Endemic Coccidioidomycosis in Northern California

An Outbreak in the Capay Valley of Yolo County

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■ ***Endemicity of coccidioidomycosis in Yolo County, outside previously known endemic areas, was confirmed by occurrence of a small epidemic. Eleven cases of clinically apparent coccidioidomycosis occurred among a group of 23 archaeology students. Eight of the cases were confirmed serologically, and three by skin test conversion alone.***

The specific site of exposure was an ancient Indian burial ground on Cache Creek near Brooks in the Capay Valley approximately 40 miles northwest of Sacramento.

SINCE THE FIRST DESCRIPTIONS of coccidioidomycosis 77 years ago, northerly limits of the endemic areas have been identified to lie, in general, in the San Joaquin Valley of California. The northernmost autochthonous cases of coccidioidomycosis have been described near Livermore, California, in the northeastern portion of Alameda County.

Yolo County has been suspected as an area in which additional cases of coccidioidomycosis have been acquired,[1] but the precise location of exposure within Yolo County in those cases recognized here could not exclude with certainty a previous exposure in the known endemic areas. We report herein an epidemic that occurred in the summer of 1968, which confirms the endemicity of Yolo County and pinpoints an area of exposure within the county.

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Description of Epidemic

An archaeology group from the University of California at Davis explored an Indian burial site near Brooks, California, in the period 16 June 1968 through 26 July 1968. On 9 July, a student member of that class was seen with pleuritic pain, fever, malaise and cough, and was found to have middle lobe pneumonia. Coccidioidomycosis was

TABLE 1.—*Clinical Data, Archaeology Class Coccidioidomycosis, Cowell Student Health Center, Summer 1968*

Case	Age	Sex	Onset of Symptoms	X-ray	Coccidioidin Skin Tests 1:100	Coccidioidin Skin Tests 1:10	Serology Date	Precipitins	Complement Fixation
1	21	M	9 July	Pos.	12 July 3mm	18 July 40mm	18 July	Pos.	Negative
							5 Aug.	Neg.	4+1:2,4+1:4,2+1:8,neg. 1:16
2	21	F	12 July	Pos.	15 July Neg.	17 July 15mm	16 July	Neg.	Negative
							Sept.	Neg.	4+1:2,1+1:4,neg. 1:8
3	28	M	12 July	Neg.	17 July 5mm		19 July	Neg.	Negative
							16 Aug.	Neg.	Negative
							27 Sept.	Neg.	4+1:2
4	19	M	22 July	Neg.	17 July Neg.	22 July Neg.	3 Sept.	Neg.	4+1:4,1+1:8,neg. 1:16
5	23	F	28 July	Pos.	17 July Neg.	22 July Neg.	19 July	Neg.	Negative
					6 Aug. 5mm	6 Aug. 10mm	2 Aug.	Neg.	Negative
							7 Aug.	Pos.	Negative
6	20	F	2 Aug. (mild)	Neg.	16 July 10mm		19 July	Neg.	4+1:8,3+1:16,2+1:32
							27 Sept.	Neg.	4+1:2,3+1:4,2+1:8,neg. 1:16
7	21	F	1-5 July	Neg.	17 July Neg.		16 July	Neg.	Negative
					24 July 25mm		5 Oct.	Neg.	4+1:2,1+1:4,neg. 1:8
8	22	F	30 Aug.	Neg.	9 Oct. 15mm		8 Oct.		Anticomplementary, positive by immuno diffusion
9	20	F	20 Aug.	Neg.	17 July Neg.	22 July 4mm	30 July	Neg.	Negative
					23 Aug. 15mm		Aug.	Neg.	Negative
10	19	M	5 July	Neg.	17 July Neg.		17 July	Neg.	Negative
					18 Oct. 10mm		18 Oct.	Neg.	Negative
11	21	F	None	Neg.	17 July Neg.	19 July Neg.	19 July	Neg.	Anticomplementary
					5 Aug. 18mm		5 Sept.	Neg.	Negative
12	20	M	1 Aug.	Neg.	17 July Neg.	22 July Neg.	19 July	Neg.	Negative
					5 Aug. 18mm		2 Aug.	Neg.	Negative
13	21	F	None	Neg.	15 July 15mm		19 July	Neg.	Negative
							20 Aug.	Neg.	Negative
14	21	F	None	Neg.	19 July 15mm		19 July	Neg.	Negative
							4 Sept.	Neg.	Negative
15	21	M	None	Neg.	17 July 13mm		19 July	Neg.	Negative
							30 Aug.	Neg.	Negative
16	20	M	None	Neg.	17 July Neg.		19 July	Neg.	Anticomplementary
17	59	M	None	Neg.	16 July Neg.	22 July Neg.	16 July	Neg.	Negative
					28 Aug. Neg.		Sept.	Neg.	Negative
18	29	M	None	Neg.	18 July 14mm		17 July	Neg.	Negative
19	18	F	None	Neg.	17 July Neg.	22 July Neg.	22 July	Neg.	Negative
							Sept.	Neg.	Negative
20	21	F	None	Neg.	12 July Neg.	22 July Neg.			
21	19	M	None	Neg.	17 July Neg.	22 July Neg.	contaminated		Anticomplementary
22	26	F	None	Neg.	17 July Neg.	22 July Neg.	17 July	Neg.	Negative
					8 Oct. Equiv.		7 Oct.	Neg.	Negative
23		M							

suspected on the basis of clinical manifestations and positive skin test response to 1:10 coccidioidin. The entire archaeology group was then tested, first with 1:100 dilution coccidioidin; and those who did not react to 1:100 were retested with the 1:10 dilution. Surveillance was continued for the duration of the archaeology course and, where possible, continued by mail with cooperating physicians thereafter.

Results of the initial survey and follow-up are recorded in Table 1. There were eight reactors to coccidioidin at the outset; four were symptomatic, and they later had positive serologic response for coccidioidomycosis (Cases 1, 2, 3 and 6, Table 1).

Four of the original reactors remained asymptomatic and serologically negative (Cases 13, 14, 15 and 18) and one student (Case 23) refused to be tested because he had lived in the San Joaquin Valley and stated he had had a previous infection. These latter five were considered not at risk.

Three persons were negative to 1:100 coccidioidin at the outset but did not return for the 1:10 test. Of these, one (Case 16) remained well throughout the observation period. One (Case 7) developed clinical disease, skin test conversion and seroconversion; and one (Case 10) later had skin test conversion and signs suggestive of disease.

Ten subjects were originally skin test negative to both 1:100 and 1:10 dilution of coccidioidin. Of these, two later developed clinical disease and

converted serologically (Cases 4 and 5); three developed strongly positive skin tests without demonstrated sero-conversion (Cases 9, 11, 12). The remaining five patients (Cases 17, 19, 20, 21, 22) showed no evidence of clinical or subclinical coccidioidomycosis.

An interesting additional case occurred in a student (Case 8) who visited the site and worked for one day, on 30 August 1968. She developed an illness in mid-September consisting of cough, pleuritic chest pain, chills and low grade fever. She recovered from the illness in about two weeks, then became aware of coccidioidomycosis through a friend and sought medical advice at the Student Health Service. A skin test carried out on 8 October was strongly positive and a single specimen of serum obtained on 8 October was found to have coccidioidal antibodies.

Soil samples were obtained from the surface and to a depth of four inches at the excavation site, but at this writing have not yielded *C. immitis* either in cultures or animals inoculated directly.

Reports of Cases

Case 1 (Table 1). A 21-year-old Caucasian man was first seen at the Student Health Center 9 July 1968 with a two-day history of cough, pleuritic pain in the right anterior region of the chest, fever, chills and malaise. He had had heavy exposure to dust in the above described archaeological effort since 19 June. An x-ray film showed segmental right middle lobe pneumonia. A skin test with 1:100 coccidioidin was read at 48 hours as equivocal (4 to 5 mm induration and very faint erythema). The patient's symptoms lessened decidedly by 11 July, but a repeat skin test with 1:10 coccidioidin resulted in a reaction 40 mm x 25 mm. On 18 July precipitins were detectable. On 5 August a serum specimen showed fixation of complement (4+ at 1:4 dilution) although precipitins had faded. The patient recovered uneventfully and by November 1968 was asymptomatic and an x-ray film showed the chest had cleared completely.

Case 2 (Table 1). A 21-year-old Caucasian woman was seen on 16 July with pleuritic pain of five days' duration which had been preceded by a sore throat occurring about one week earlier. Skin test (1:100 coccidioidin) was negative at this time but an x-ray film showed pneumonia in the superior segment of the left lower lobe and she was admitted to the hospital. A repeat coccidioidin skin test with a 1:10 dilution on 17 July was positive with 14 mm x 15 mm of induration. This patient had a previous history of acute glomerulonephritis and with the current illness albuminuria and hematuria developed. These conditions cleared completely by 13 August 1968. Antistreptolysin 0 titer remained negative (less than 50 Todd units). Coccidioidal serology on 16 July was negative but when retested in early September a specimen of serum fixed complement (4+ at 1:4 dilution by overnight complement binding). At present there is a residual radiographic density in the area of the previous pneumonitis, although the patient is in good health and under the care of her personal physician.

Case 5 (Table 1). A 20-year-old Caucasian woman was found to be skin test negative at the original survey, had a clear x-ray film of the chest, and on 19 July coccidioidal serology was negative. The patient finished her course of study on 26 July and went to the Sierra Nevada Mountains where her husband was employed for the summer. She had been provided with information about coccidioidomycosis and a letter of instruction to give to her physician in case of illness. She was asked to have serologic and skin tests repeated in August in any case. On 28 July pleuritic pain developed on the right side. She was seen by a physician in Jackson, California, where a "spot" was noted on an x-ray film of the chest. Penicillin was given but chills, cough, fever and more severe pleuritic pain and erythema nodosum developed. The patient returned to her home near Sacramento, California, and was seen there by her personal physician, who made a tentative diagnosis of coccidioidomycosis. Because it was felt necessary that she be isolated (incorrectly, in our opinion), and no private isolation room was available, she returned to the Student Health Center and was admitted on 5 August after an roentgenogram of the chest showed consolidation of the superior segment of the right lower lobe. Coccidioidin skin test (1:100 dilution) produced 5 mm of induration and erythema, while the 1:10 dilution yielded a 10 mm reaction. On 7 August precipitins were detected in the serum. Erythema nodosum present during the acute phase subsided after one week and the patient was released to the care of her personal physician. We have no follow-up to date.

Case 10 (Table 1). A 19-year-old Caucasian male student when originally skin tested on 16 July 1968 had no reaction to 1:100 coccidioidin.

TABLE 2.—*Average Monthly and Seasonal Precipitation 1967-1968 at Various Stations in Yolo County**

Station	*July*	*Aug.*	*Sept.*	*Oct.*	*Nov.*	*Dec.*	*Jan.*	*Feb.*	*Mar.*	*Apr.*	*May*	*June*	*Season*
Brooks	.01	.02	.19	.96	1.75	4.17	4.06	4.10	2.63	1.31	.60	.20	20.00
Clarksburg	.01	.01	.21	1.10	1.57	2.95	3.45	3.44	2.39	1.61	.53	.09	17.36
Davis	..	.01	.17	.76	1.37	3.41	3.29	3.25	2.14	.36	.57	.13	16.46
Dunnigan	..	.01	.26	1.17	1.55	3.34	3.13	3.11	2.12	.39	.55	.16	16.79
Guinda	.01	.03	.53	.79	1.82	3.23	6.42	3.72	3.25	.97	.59	.13	21.49
Knights Landing	..	.03	.17	.78	1.46	3.35	2.99	2.92	2.22	1.42	.54	.22	16.10

*U.S. Soil Conservation Office, Woodland, Calif.

TABLE 3.—*Suspected Autochthonous Coccidioidomycosis —A Review of Recorded Diagnosis of Four Yolo County Hospitals, 1958-1968*

Age	*Sex*	*Possible Origin of Infection*
45	M	Rumsey
50	F	Dixon or Winters
37	M	Davis
64	F	Winters
22	M	Davis
35	M	Dixon
61	M	Guinda

He was retested on 18 October with 1:100 coccidioidin and showed a 15 mm reaction. In the interim he had had a chronic rash lasting about one month (presumed to be caused by poison oak) which had been treated with steroids, but had subsequently become asymptomatic. Coccidioidal serologic tests remained negative through 18 October 1968.

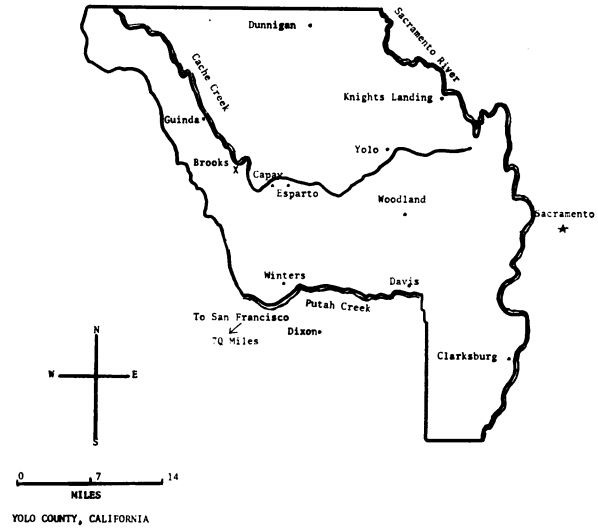

Figure 1.—Map of Yolo County with the approximate site of exposure (X) at Cache Creek near Brooks.

Characteristics of the Endemic Region

Known endemic areas,[2] like those of Maddy's Lower Sonoran Life Zone,[3] are characterized by scant rainfall, hot dry summers, alkaline soil, mild winters and sparse flora. The Capay Valley of Yolo County (Figure 1) in Northern California, and the specific site near Brooks, California, have these general characteristics although the soil is neutral, of physical class 2S-3, a 3 percent clay loam.[4] The elevation above sea level of the site is approximately 300 feet. Rainfall in this area is moderate, occurring mostly in winter and spring (Table 2). The general climatic and terrain conditions of this area exist in the foothills of the central Sacramento Valley as far north as Red Bluff, California. Reference to the "Life-zone" map of Grinnell[5] indicates that the Capay Valley lies outside (west of) the Lower Sonoran Life Zone.

The excavation site lay on either side of a dirt road which parallels Cache Creek in its course through a small meadow. The flat meadow is irrigated and farmed, the irrigation ditch running beside the road.

Discussion

The archaeological group described above concentrated its work during the academic Summer Session only at the above-described diggings, and there is little doubt that the reported cases of coccidioidomycosis were acquired at that site. With this demonstration, Yolo County can be added to the known endemic areas for coccidioidomycosis. The nearest previously demonstrated endemic area is the Livermore Valley, approximately 80 miles to the south. Several isolated cases of coccidioidomycosis in humans have been reported in Yolo County in the past. A ten-year review of coccidioidomycosis cases in four hospitals in Yolo County (1958-1968) reveals a number of cases which may have been autochthonous (Table 3). Heretofore, it has not been possible, however, to exclude the possibility that these infections resulted from visiting known endemic areas,

or from fomite transfer. For example, Pulford and Larson[1] described a fatal case of coccidioidomycosis in a male resident of Woodland. The apparent onset of his illness was in November 1926, although he had been to the San Joaquin Valley (Modesto) on three occasions in August 1926. An additional local case of coccidioidomycosis was recently proved in a simian subject kept out of doors in the Davis area for the past three to four years.[6]

The occupational considerations in this episode are noteworthy. Archaeology is one of the vocations which commonly involve exposure to dust. Other examples of such vocations are construction, surveying, agriculture, oil drilling, anthropology. In the present case soil was removed from the study site and screened in a rocker-type screen, which in dry conditions exposes the operators and those nearby to large amounts of dust. Outbreaks have occurred among archaeological and anthropological groups in endemic areas of California several times in recent years.[7,8,9]

Among those measures which should be helpful in controlling exposures are the following: skin testing of persons who are to work in endemic areas; dust control measures; careful medical follow-up of exposed individuals; educational programs aimed at those in high risk occupational groups as well as those professional or managerial people dealing with such groups. While no specific measure can be recommended it should be helpful to attempt to minimize exposure to dust.[10]

The increasing use of heavy equipment in construction and agriculture that exposes operators to dust, and increasing archaeological and anthropological interest in the North American Indian are likely to lead to other exposures and possibly to documentation of additional areas of endemicity. Awareness of this possibility by physicians should be helpful in early discovery of new cases, and their proper management.

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DRUG COMPLICATIONS OF ANEMIA IN PREGNANCY

"Anemia is a common factor — in fact, it's an occupational hazard — of the multigravida, especially in indigent populations. Iron deficiency and megaloblastic anemias do not respond as well, and in fact sometimes will not respond at all, to therapy when chloramphenicol (trade named Chloromycetin) has been used as a drug for treatment of infection. It is also thought, but not as clearly demonstrated in the literature, that tetracycline will do the same; and both of these drugs do inhibit protein synthesis."

—WILLIAM A. LITTLE, M.D., Miami

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