TUBERCULOSIS IN INFANTS AND YOUNG CHILDREN*

By Lloyd B. Dickey, M. D.
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Discussion *by Ernst Wolff, M. D., San Francisco; Philip H. Pierson, M. D., San Francisco; Esther B. Clark, M. D., Palo Alto.*

OUR ideas in regard to the resistance of the infant to tuberculous infection have changed considerably in the last few years. Reuben and Smith,[1] Hempelmann,[2] Lemaire,[3] McLean and Jeidell,[4] Krause,[5] Drolet,[6] Langer,[7] Wahlquist and Myers,[8] and Asserson,[9] have shown that many infants become infected with tuberculosis without developing signs of serious tuberculous disease. In these reports the mortality rates are very much higher in those series in which only hospital, or sick children were examined. As series are reported that include out-patient infants, suffering from minor ailments, or from none at all, the mortality rate very much diminishes, although the number of patients exhibiting evidence of a tuberculous infection remains relatively high.

Asserson's report, which included a study of 4003 hospital and clinic infants under two years of age, and 1656 infants of the same age, attending baby health centers, showed an incidence of tuberculous infection of 11.4 per cent in the former group and of only 3 per cent among the well babies. "The results of this study indicate that the infant's resistance to tuberculous infection is better than it was formerly believed to be; on the other hand, the infant's lack of resistance to tuberculous disease appears to be relatively low, a fact long recognized." The report also indicates that the incidence of tuberculous disease in infants is a matter of continued exposure, and that "infants who receive their infection in a more casual and less continuous way show marked resistance to tuberculous infection."

During the course of the work done under the auspices of the San Francisco Tuberculosis Association, in which tuberculin testing was done on dispensary patients, regardless of complaint, we frequently saw positive intracutaneous tests on infants and young children with no symptoms referable to tuberculosis other than a history of exposure in a few instances. Most of those that it was possible to follow, developed no symptoms later. Others of course, with positive skin tests at an early age, already had symptoms, signs, or roentgenological evidence of tuberculous disease. A few of these have carried considerable disease for a period of a year or more.

During our investigation, as soon as the tuberculin tests were read and recorded as positive, a complete history was taken, with special reference to tuberculosis; a complete physical examination was done; roentgenological studies were completed, which included a fluoroscopy, and lateral and anteroposterior chest plates. With these data at hand all cases were classified—in regard to their tuberculous condition—as active disease, suspected disease, or as healed. Those with symptoms or physical signs in addition to roentgenological evidence of disease were called active; those without symptoms or signs, but with roentgenograms which might be evidence of tuberculous disease were classed as suspected; those with no signs or symptoms, and with roentgenograms which showed definite calcifications without other parenchymal involvement were classified as healed.

One hundred and fifty-two infants under one year of age were tested with a 1/10 mg. dose of Koch's old tuberculin, intracutaneously. Seven, or 4.6 per cent, reacting positively; 161 children tested between the ages of one and two gave twenty-two positive reactions, or 13.7 per cent; between the ages of two and three, 171 were tested, nineteen, or 11.1 per cent, were positive; while of those between three and four, 254 were tested, with fifty-seven, or 22.4 per cent, reacting positively. This age incidence of infection is charted in Fig. 1, together with the percentage of

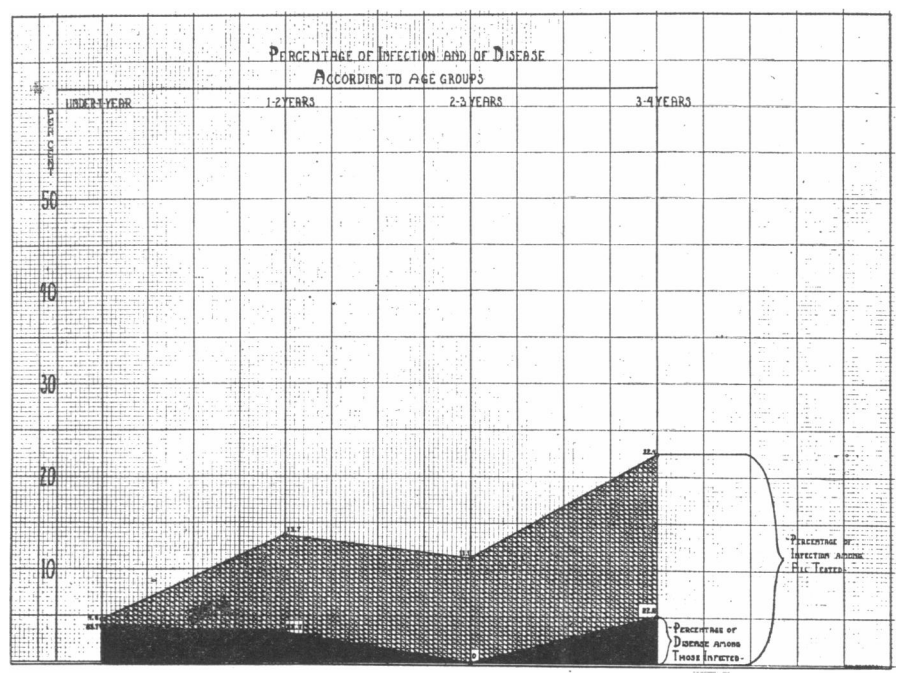

Figure 1

* From the Department of Pediatrics, Stanford University Medical School, San Francisco.

* Read before the Pediatrics Section of the California Medical Association at its Fifty-Seventh Annual Session, April 30 to May 3, 1928.

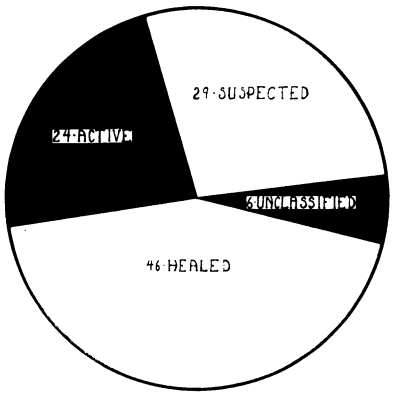

Fig. 2.—Classification of 105 cases.

active disease in each age group of the infected. These four groups made a total of 738 children under four years of age, 105 of which were positive reactors to tuberculin, an incidence of 14.2 per cent.

Of our 105 cases of tuberculous infection in children under four, twenty-four were classified as active, twenty-nine as suspected, forty-six as healed, and in six a classification was not possible, due to incomplete records (Fig. 2).

Most of these 105 children have been followed from three months to two and a half years. Those who have disappeared from our observation are a relatively small number, nine in all. Of these only two were thought to have been acutely ill of tuberculous disease at the time of their disappearance.

Five children, or 0.66 per cent, of the 738 tested are known to be dead, which is 4.7 per cent of the 105 known to have had a tuberculous infection; of these one was under one year of age, three were in the one to two year group, and one was between three and four years of age. All of these mortalities except one were in the group classified as active. The one exception was in the group of suspected cases, where the patient died of a sarcoma without developing marked symptoms of tuberculosis. The four other fatal cases included one of miliary tuberculosis, one of tuberculous bronchopneumonia, one of hilum node tuberculosis, and one of combined pulmonary and bone disease.

In the remaining twenty cases in the active group are included four cases of pulmonary tuberculosis, three of hilum node tuberculosis, two of bone disease, five of tuberculosis of the cervical lymph nodes, and three cases of pleurisy with effusion. In three the focus might have been either pulmonary or in the hilum nodes.

At the present time, then, from three months to two and one-half years after being first seen, seventeen of the twenty-four active patients are known to be living, and three have disappeared from observation. Of the seventeen known to be living, nine are completely well and symptomless, three are ill at home with symptoms of tuberculosis, and five are in hospitals for tuberculous patients.

Of the twenty-nine cases classed originally as suspected, one is dead, two are ill with symptoms of tuberculosis, three have disappeared, while twenty-three are well.

Of the forty-six cases classed as healed, one has been lost, the other forty-five were well when last seen, and have never had signs or symptoms of active tuberculous disease other than the original positive tuberculin test.

In the group of twenty-four active cases, nine, or 37.5 per cent, had definite histories of exposure in the home to tuberculosis; in the twenty-nine suspected cases, nine, or 31 per cent, were known contacts; in the forty-six cases of healed tuberculosis, ten, or about 21.8 per cent, were known to be contacts. For the total group of 105 there were twenty-nine known contacts, an incidence of 27.6 per cent.

The present condition of the patients in the classified groups is shown graphically in Fig. 3.

The following case reports were selected at

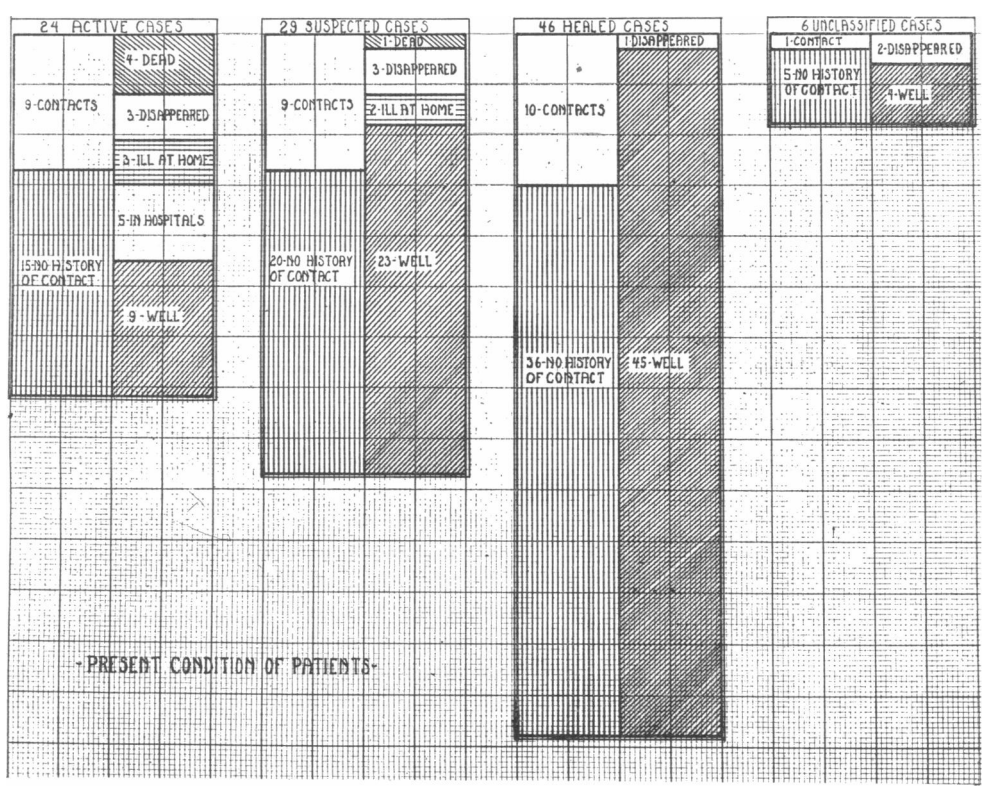

Figure 3

random from among those in which abnormal roentgen shadows could be demonstrated.

CASE REPORTS

CASE 1.—E. S., boy, age five months. Complaint: failure to gain in weight for the past six weeks. Brother was actively tuberculous and lived in intimate contact with the baby for the first four months of its life. Tuberculin test very strongly positive, 20 by 20 millimeters in diameter. Physical examination showed enlarged anterior fontanelle, spleen enlarged and palpable 3 centimeters below the costal margin. Roentgenogram showed density in upper lobe of left lung, a rounded area of density to the left of the trachea thought to be probably an enlarged gland, enlargement of the spleen, thymic enlargement. (See Fig. 4.) This was classified as active disease. Baby ran an afebrile course in the hospital and began to gain on a proper formula. Roentgenogram taken three three weeks later showed thymic enlargement to have disappeared, density in left upper lobe unchanged, and the appearance of a small amount of what was probably interlobar fluid. At this time patient ran a course of fever as high as 103 degrees F., lasting for a week, and developed an intercurrent otitis and pyelitis from which it recovered. One month later, developed a typical pertussis. Roentgenogram at this time showed no changes over the previous one. Patient recovered from the pertussis, and was put on quartz-light therapy. Roentgenogram taken eight months from time of first visit showed thymus again enlarged, disappearance of interlobar fluid, and spleen of normal size. (See Fig. 5.) Child well at this time, gaining normally. Still had some cough. At age of twenty months reported well.

CASE 2.—D. M., boy, age ten months. No complaints. Visited the clinic because two weeks previously the mother had been diagnosed as an active case of open pulmonary

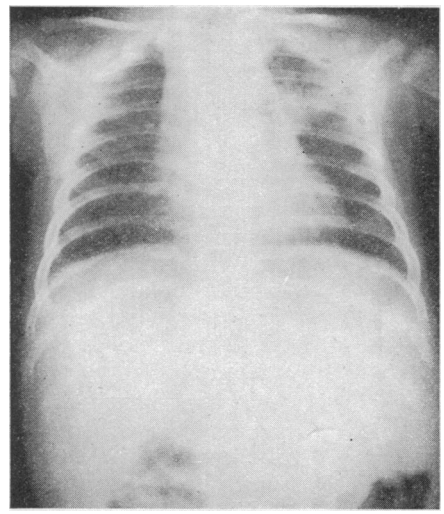

Fig. 4 (Case 1).—Boy, five months

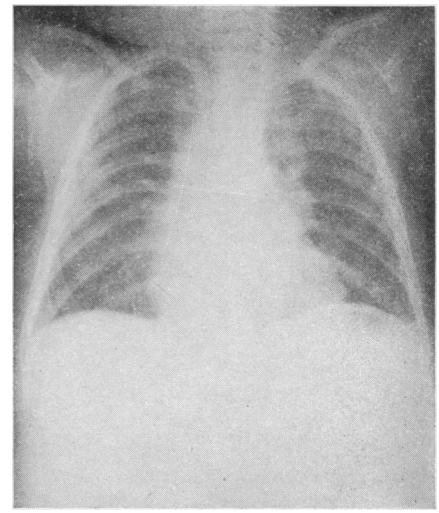

Fig. 5 (Case 1).—Eight months later than Fig. 4

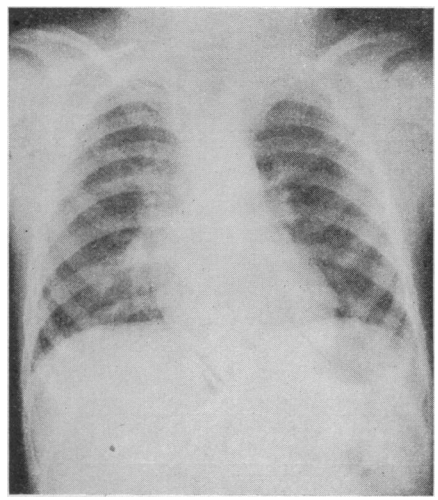

Fig. 6 (Case 3).—Girl, age three years

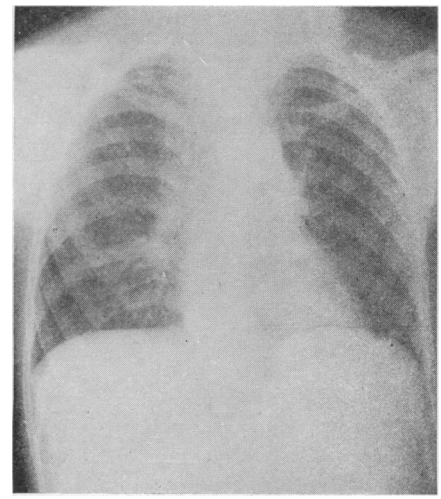

Fig. 7 (Case 3).—Two and one-half years after (Fig. 6)

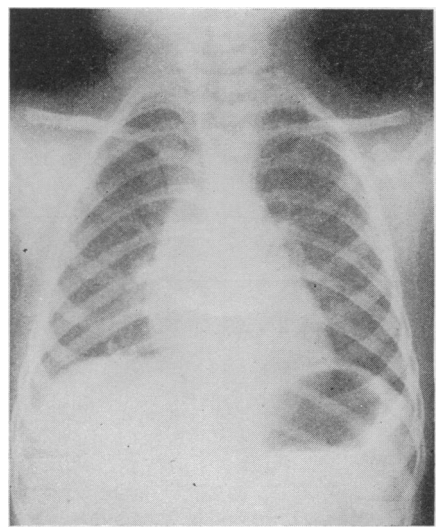

Fig. 8 (Case 4).—Girl, age two and one-half years

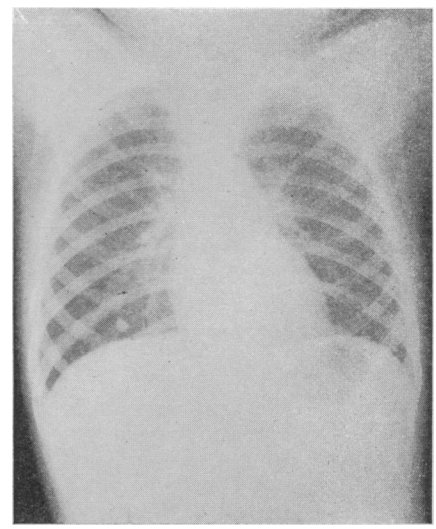

Fig. 9 (Case 4).—One year later than Fig. 8. Note much increase in calcification, especially of solitary node in right lower lobe

tuberculosis. Tuberculin test positive. Physical examination revealed child of normal weight. Fine râles at the right base posteriorly. Roentgenograms showed lung roots increased in dimensions and density, and the presence of enlarged glands; lung fields somewhat mottled with mottling distributed along the major bronchial branches; no calcification evident. This case was classified as active, but the child has never developed any symptoms, and at the age of eighteen months is entirely well. Roentgenograms at this time show no decrease in size of glands, no calcification, but mottling somewhat less.

CASE 3.—V. M., girl, age three. No presenting symptoms. Mother died of tuberculosis two months previous to first visit of patient. Physical examination showed cervical adenopathy, moderate, but otherwise was negative. Tuberculin test was positive, with an indurated area of 18 by 22 millimeters, with a more extensive erythema. Roentgenograms showed much fuzzy and irregular density along the bronchial tree, with a patch of density in lower inner portion of right lower lobe. (See Fig. 6.) Patient was considered as actively diseased. During the period of observation of two years and six months, she developed no symptoms except those of frequent colds, and cough at times of having colds. Roentgenogram taken showed increased density along the bronchial tree as compared with previous films, with roentgenologist reporting "definite peribronchial tubercles." (See Fig. 7.)

CASE 4.—A. V., girl, age two years six months. Complaint: painful swelling of neck. Mother had died of pulmonary tuberculosis two months previously. Physical examination revealed large mass, indurated, in right posterior triangle, with the central portion red and fluctuant. Many coarse râles throughout the chest. Tuberculin was positive with an induration of 15 by 16 millimeters, and an erythema of 21 by 28 millimeters. Pus from gland obtained by aspiration showed no acid-fast bacilli, and subsequent animal inoculation was negative. Roentgenogram of chest showed heavy peribronchial adenopathy, with two or three spots of calcification in the parenchyma of the right lung, with a large one in the right lower lobe. (See Fig. 8.) This case was classified as suspected. Heliotherapy was prescribed. One year later the child was well, roentgenogram unchanged except for much increase in the calcification. (See Fig. 9.)

COMMENT

The number in this series of cases is, of course, much too small from which to draw any mortality statistics, but there are many of these children who give proof of the fact that infants and young children may carry tuberculous infection with few symptoms. Some of them may have considerable resistance also to rather extensive tuberculous disease. Eighty-one of our series of 105, or about 77 per cent of those known to be tuberculous, are entirely free of symptoms and well from three to thirty months after they were first seen.

Our ever increasing knowledge, then, of tuberculous infection and disease in the infant has made us hesitant about predicting the fate of those merely infected with tuberculosis. We find also that we have made mistakes in the prognosis of many suffering from considerable disease. Has part of this been due, not only to our lack of knowledge of the course that tuberculosis may run, but also to the fact that small children as well as adults are becoming more resistant to the disease than formerly? Calmette has possibly shown by his extensive researches that a certain amount of immunity may be acquired by the infant when avirulent tuberculous organisms are taken into the body in large numbers.* It is more than possible that this same phenomenon is going on under our very eyes in a large number of children, and in a natural way, and would explain the fact that many children become infected with tuberculosis early in life, and remain free from symptoms of tuberculous disease.

CONCLUSIONS

1. Tuberculous infection is fairly common in infancy and early childhood.

2. In the absence of symptoms and roentgen-ray findings these patients carry the infection usually without developing evidence of marked disease.

3. Occasionally those having marked evidence of disease may carry the disease for a considerable time with no increase of signs or symptoms.

4. Seventy-seven per cent of the children under four years of age in our series that were positive reactors to tuberculin developed no evidence of tuberculous disease.

5. The intracutaneous test and the roentgen ray are the most valuable aids in diagnosis.

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DISCUSSION

ERNST WOLFF, M. D. (516 Sutter Street, San Francisco).—Doctor Dickey's paper is the first valuable study to reveal the incidence of tuberculous infection in infants and young children in San Francisco. His figures are similar to the results of American and European statistics, obtained by the same technique. This striking similarity of results in localities, which

* Greenwood has recently questioned Calmette's statistical analysis (British Medical Journal, May 12, 1928, p. 793).

differ widely in social, racial and climatic conditions indicates that the mechanism of so-called "casual" exposure is the deciding one that brings about the positive tuberculin reaction in infants and runabouts.

Concerning the related histories in which the favorable course of active or suspected tuberculosis is described it is interesting to note that in three out of four cases the infection ceased with the death of the tuberculous mother or the removal of the tuberculous contact case from the home to the hospital. In the fourth case the active tuberculous mother very likely was separated from the baby after the first examination. On the other hand, it is our experience that active lung infiltrations in older children are often observed when they are constantly superinfected by immediate contact. There may be some direct relation between the healing of the tuberculous process and the ceasing of the source of infection. This relation may count for the favorable course in the related cases, without discussing the question of increasing resistance to tuberculosis in mankind.

PHILIP H. PIERSON, M. D. (490 Post Street, San Francisco).—This paper of Doctor Dickey shows a study of a group of children, some contact cases and some where no contact was evident. Tuberculous infection may be present without any manifestations, subjectively or objectively. Tuberculous disease may also be present without objective or subjective signs, and even when present are not specific enough directly to guide us either in diagnosis or prognosis. This very fact should make us more careful to view children from the broadest possible standpoint, and make use of the two most valuable aids—roentgenography and the tuberculin test.

The work of Valtis in Calmette's laboratory has shown that certain forms of tubercle bacilli not only pass through a Chamberlin filter, but also through the placenta, giving no localizing symptoms of tuberculous disease, nevertheless setting up a protective reaction in the tracheobronchial lymph nodes. If this work continues to be verified, it may revise our ideas as to antenatal infection.

This source of early infection together with small exogenous infections, where the general health of the individual receives special attention, probably accounts for the fact that many of our children respond very well and the disease becomes arrested and cured more often than we originally thought. A case of healed general miliary tuberculosis that I reported a few years ago, and others that are on record, show the wealth of resistance which may be summoned to the aid of many children.

In conclusion let us carry this thoughtful point of view in considering the children who come to us and recognize that tuberculosis, if considered from this broad point of view and carefully treated, may have a very hopeful outlook and that infected children may recover, leaving no evidence of a previous tuberculous infection.

ESTHER B. CLARK, M. D. (300 Hamilton Avenue, Palo Alto).—Doctor Dickey has made a splendid contribution to the study of tuberculosis in children. The incidence of tuberculosis as revealed by the tuberculin intracutaneous test is undoubtedly higher in young children than is generally believed. A knowledge of the probable fate of a young child or infant who is known to be harboring tubercle bacilli is of very great prognostic importance. Such knowledge can only be gained by observation over long periods of time of children who have early in their lives been found to be infected. Doctor Dickey's observations, while covering a relatively short period of time, would indicate that the outlook for the infected child who is free from symptoms is usually good.

Clinically it is often extremely difficult or impossible to decide whether or not a child presenting any of several symptoms or signs and a positive tuberculin and a chest plate with indecisive markings, is actually suffering from tuberculosis or not. In children with such obscure and indefinite findings a negative tuberculin gives more real information and is of more significance than is a positive tuberculin.

COCCIDIOIDAL GRANULOMA*

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DISCUSSION *by Roy W. Hammack, M. D., Los Angeles; W. T. Cummins, M. D., San Francisco; Norman Epstein, M. D., San Francisco.*

THE results of some observations on the efficacy of colloidal copper in the treatment of coccidioidal granuloma were presented at the fifty-sixth annual session.[1] Since the reading of that paper, which was based upon the treatment of two patients, I have had the opportunity of further observation of one of the two originally reported and, in addition, have studied the effects of colloidal copper upon four others. Through experimental work upon guinea-pigs, I have attempted to ascertain the methods and factors concerned in the transmission of this infection. The results I shall present to you after a brief outline of the histories of the four recent patients. Following are the case histories:

CASE REPORTS

CASE 1.—E. M., male, thirty-nine years of age, negro, cement worker, born in Texas and resident for the past four years in Los Angeles County, was admitted to the Los Angeles Hospital, April 5, 1927, and discharged August 3, 1927.

He complained upon admission of weakness, cough, night sweats, loss of weight, pain in the neck and left shoulder, and swelling below the left clavicle.

Present trouble started three months before with a "cold" characterized by fever, coughing, night sweats and weakness. Home treatment was ineffective; after a month he experienced pain in the proximal end of the left clavicle, followed in a few days by a noticeable swelling which has increased in size until the present time.

Examination showed a patient acutely ill and extremely weak. Temperature and pulse curves were of a septic character. Cough persistent and expectoration profuse. Examination revealed several variously sized fluctuating tumor masses, the most conspicuous of which were situated below the left clavicle and sternal regions.

X-ray study showed a mediastinal mass not distinctive of its origin.

In the pus aspirated from an abscess the coccidioides immitis was found, culturally and microscopically.

Treatment, colloidal copper. After the fourth injection improvement began and continued progressively until August 3, 1927, when voluntarily he left the hospital, much improved but not completely cured. Unfortunately I do not know his present physical condition. It is significant that, in spite of his critical condition upon entering the hospital, he was able to leave in the

* Read before the Dermatology and Syphilology Section of the California Medical Association at its Fifty-Seventh Annual Session, April 30 to May 3, 1928.

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