# Histoplasmin, Coccidioidin, And Tuberculin Sensitivity Among School Children In Two Texas Counties

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*Although the general areas of histoplasmosis and coccidioidomycosis prevalence are well known, few studies of these diseases have been made in areas where both exist. Reactors to histoplasmin and coccidioidin, as well as tuberculin, among a group of Texas school children are reported in this study.*

THE ENDEMIC areas of histoplasmosis and coccidioidomycosis appear to extend into Texas, the former from the northeast, the latter from the southwest. Observations on histoplasmin sensitivity in Texas indicate approximately 30 percent of the young adults are positive histoplasmin reactors. Among 209 lifetime residents of Texas attending the University of Chicago from 1946 to 1948, 61, or 29 percent, were found to be positive reactors to the histoplasmin skin test (*1*). Palmer's survey among student nurses yielded 21 positive reactors, 34 percent, of the 61 Texans tested (*2*). In a survey at Vanderbilt University, Christie and Peterson reported 7 positive histoplasmin reactors, 26 percent, among the 27 Texas residents tested (*3*).

These investigators made no effort to divide Texas into areas of histoplasmin sensitivity, but considered the State as a whole. The only report of a survey in a specific area is that of Forbes and Chang (*4*), who tested 441 infants and children in Dallas hospitals. This report showed a rise in sensitivity rates with age, reaching about 17 percent in the 12- to 15-year group. Since illness decreases skin sensitivity, it is probable that sensitivity among healthy children in this area would be higher.

In 1953, a survey of histoplasmosis and coccidioidomycosis in Texas was stimulated by the United States Army, which was concerned with the prevalence of fungus diseases in the area about Fort Hood where large numbers of men are trained. The location of Fort Hood and its relation to Bell and Coryell Counties are shown in figure 1. Tests were given only in Gatesville in Coryell County and Killeen in Bell County. These towns are at opposite ends of Fort Hood and are considered representative of the two counties. Landscape and climate are similar throughout the area.

Tuberculin tests were done also to furnish data to compare with similar surveys in other parts of the United States. In addition to the skin testing, a 35-mm. X-ray of the chest was obtained for each individual. A portable X-ray unit was used. The films were read by H. E. Smith of the Texas State Department of Health. Results of the X-ray survey are not considered in this paper.

## Materials and Methods

The study was conducted between May 4–7, 1953. Tuberculin, histoplasmin, and coccidioidin tests were done simultaneously by intradermal injection of 0.1 cc. of the appropriate antigen. The tuberculin and coccidioidin tests

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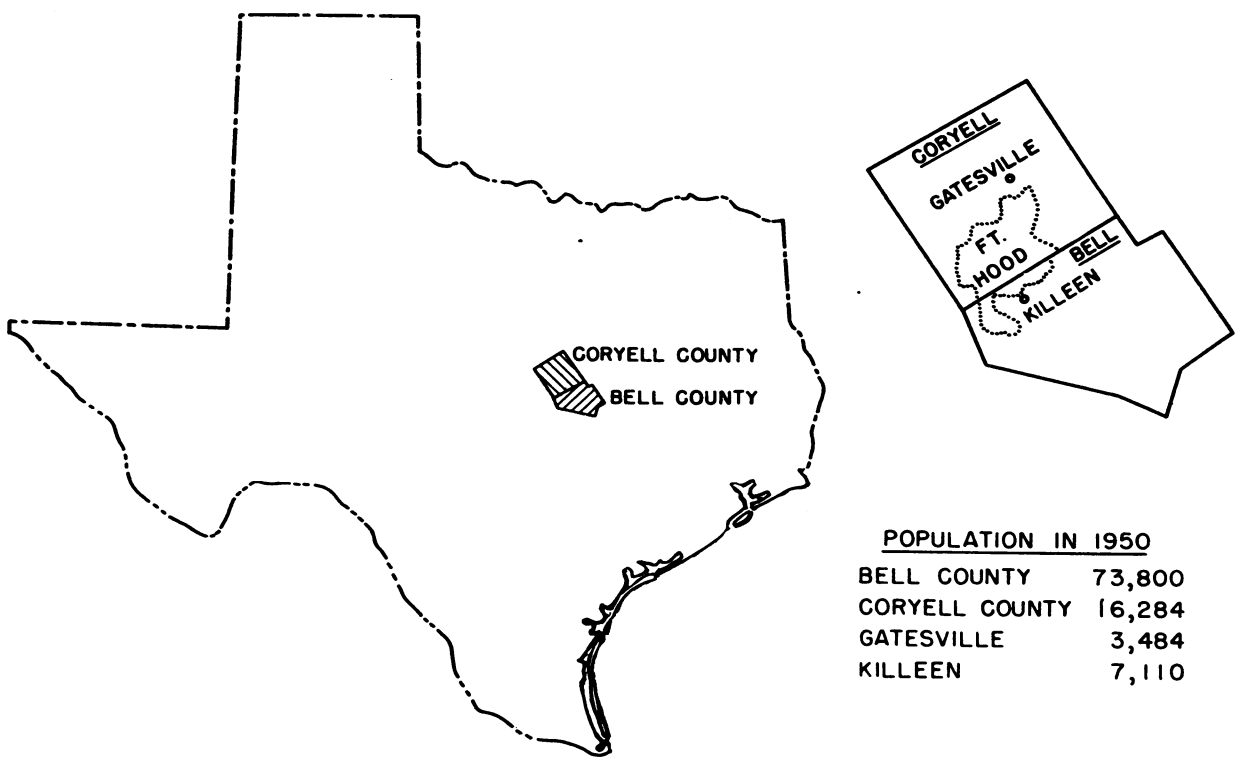
were placed on the volar surface of the left forearm, and the histoplasmin test was similarly placed on the right forearm. The injections were given by teams of three experienced persons, each using a separate set of syringes and needles and each injecting a single antigen. The tests were inspected 48 hours after injection, and measurements of the transverse diameter of erythema and induration were made by two experienced readers. Reactions were considered positive if the area of induration was 5 mm. or more in diameter without regard to erythema.

The tuberculin dosage was 0.0001 mg. in 0.1 cc. of diluent. The histoplasmin (lot HKC–5) prepared and titrated by the methods of Shaw, Howell, and Weiss (*5*), was administered in a dilution of 2:1000. This histoplasmin and dilution are equivalent in potency to earlier products (*1*, *2*). The coccidioidin was used in a dilution of 1:100.

A questionnaire, including parental consent form, was distributed to each student prior to the test. This form included identifying information, date of birth, sex, length of residence in Bell and Coryell Counties, and appropriate space for recording the results of the skin tests and the X-ray number. On completion of the survey these records were transferred to punchcards from which the desired tabulations were obtained.

Skin tests were given to 2,838 persons in the public schools at Gatesville and Killeen, Tex. Twenty nonwhite persons and 109 adults were eliminated from the analysis, leaving a total of 2,709. All of these children were considered in the analysis of the tuberculin results. Lifetime residents only were considered in analyzing the results of the histoplasmin and coccidioidin tests. Any person living at least 80 percent of his life in the Bell-Coryell County area was considered a lifetime resident. This criterion eliminated approximately half of those tested, since the children of army personnel at Fort Hood, a rather transient group, constituted a large proportion of the total school population. The data analyzed for histoplasmin and coccidioidin sensitivity, then,

**Figure 1. Area of residence of persons given skin tests in Bell and Coryell Counties, Tex.**



represents the indigenous population of Bell and Coryell Counties, essentially a rural area.

As used in the text, "rates" or "sensitivity rates" refer to the prevalence of positive reactors to the various antigens.

## Results

*Differences between schools.* The number and percent of positive reactors to histoplasmin in the Gatesville and Killeen public schools are shown in table 1 and figure 2. Since the towns are approximately 30 miles apart, it was considered desirable to compare the sensitivity rates. As the rates for the two schools were approximately the same, for purposes of analysis, the results from the two areas were combined.

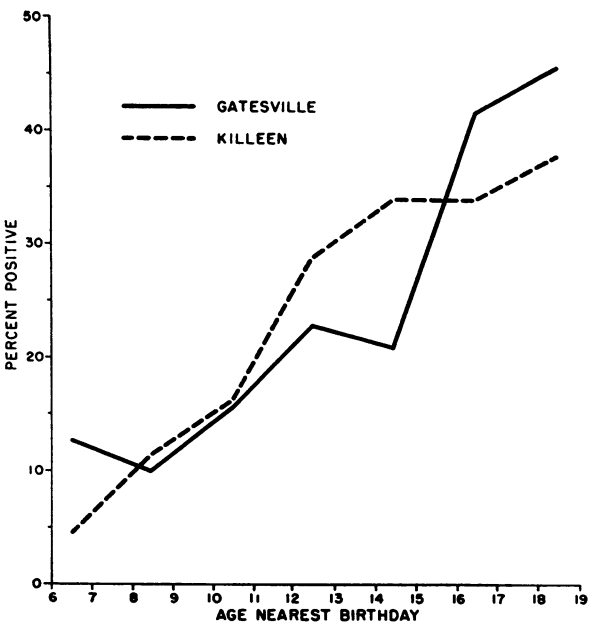
**Table 1. Histoplasmin sensitivity prevalence among Gatesville and Killeen lifetime resident public school children, Tex.**

| Age nearest birthday | Gatesville | | | Killeen | | |
|---|---|---|---|---|---|---|
| | Number tested | Number positive | Percent positive | Number tested | Number positive | Percent positive |
| 6–7 | 79 | 10 | 12. 7 | 67 | 3 | 4. 5 |
| 8–9 | 141 | 14 | 9. 9 | 131 | 15 | 11. 5 |
| 10–11 | 129 | 20 | 15. 5 | 148 | 24 | 16. 2 |
| 12–13 | 101 | 23 | 22. 8 | 139 | 40 | 28. 8 |
| 14–15 | 96 | 20 | 20. 8 | 109 | 37 | 33. 9 |
| 16–17 | 53 | 22 | 41. 5 | 115 | 39 | 33. 9 |
| 18–19 | 22 | 10 | 45. 5 | 53 | 20 | 37. 7 |
| Total | 621 | 119 | 19. 2 | 762 | 178 | 23. 4 |

*Tuberculin sensitivity.* Table 2 and figure 3 show the number and percent of positive reactors among the 2,709 white children tested. The rates were relatively low, rising from 1.8 in the 6- to 7-year age group to 6.1 in the 16- to 17-year age group. There was a clear-cut rise in rates with age. The overall rate was 4.0 percent. Four of the 18 Negro children tested were positive to tuberculin.

*Histoplasmin sensitivity.* The data on the frequency of positive reactions to histoplasmin are given in table 3 and figure 3. These data, confined to the 1,383 white lifetime residents tested, show progressively increasing rates of

**Figure 2. Prevalence of histoplasmin sensitivity among lifetime residents in Gatesville and Killeen schools, Tex.**




sensitivity with age. The 6- to 7-year age group had 8.9 percent positive and the oldest age group, 18- to 19-year olds, had 40.0 percent positive reactors. The overall percentage of positive reactors was 21.5 percent.

*Coccidioidin sensitivity.* Few of the lifetime residents of Bell and Coryell Counties reacted to this antigen (table 3 and fig. 3). Although the rates were low, they were based on a relatively large sample and show a tendency to increase with age, from less than 1 to almost 3 percent. The low rates of sensitivity

**Table 2. Number and percent positive tuberculin reactors among white school children in Bell and Coryell Counties, Tex.**

| Age nearest birthday | Number tested | Number positive | Percent positive |
|---|---|---|---|
| 6–7 | 325 | 6 | 1. 8 |
| 8–9 | 578 | 16 | 2. 8 |
| 10–11 | 581 | 27 | 4. 7 |
| 12–13 | 448 | 19 | 4. 2 |
| 14–15 | 379 | 17 | 4. 5 |
| 16–17 | 279 | 17 | 6. 1 |
| 18–19 | 119 | 7 | 5. 9 |
| Total | 2, 709 | 109 | 4. 0 |

to coccidioidin suggest that coccidioidomycosis is not endemic in this region of Texas. A number of coccidioidin reactors were noted among the "nonlifetime" residents. These occurred among persons whose major residence had been in western Texas.

*Sex differences in histoplasmin sensitivity.* The positive reactions among males and females are shown in table 4 and figure 4. The overall frequency was higher among males than females (26 versus 17 percent). This has been noted in other surveys (*6*, *7*). However, the rates were essentially equal up to the 12- to 13-year age group. Another difference between the male and female rates was the failure of the female rates to show a marked increase with age beyond the 10- to 11-year group. In fact, the rates for females above this age were almost constant. The only rise occurred in the 18- to 19-year group, where only 29 girls were tested. The reasons for these sex differences are not known.

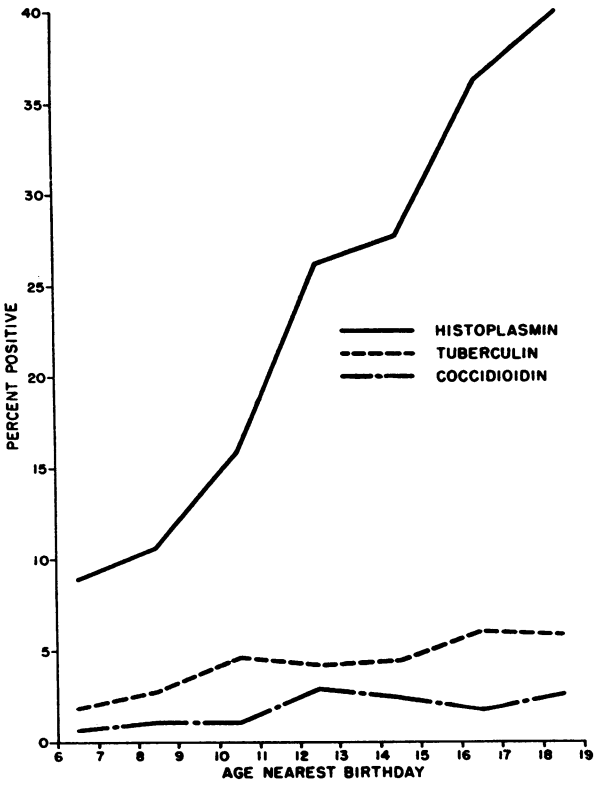
*Cross reactions.* Cross reactions in patients tested with histoplasmin and coccidioidin have been reported (*8*). The comparison of the size of the reaction to histoplasmin and to coccidioidin in the same children is shown in table 5. It appears that some of the coccidioidin reactions were cross reactions. This was indicated by the number of children who showed a smaller reaction to coccidioidin than to histoplasmin.

**Table 3. Number and percent positive reactors to histoplasmin and coccidioidin among lifetime residents of Bell and Coryell Counties, Tex.**

| Age nearest birthday | Number tested | Histoplasmin | | Coccidioidin | |
|---|---|---|---|---|---|
| | | Number positive | Percent positive | Number positive | Percent positive |
| 6–7 | 146 | 13 | 8.9 | 1 | 0.7 |
| 8–9 | 272 | 29 | 10.7 | 3 | 1.1 |
| 10–11 | [1] 277 | 44 | 15.9 | 3 | 1.1 |
| 12–13 | 240 | 63 | 26.3 | 7 | 2.9 |
| 14–15 | 205 | 57 | 27.8 | 5 | 2.4 |
| 16–17 | 168 | 61 | 36.3 | 3 | 1.8 |
| 18–19 | 75 | 30 | 40.0 | 2 | 2.7 |
| Total | 1,383 | 297 | 21.5 | 24 | 1.7 |

[1] One child in this group was tested with histoplasmin but not with coccidioidin.

**Figure 3. Prevalence of histoplasmin and coccidioidin sensitivity among lifetime resident school children, and of tuberculin sensitivity in all school children, Bell and Coryell Counties, Tex.**




Many of the coccidioidin reactions were specific reactions and not cross reactions. This was clearly shown in the 52 children who reacted to coccidioidin but were negative to histoplasmin. Of these, 14 were positive reactors. In 13 other children, the reactions to coccidioidin were larger than to histoplasmin.

## Discussion

Although the purpose of this survey was to determine the prevalence of sensitivity of histoplasmin and coccidioidin, the tuberculin rates also proved interesting. The tuberculin rates among children in this rural area of Texas were surprisingly high. In comparing rates obtained under similar circumstances with the same lot and dose of tuberculin, the Texas rates were found to be twice as high as those among the suburban children in the vicinity of Cincinnati, Ohio (*6*). While the Texas rates appeared

to be about half as great as rates observed in Kansas City, Mo., (*6*) they were still surprisingly high for a rural area. These rates were not accounted for by the presence of large numbers of Mexican or Latin American children, since less than 5 percent of the children tested were of such origin. The presence of Negroes did not complicate the picture, since they were not included in the analysis.

**Table 4. Histoplasmin sensitivity prevalence according to sex among lifetime resident school children of Bell and Coryell Counties, Tex.**

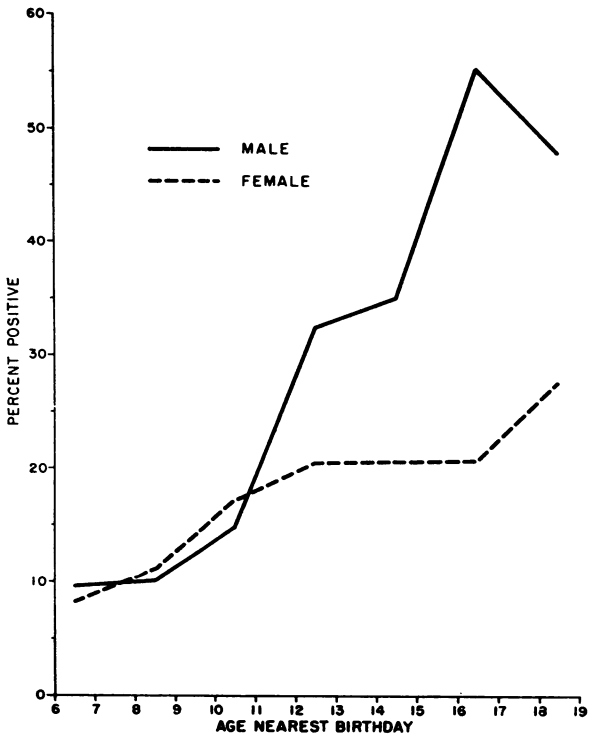
| Age nearest birthday | Male | | | Female | | |
|---|---|---|---|---|---|---|
| | Number tested | Number positive | Percent positive | Number tested | Number positive | Percent positive |
| 6–7 | 73 | 7 | 9. 6 | 73 | 6 | 8. 2 |
| 8–9 | 138 | 14 | 10. 1 | 134 | 15 | 11. 2 |
| 10–11 | 149 | 22 | 14. 8 | 128 | 22 | 17. 2 |
| 12–13 | 118 | 38 | 32. 2 | 122 | 25 | 20. 5 |
| 14–15 | 103 | 36 | 35. 0 | 102 | 21 | 20. 6 |
| 16–17 | 76 | 42 | 55. 3 | 92 | 19 | 20. 7 |
| 18–19 | 46 | 22 | 47. 8 | 29 | 8 | 27. 6 |
| Total | 703 | 181 | 25. 8 | 680 | 116 | 17. 1 |

The histoplasmin sensitivity rates also deserve comment. While the exact prevalence of histoplasmosis in Texas has never been determined, a number of cases have been reported from Veterans Administration hospitals, Army hospitals, and other sources.

Preliminary studies mentioned earlier (*1–4*) had not indicated such a high prevalence of sensitivity among lifetime residents. The fact that 40 percent of the children were sensitive at the age of 18 certainly points up the problem for physicians in this area. It might also be appropriate to mention that *Histoplasma capsulatum* was isolated from 1 of 30 soil samples taken from the Fort Hood reservation. Also, this fungus has been isolated from the soil obtained from northeastern Texas near the Arkansas-Louisiana border.

Cross reactions between fungus antigens appear to be common. This is illustrated by the results of Smith and associates (*8*) showing cross reactions in humans between coccidioidin and histoplasmin. Also, cross reactions between histoplasmin and blastomycin in humans have been reported (*6*). There is some evidence of cross reactions between histoplasmin and coccidioidin in these studies as evidenced by the finding that 45 persons reacted to both tests whereas, on a chance basis, only 13 reactions would have been expected. There was also evidence of specific sensitivity to both antigens.

**Figure 4. Prevalence of histoplasmin sensitivity by sex among lifetime resident school children of Bell and Coryell Counties, Tex.**




## Summary

Histoplasmin, tuberculin, and coccidioidin skin tests were made on 2,838 persons in Bell and Coryell Counties, Tex. Tuberculin sensitivity was found to be relatively high for a rural area. Histoplasmin sensitivity among lifetime resident school children was found to increase with age, reaching 40 percent positive in the 18- to 19-year age group, indicating a prevalence of sensitivity somewhat higher than had been expected for this area. The coccidioidin prevalence was low, which seems to

**Table 5. Comparison of the size (in millimeters) of the histoplasmin and coccidioidin reactions in the same child (induration only)**

| Coccidioidin \ Histoplasmin | 0 | 1–4 | 5–9 | 10–14 | 15–19 | 20 and over | Total |
|---|---|---|---|---|---|---|---|
| 0 | 2, 135 | 32 | 326 | 181 | 14 | 3 | 2, 691 |
| 1–4 | 38 | 4 | 15 | 4 | 3 | 0 | 64 |
| 5–9 | 10 | 1 | 10 | 12 | 5 | 0 | 38 |
| 10–14 | 2 | 0 | 4 | 5 | 0 | 1 | 12 |
| 15–19 | 1 | 1 | 0 | 1 | 1 | 0 | 4 |
| 20 and over | 1 | 0 | 5 | 1 | 0 | 0 | 7 |
| Total | 2, 187 | 38 | 360 | 204 | 23 | 4 | 2, 816 |

indicate that *Coccidioides immitis* is not endemic to this area.

It would appear from the known geographic distribution of histoplasmin sensitivity that the rates of reaction probably are even higher as one moves eastward from this area. Physicians in the entire area should therefore be alerted for possible cases of histoplasmosis. As mentioned above, the cases of histoplasmosis which have been reported from Texas have been confined to the large medical centers and Veterans Administration hospitals. Since the infection is generally more common in rural areas, it is probable that large numbers of cases are being missed.

The low rate of coccidioidin sensitivity in Bell and Coryell Counties is noteworthy since the endemic area of coccidioidomycosis has not been too well defined in Texas. It is well known that western Texas and the Rio Grande River Valley are in the endemic area since cases have been reported in these locations (*9*). However, the extension of this area to the north and east has not been well delineated. From these studies it appears that this infection is not common in the central area of Texas around Fort Hood. The reasons for the occurrence of almost 2 percent coccidioidin reactors among lifetime residents are not evident. It might be due to the presence of only a few spores in the soil or to unknown visits into the high area of sensitivity. It should be remembered also that the prevailing winds blow from western and southern Texas over this area and might conceivably disseminate the spores of *C. immitis*.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#### REFERENCES


(*1*) Loosli, C. G., Beadenkopf, W. G. Rice, F. A., and Savage, L. J.: Epidemiological aspects of histoplasmin, tuberculin, and coccidioidin sensitivity. Am. J. Hyg. 53: 33–57 (1951).

(*2*) Palmer, C. E.: Geographic differences in sensitivity to histoplasmin among student nurses. Pub. Health Rep. 61: 475–487 (1946).

(*3*) Christie, A., and Peterson, J. C.: Histoplasmin sensitivity. Am. J. Pediat. 29: 417–432 (1946).

(*4*) Forbes, G. B., and Chang, C. C.: Histoplasmin and tuberculin sensitivity in Texas infants and children. Pub. Health Rep. 68: 320–322 (1953).

(*5*) Shaw, L. W., Howell, A., and Weiss, E. S.: Biological assay of lots of histoplasmin and the

selection of a new working lot. Pub. Health Rep. 65: 583–604 (1950).
(6) Furcolow, M. L., Schwarz, J., Hewell, B. A., and Grayston, J. T.: Incidence of tuberculin, histoplasmin, and blastomycin reactors among a group of school children. Am. J. Pub. Health 43: 1523–1531 (1953).
(7) Prior, J. A., and Allen, M. F.; Geographic distribution of histoplasmin and tuberculin reactors among Ohio State University freshmen and student nurses training in Columbus, Ohio, hospitals. Pub. Health Rep. 62: 1608–1617 (1947).
(8) Smith, C. E., Saito, M. T., and Beard, R. R.: Histoplasmin sensitivity and coccidioidal infection. I. Occurrence of cross reaction. Am. J. Pub. Health 39: 722–736 (1949).
(9) Smith, C. E.: Diagnosis of pulmonary coccidioidal infection. California Med. 75: 385–394 (1951).