

## ORIGINAL ARTICLES

## Scientific and General

COCCIDIOIDOMYCOSIS: IN THE WESTERN  
FLYING TRAINING COMMAND\*

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THAT the unprecedented opportunity for study of coccidoidal infection which the mobilization and training of troops in the southwestern United States provided was not neglected, was due to the foresight of Colonel (now Brigadier General) Charles R. Glenn and his successors, Colonel Healy and Colonel Britton. Anticipating the situation which actually arose, they enlisted the cooperation of Dr. Charles E. Smith, as a Surgeon General's consultant representing the Army Epidemiological Board and, even before mobilization began, set in action a program of study and control which still functions, and which has already yielded information of inestimable value about this rather little known disease. That there was a hazard in putting troops into this area was recognized in the beginning. The decision that the climatic advantages for flying outweighed the hazard of coccidioidomycosis has been amply justified. The accident rate in flying training in this command has been the lowest in the country, and favorable flying weather has been the most important factor in achieving this record. Lives saved in this way far outnumber lives lost from coccidioidomycosis. And the incidental benefit with which we are concerned today is the unique clinical and laboratory experience furnished for observations on coccidioidomycosis. Unfortunately it is not yet possible to release exact figures of the numbers of men involved, and the final statistical analysis of our observations must rest until the war is over. But it is possible to give you an idea of what was involved in the program of the Western Flying Training Command. All new personnel coming on air fields are skin-tested when they arrive, and the negative reactions are retested six months later or when they leave the field if before this time has elapsed. All suspicious clinical cases in the dispensaries and hospitals are skin-tested during the course of the disease, and in addition specimens of blood are sent to Dr. Smith for confirmatory evidence when indicated. A campaign of medical education has been instituted, due to the fact that coccidioidomycosis was just news to most of the medical officers. A manual was

prepared with x-ray reproductions, and this was distributed to all the stations and to many of the individual officers. A coccidioidomycosis control officer was appointed to supervise the data collected and to assist in the education of personnel. Dr. Charles E. Smith has visited the valley stations regularly once a month, and has been in constant consultation with Colonel Healy, Surgeon, Western Flying Training Command. As a result of this program, over a quarter of a million skin tests have been given, a thousand or more clinical cases recognized, nine complete autopsies done, and an enormous mass of statistical material has been collected.

## GEOGRAPHICAL LIMITS OF THE ENDEMIC AREA

When these results are available it will be possible for the first time to define precisely the geographical limits of the endemic area—we are already prepared to state that the San Joaquin Valley is not the worst area by any means. We will have a pretty accurate measure of probable morbidity and mortality in any given area, of the percentage of subclinical to clinical cases, and the percentage of erythema nodosum, cavitation, and dissemination to be expected. We will be able to give an estimate of the economic cost and probably an improved picture of the clinical course and clinical types. This is the particular theme of my remarks today. The other data must wait until all the returns are in; but when it does come it will furnish, I believe, definitive answers to many questions.

## CLINICAL CLASSIFICATIONS

From the clinical point of view various classifications are made. Dr. C. E. Smith has recently proposed one in the *Medical Clinics of North America*. The question is still open, so I propose yet another of my own. It seems to me that some clinical value may be had from grouping the cases as follows:

1. Primary.
2. Intermediate (or Pulmonary).
3. Advanced (or Disseminated).

The *Primary* form in the great majority of cases is subclinical. The only evidence of its having occurred is the finding of a positive skin test in an individual who was previously negative. This change of positive from negative will occur in about 10 per cent of personnel in the all over portion of this command, which includes both endemic and nonendemic areas, within six months. But some stations have reported as high as 80 per cent of the post population who stay six months turning positive. As the medical personnel and the men themselves become more aware of this disease, more and more of these subclinical cases will be recognized and properly diagnosed. Frequently, what would ordinarily pass as a cold or a mild influenza, "desert rheumatism," etc., is properly diagnosed as coccidoidal infection, when it is suspected. When erythema nodosum occurs, as it often does in this primary stage, the diagnosis, of course, is suspected much more frequently. There is no sharp borderline between

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this stage and the pulmonary phase, because many of the more severe cases show varying degrees of respiratory involvement.

The *Intermediate (or Pulmonic)* stage is the one which is most frequently recognized clinically. This is an acute, subacute, or chronic pulmonary inflammation. Almost all degrees of pulmonary involvement are seen, from a mild bronchitis, with or without hilar gland enlargement, to a massive or disseminated pulmonary consolidation. The resemblance to tuberculosis has often been stressed, but there are certain differences which are recognizable with experience. Our roentgenologists seldom mistake it now. The clinical symptoms in relation to the x-ray findings show also certain definite differences from tuberculosis. Perhaps the most marked is the relatively better prognosis. In relation to the amount of pulmonary involvement a patient with coccidioidal infection will recover, where the outlook would be exceedingly grave were the diagnosis tuberculosis. But when the lesion is primarily apical, the confusion may be truly difficult. And with certain lower lobe lesions the resemblances to virus pneumonia are often striking. Cavities occur rather frequently, but have a much better outlook than do tuberculous cavities. They have thinner walls as a rule, and often occur spontaneously, so to speak, i.e., without a preceding area of consolidation. They show a very marked tendency toward spontaneous closure, although some have been observed to be open for seven months. There is another curious lesion almost pathognomic of this disease. This consists of a well-circumscribed nodule which looks very much like a metastatic carcinoma. These nodules are usually unaccompanied by symptoms, but are very slow in resolving. We have seen multiple patches of rather dense consolidation scattered all through both lung fields. In one such, about twenty small cavities developed, which closed, however, rather promptly, and the patient made a complete recovery. There are a few who develop massive consolidations and then recover, but this is usually seen in the fatal disseminated cases. We have found that about one-sixth of all cases which occur on every field are diagnosed as clinical coccidioidomycosis, and of these so diagnosed about 20 per cent will show skin lesions, usually erythema nodosum.

In the *Advanced (or Disseminated)* form, literally anything can happen. This outcome would seem to be about 100 times as likely to occur in the colored as in the white soldier. The mechanism of the occurrence of dissemination is not known, nor is the time in relation to the onset of the disease. The shortest time from onset to death was 63 days, the longest time was 200 days—the average elapsed time in the fatal cases was 3-4 months from onset to death. Thus it would appear, and a study of the records confirms, that dissemination, if it occurs, is likely to occur early. There has been one doubtful case of late dissemination almost five years after residence in an endemic area, but we have not observed any such. This is naturally a question of

prime importance, for if we are going to see a large number of late disseminations from the men who have been infected in the desert area, the problem will be very difficult. In the disseminated cases almost every organ of the body has been involved. All the fatal cases showed pulmonary involvement, all showed lymph gland involvement, all but one showed some involvement of bones, the calvarium or meninges was involved in five cases, two out of the nine showed involvement of the spleen. In some cases the whole body was literally riddled with cold abscesses. A curious, and I believe previously unobserved finding, was involvement of the heart muscle in three cases. These showed infiltrations between the muscle fibres in which spherules were found, and in one case a small cold abscess in the wall of the ventricle. Unfortunately, EKG's were not made on these cases, but EKG studies are now being made on all, and one case is under observation now which shows abnormalities in the T-waves which may be significant. We have seen, incidentally, no less than four instances of pericardial effusion in patients who are apparently recovering. There have been a few cases of dissemination where apparent recovery occurred. The complete figures on these are not yet available, but seem to be about 20 per cent of the whole number of disseminations. That dissemination may be impending can often be anticipated from a rising titre in the complement fixation test. We have discovered no treatment that affects the course in any way. The sulfones are futile; our one case treated with penicillin received no benefit, and in vitro tests indicate that the fungus is not susceptible to penicillin. This has been confirmed elsewhere. Disseminated coccidioidomycosis was, as you all know, the first recognized manifestation and it is a truly terrible disease, especially for the darker skinned races.

#### SUMMARY

This now is a summary of our present ideas on coccidioidomycosis. It is an endemic disease in the San Joaquin Valley of California, the whole of Arizona and New Mexico, western Texas, northern Mexico, southern Nevada, and probably Idaho. A very large percentage of those who spend time in this region will be infected, generally with the inapparent subclinical form of the disease. Under the closest scrutiny one-sixth of the infections will be diagnosed and in practically all of the diagnosed cases some pulmonary involvement will be found. About 20 per cent of diagnosed cases will show skin lesions, and about 1 per cent of the diagnosed cases will develop dissemination, and four-fifths of these will die. The pulmonary involvement will always be found in the fatal cases, but in itself is rarely, if ever, the cause of death. We believe dissemination is less likely if the intermediate cases are kept at rest until the process subsides, but must confess ignorance at present as to the time or the route of dissemination. There is no specific treatment. (Slides.)

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