Coccidioidin Sensitivity Among School Children in Phoenix (Skin Test and X-ray Survey)*

JOHN EMMETT, M.D.[†]

Communicable Disease Center, Public Health Service, Atlanta, Ga.

THE appellations "San Joaquin" and "Valley Fever" for a time not only signified the relatively benign, pulmonary disease caused by the fungus *Coccidioides immitis*,¹⁻⁴ but also defined its area of endemicity. Since that time the endemic area has been broadened to include much of the Southwestern United States⁵⁻⁹ and the term coccidioidomycosis includes both benign and disseminated ("coccidioidal granuloma") forms of the disease.

In a stable population in an endemic area the problem of coccidioidomycosis is mainly a pediatric one, exposure and the development of immunity having rendered adults nonsusceptible. In migratory populations and in resort areas, however, the problem may also involve adults, as was evidenced by the experience of large numbers of susceptible military personnel brought into endemic areas during the recent war.¹⁰⁻¹²

The present paper reports for the first time data regarding sensitivity to coccidioidin, analyzed according to age, sex, nationality, length of residence, and school attended, for a group of "normal" children living in the endemic area of Phoenix, Ariz.

MATERIAL AND METHODS

One thousand, eight hundred and sixty-nine grade school children ages 5 to 17 were skin-tested for sensitivity to coccidioidin and tuberculin, and all positive reactors and a group of 228 negative

controls received photofluorographic (70 mm.) chest films. The children were pupils of three city schools unselected beforehand for any specific factors. But School C was located in an unpaved, hence dustier, area of the city than Schools A and B, which were located in paved areas. The children compose two large nationality groups, which are classified as American and Spanish-American. A group of 13 American Indians and Chinese make up the total. Seventytwo adults were skin-tested and revealed 51 per cent positive reactors to coccidioidin, which figure is used only for comparison.

Coccidioidin 1:100, as recommended and graciously supplied by Dr. C. E. Smith,¹³ and tuberculin 1:10,000 (O.T.), were used as antigens, with 0.1 ml. of each injected intradermally into the left and right forearms respectively. Conspicuously differentiated, separate sets of new tuberculin syringes and needles were used for each antigen. The schools were tested in alphabetical order at one week intervals and all tests and readings were done by the same person. Reactions which presented an area of reddened induration more than 5 mm. in diameter at the end of 48 hours were considered positive.¹⁴ Only four severe

^{*} Presented before the Epidemiology Section of the American Public Health Association at the Seventyninth Annual Meeting in San Francisco, Calif., November 2, 1951.

[†] Now assigned to Los Angeles City Health Department, Los Angeles, Calif.

reactions occurred, and these responded well to the use of a sling for the involved arm and to the application of warm wet dressings.

RESULTS

Of the total tested, 794 (42 per cent) revealed positive skin reactions to coccidioidin. There was no statistically significant difference between the sexes. The Spanish-American children, with 61 per cent positive reactors, were significantly higher than the American children, with 39 per cent. Table 1 presents the data analyzed according to age, nationality, and school attended. Sensitivity to coccidioidin as revealed by a positive skin test is observed to increase with increase in age for both nationalities and in all schools. It will be noted that School C reveals consistently higher percentages of positive reactors for each nationality than either of Schools A or B, and this difference is significant. The difference between

Schools A and B is not significant and they have been combined.

The data in Table 1 represent both lifetime and non-lifetime residents combined. Since the latter groups include migrants from both endemic and nonendemic areas, the effect of residence in the endemic area of Phoenix can be examined more clearly by analyzing the lifetime residents alone, as is done in Table 2. Lifetime residents are defined as those who have spent all, or all of their lives with the exception of not more than 6 months, in Phoenix. Age and length of residence for this group are, of course, essentially identical. Figure 1 illustrates the increase in percentages of positive reactors that occurs with increasing length of residence in Phoenix, and compares the nationalities and schools. It will be noted that the differences between the nationalities are less and that the curves tend to coincide.

Comparison of lifetime with non-lifetime residents in the same age and resi-

TABLE	1
-------	---

Reactors to Coccidioidin, Grade School Children, Phoenix, Ariz., 1951, by Age, Nationality, and School

	American						Spanish-American				
Ages	Schools	A	В	с	A and B	Totals (ABC)	A	В	с	A and B	Totals (ABC)
5-6	Positive	5	11	27	16	43	0	1	7	1	8
	Tested	17	75	91	92	183	2	4	19	6	25
7 8	Р	20	29	63	49	112	3	5	18	· 8	26
	Т	74	139	141	213	354	8	16	34	24	58
9–10	T P	17	48	69	65	134	6	6	18	12	30
	Т	72	154	140	226	366	8	12	29	20	49
11-12	P T	32	12	93	44	137	6	5	30	11	41
	Т	104	33	140	137	277	14	ž	.40	21	61
13-14	Р	49	_	88	49	137	13	2	55	15	70
	Ť	163	_	123	163	286	28	2	72	30	102
15-16	Р	4		18	4	22	- 8	ó	26	8	34
	Т	21	_	28	21	49	14	ŏ	32	14	34 46
					Per cents	Positive					
5-6		29.	15.	30.	17.	23.			37.		
7-8		27.	21.	45.	23.	32.			53.	33.	
9-10		24.	31.	49.	29.	37.			62.	60.	
11-12		31.	36.	66.	32.	49.			75.	52.	
13-14		30.	'	71.	30.	48.			76.	50.	
15-16		19.		64.	19.	45.			81.	57.	
					Tota	ls					
	Positive	127	100	358	227	585	36	19	154	55	2 0 9
All ages	Tested	451	401	663		1,515	74	41	226	115	341
	% Positive	28.	25.	54.		39.	49.	46.	68.	48.	61.

Coccidioidin Sensitivity

TABLE 2

	Schools		A merica	n	Spanish-American			
Ages		A and B	c	Totals	A and B	c	Totals	
5 - 6	Positive	11	16	27	1	6	7	
	Tested	54	47	101	3	14	17	
7- 8	Р	17	32	49	5	12	17	
	Т	83	80	163	12	23	35	
9–10	Р	29	29	58	8	12	20	
	Ť	87	52	139	15	19	34	
11-12	Р	13	30	43	5	16	21	
	Ť	30	42	72	11	24	35	
13–14	Р	17	27	44	10	28	38	
	Ť	37	35	72	20	38	58	
15-16	· P	2	4	6	3	16	19	
	Т	2 4	6	10	3 8	20	28	
			Per cer	ts Positive				
5-6		20.	34.	26.		43.	41.	
7-8		20.	40.	30.	42.	52.	49.	
9-10		33.	56.	42.	53.	63.	59.	
11-12		43.	71.	60.	45.	66.	60.	
13-14		46.	77.	61.	50.	74.	65.	
15-16				60.		80.	68.	
			Total	s all Ages				
	Positive	89	138	227	32	9 0	122	
All ages	Tested	295	262	557	69	138	207	
-8-5	% Positive	30.	53.	40.	46.	65.	59.	

Reactors to Coccidioidin, Grade School Children, Phoenix, Ariz., 1951, Lifetime Residents, by Age, Nationality, and School

dence groups reveals no significant difference between them, nor does comparison of 5-11 year olds with 11-17year olds of the same length of residence in Phoenix. It is apparent, therefore, that length of residence in the endemic area governs sensitivity to coccidioidin and the increase associated with increase in age is a reflection of this fact.

X-RAY RESULTS

The 70 mm. chest films revealed no cases of active pulmonary disease or cavitation. A dozen children were recommended for larger films and/or 6 month follow-up. All films were read by an experienced radiologist who was unaware at the time of reading which films were those of positive reactors to the skin tests. The 228 negative controls were read, in addition, by another radiologist and by an internist. Only when all three readers agreed on the presence of pulmonary calcification in these films was such calcification tallied. Accordingly, 13 per cent of the positive skin test reactors and 14 per cent of the negative controls presented evidence of pulmonary calcification.

Regarding the skin tests with tuberculin a total of 312, or 17 per cent, were positive reactors. The percentages positive increased with increase in age for both nationalities alike.

DISCUSSION

The gross data in Table 1 show differences between Americans and Spanish-Americans which refinement largely eliminates. Taking into account the smaller numbers of Spanish-Americans leads us to conclude that the differences between the groups are more apparent than real and do not represent a real nationality difference but rather a hidden correlation of exposure.

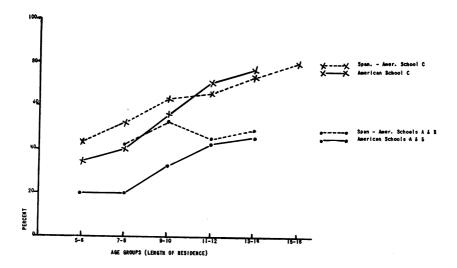


FIGURE 1—Positive Reactors to Coccidioidin. Grade School Children, Lifetime Residents, Phoenix, Ariz., 1951 Comparison by Age, Nationality, and School.

The significantly higher percentages of positive reactors in School C is most reasonably accounted for by the fact that the children attending it live in an unpaved, dustier section of the city. The reduction in the incidence of infection that has been achieved by dust control as reported by Dr. C. E. Smith substantiates this view.

Our data do not inform us as to loss of sensitivity to coccidioidin, although the gross data show a decrease in the oldest age group.

The fact that 14 per cent of the children negative to both coccidioidin and tuberculin presented evidence of pulmonary calcification on the 70 mm. photofluorograph suggests the possibility that the calcification is due to histoplasmosis. Some of these children were migrants from areas where this disease occurs. However, they were not tested for sensitivity to histoplasmin.

SUMMARY

The findings of a survey of 1,869 Caucasian school children between the ages of 5 and 17 in Phoenix, Ariz., skintested with coccidioidin and tuberculin and photofluorographed, are presented. The children showed no significant differences in sensitivity to coccidioidin on the basis of sex or nationality. Sensitivity to coccidioidin was found to increase with length of residence in Phoenix and children living in a dusty area of the city showed higher proportions of positive reactors than those living in less dusty areas.

CONCLUSION

1. Sensitivity to coccidioidin as revealed by skin test among grade school children in Phoenix is directly related to length of residence in the endemic area and is of relatively long duration.

REFERENCES

- Rixford, E., and Gilchrist, T. C. Two Cases of Protozoan (Coccidioidal) Infection of the Skin and Other Organs. *Rep. Johns Hopkins Hosp.* 1:209, 1896.
- Gifford, M. A. Coccidioidomycosis, Kern County. Kern County Health Department Annual Report, 1935-36.
- 3. Dickson, E. C. "Valley Fever" of San Joaquin Valley and Fungus Coccidioides. California & West. Med. 47:151 (Sept.), 1937.
- Smith, C. E. An Epidemiological Study of Acute Coccidioidomycosis with Erythema Nodosum. Proc. Sixth Pac. Sci. Cong. 5:797, 1939.

- Baker, E. E., Mrak, E. M., and Smith, C. E. The Morphology, Taxonomy and Distribution of *Coccidioides Immitis* Rixford and Gilchrist, 1896. *Farlowia* 1:199, 1943.
- Brown, O. H. Coccidioides Infection in Arizona— Allergic Factors in Nodules? Southwestern Med. 23:131 (Apr.), 1939.
- Schenken, J. R., and Palik, E. E. Coccidioidomycosis in States Other than California, with Report of Case in Louisiana. Arch. Path. 34:484 (Sept.), 1942.
- S. Caldwell, G. T. Secondary Granulomatous Coccidioidomycosis—Coccidioidal Granuloma. Texas State J. Med. 38:376 (Oct.), 1942.
- Smith, C. E. Medical Progress. Recent Progress in Pulmonary Mycotic Infections. *California Med.* 67:179 (Sept.), 1947.
- 67:179 (Sept.), 1947.
 10. Goldstein, D. M., and Louie, S. Primary Pulmonary Coccidioidomycosis. Report of Epidemic of 75 Cases. War Med. 4:299 (Sept.), 1943.
- To Cases. War Med. 4:299 (Sept.), 1943.
 Beare, W. K. Primary Pulmonary Coccidioidomycosis. Air Surgeon's Bull. 2:397 (Nov.), 1945.
- 12. Smith, C. E., Beard, R. R., Whiting, E. G., and Rosenberger, H. G. Varieties of Coccidioidal In-

fection in Relation to the Epidemiology and Control of the Diseases. A.J.P.H. 36, 12:1394 (Dec.), 1946.

- Smith, C. E., et al. The Use of Coccidioidin. Am. Rev. Tuberc. 57:330 (Apr.), 1948.
- 14. Aronson, J. D. The Purified Protein Derivative. Am. Rev. Tuberc. 30:727 (Dec.), 1934.

ACKNOWLEDCMENTS—Grateful acknowledgment is made to A. D. Langmuir, M.D., and M. L. Furcolow, M.D., and to R. E. Lewis of the Communicable Disease Center, Public Health Service, for their suggestions and help with the data; to C. E. Smith, M.D., of the University of California, for his gracious supply of antigen; and to G. C. Crecelius, Ph.D., of the Arizona State Department of Health, and Trevor Browne, M.D., school physician, Phoenix public schools, for their enthusiastic aid with the details of the survey.

Postdoctoral Awards in Statistics

The Committee on Statistics of the University of Chicago has established. under a five year grant from the Rockefeller Foundation, a program of postdoctoral awards to provide training and experience in statistics for scholars whose main interests lie outside that field. Three awards of \$4,000 or more will be made annually to holders of a doctorate or equivalent in the biological, the physical, and the social sciences. In addition, office space will be provided and \$600 to \$1,000 made available for clerical and other assistance. There will be no tuition charges.

Applicants must have the doctor's de-

gree except in the case of recognized research workers whose experience and accomplishments are clearly the equivalent. Candidates whose mathematical preparation includes less than the usual sophomore year of calculus will not ordinarily be considered, but previous training in statistics is not required. Preference will be given to candidates having research programs under way.

Further information from Committee on Statistics, University of Chicago, Chicago 37. Applications for the academic year 1952–1953 should arrive by April 1, 1952.