site of inoculation with subsequent pigmentation and desquamation. The 25 mg. dose of avian tuberculin was given in order to check these observations and to note what would occur with the stronger reagent. In seventy-two hours, when the ordinary reaction has begun to recede, the area involved in this test had become greater than ever, and two days later unusual signs of severe necrosis developed.

Here is presented then a case of Hodgkin's disease or glandular tuberculosis, which undoubtedly gives a typical tuberculin reaction to avian type tuberculin. In the tests described above no such reaction occurred. Case 1 can therefore be utilized as a positive control indicating the avian tuberculin which was used to be active.

From a review of the literature, it appears that the prognosis in infections due to the avian type tubercle bacillus is much better than in Hodgkin's disease. Lowenstein's
picture of avian tuberculosis is not one of a severe infection. After operation in these cases, the patients seem to pass an uneventful convalescence, while in cases of Hodgkin's disease, the malady spreads rapidly or slowly as the case may be to regional lymph glands, eventually leading to death.

The natures of these two types of ailments being thus distinctly different make it somewhat difficult in visualizing the avian tubercle bacillus as the etiological factor in Hodgkin's disease. The finding of this organism in any disease of the lymphatics might be looked upon in the same light as the accidental finding of any other, as a secondary invader after the loss of resistance; though it must be admitted that in cases of Hodgkin's disease, or any other disorder of the lymphatics, wherein the avian tubercle bacillus is found, it may prove a contributor to the pathological picture shown in these cases, yet not be pathognomonic of Hodgkin's disease.

The result of observation in Case 2 and in Case 3 shows that the findings in these two latter cases simulate to a great degree those of previous findings in individuals reacting to the human type tuberculin. There is nothing of interest to note in connection with either of these two cases, neither of which it appears have ever had a tissue section.

It is of interest to speculate, however, as to what these results might indicate. If all three are actual cases of Hodgkin's disease, the avian tuberculin test is very inconsistent in its appearance in that affection.
If this supposition should prove to be a fact, it would seem to the writer that all three cases should react to avian tuberculin in a similar manner provided the theory of L'Esperance, regarding the relationship of Hodgkin's disease and the avian tubercle bacillus is true; if the avian tubercle bacillus is present in these cases, a typical tuberculin reaction should be elicited in them to avian tuberculin.

If Case 1 is Hodgkin's disease and the other two are not, there is the possibility that all cases of Hodgkin's disease show hypersensitivity to avian tuberculin. If, however, none of the three are Hodgkin's disease, Case 1 has the possibility of being a mixed infection due to the avian and human types of tubercle bacilli.
SUMMARY

I Cultures of Tuberculous Material.

Out of a total of 158 cultures of tuberculous material taken from as many cases from two modern tuberculosis sanitariums, 114 having a diagnosis of pulmonary; 7 renal; 6 intestinal; 2 bone and 1 glandular tuberculosis, not a single culture of the avian tubercle bacillus was found. The media used was Petroff's Gentian Violet Egg and Korper's Glycerine Violet Potatoe. The cultures were incubated at 41 C. and were discarded after ten weeks when no growth was visible with a hand lens. Acid-fast bacilli having the morphology of the tubercle bacillus were seen on smears made simultaneously with the inoculation of the culture tubes in 120 of the 158 specimens. No organisms which were capable of growth at 41 C. were found, although cultures made from some of the same material produced growth at 37 C.

II Avian Tuberculin Tests.

Twenty-four children under twelve years of age who gave no history of contact with tuberculosis were tested simultaneously by the intracutaneous method with a solution of human tuberculin containing 0.2 mg. tuberculim per dose, and with avian tuberculin which was found to give best results when 0.4 mg. were contained in a dose; with the result that none of them reacted to the human type of tuberculin, and the avian test appeared exactly as did the human.
Likewise, eighteen adults suffering with active tuberculosis, four children under twelve years of age giving histories of tuberculosis contact, and three adults giving neither history of contact nor history of tuberculosis were tested in the same manner with the same tuberculin. All reacted with varying intensity to the human type tuberculin, and all showed reddened diffuse areas which rapidly disappeared about the sites of inoculation with the avian tuberculin. None of these avian reactions resembled the typical reaction to human tuberculin, but all showed a peculiar type of "cross-reaction".

Three cases of suspected Hodgkin's disease were tested in the same manner with the same reagents, with the result that one case gave a reaction to the avian tuberculin greatly simulating that which it gave to the human type tuberculin (moderately severe), and the other two gave reactions resembling those described as occurring in persons who react to human type tuberculin. One of the latter two cases gave a moderately severe reaction, and the other reacted quite severely to the human type tuberculin. The avian tuberculin reactions in these two may be called negative, and it is therefore supposed that

1. If all three cases are Hodgkin's disease, the avian tubercle bacillus is not regularly associated with Hodgkin's, or
2. If Case 1 only is Hodgkin's disease, the possibility remains that the avian tubercle bacillus is its etiological factor, or
3. If none of the three prove to be Hodgkin's disease, Case 1 is probably a mixed infection due to the avian and human types of tubercle bacilli.

CONCLUSIONS

After consideration of the foregoing observations, the following conclusions seem evident:

1. Not one case of avian tuberculosis was found among 114 cases of pulmonary tuberculosis; 7 cases of renal tuberculosis; 6 cases of intestinal tuberculosis; 2 cases of bone; or the one case of glandular tuberculosis.

2. The incidence of the occurrence of unrecognized avian tuberculosis in our modern tuberculosis sanitaria is so low as to cause its existence to be doubtful.

3. The 0.4 mg. dose is a very dependable dosage of avian tuberculin for intracutaneous skin tests.

4. Avian tuberculin similar to the human type tuberculin does not bring about a reaction in normal children under twelve years of age.

5. Reactions to avian tuberculin in tuberculous persons are characterized by a transient spreading diffuse type of reddened zone, not greatly simulating the true type of tuberculin reaction.

6. Avian tuberculin skin tests on individuals suffering with tuberculosis due to the human type tubercle
bacillus reveal a high degree of "cross-reactions" with the human type tuberculin tests.

7. Such "cross reactions" become confusing when large quantities of avian tuberculin are utilized for making the tests.

8. Results of tests on three possible cases of Hodgkin's disease reveal one case giving a typical tuberculin reaction to both avian and human tuberculin respectively and the other two, the observed type of reaction brought about by the usual reactor to human type tuberculin.

9. A fair degree of specificity to avian tuberculin was indicated in the one typical tuberculin reaction observed in the above mentioned case wherein both avian and human types of reaction could not be differentiated.

10. This case is an involvement with which the avian tubercle bacillus is probably associated in an unknown capacity lending its influence either as a factor in a mixed avian and human glandular tuberculous infection, or as a secondary invader in Hodgkin's disease.
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KEY TO PHOTOGRAPHS

Figure 1. Negative avian and human type tuberculin tests 24 hours after inoculation.

Figure 2. Moderate human type reaction and negative avian, 24 hours after inoculation.

Figure 3. Reactions in Case 1 at 24 hours.

Figure 4. At 48 hours.

Figure 5. At 72 hours.