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Tempest From Tehachapi Takes Toll or Coccidioides Conveyed Aloft and Afar

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New cases of acute primary coccidioidomycosis in large numbers resulted from a windstorm that blew through Kern County, California, on December 20, 1977. In most of these cases clinically apparent infections developed in early and mid-January 1978 and occurred not only in persons exposed directly to the dust raised by the windstorm but also among those in many areas to the north and west of Kern County. The exposure to the dustborne Coccidioides immitis was brief because of the arrival of drenching rains, but the continued heavy rainfall increased the potential for large numbers of cases of coccidioidomycosis to occur in the summer-fall season.

TO THE EXPORTS from Bakersfield, California, and environs—oil, livestock, cotton, potatoes, grapes, Merle Haggard, Buck Owens—can be added one of dubious value, coccidioidomycosis. During the first five months of 1978 a remarkable number of new cases of acute primary coccidioidomycosis were recognized in California. These resulted from the dust storm that blew through Kern County on December 20, 1977, depositing tremendous amounts of soil and arthrospores of Coccidioides immitis to the north and west of this southern-most county of the San Joaquin Valley. The heavy deposit of windblown dirt in Kern County was phenomenal. One resident described the deposition of dirt in her swimming pool as resembling "the result of a Fleet's enema." These winds in Kern County provided fallout of soil in the northern and coastal areas of San Francisco, Marin County, Sacramento, the east bay, and Santa Clara and Monterey counties, cities in the northern Sacramento Valley, and as far north as Oregon.

The northern areas were not directly affected by the ground level windstorm that had struck Kern county but the dust was lifted to several thousand feet elevation and, borne on high currents, the soil and arthrospores along with some moisture were gently deposited on sidewalks and automobiles as "a mud storm" that vexed the residents of much of California. The dust storm climaxed a year of drought in California that interestingly, besides its desiccation of the state, had also been accompanied by the lowest number (375) of reported cases of coccidioidomycosis in recent years.

The first illnesses of the new outbreak became apparent in late December. January 1, 1978, was the date on which symptoms that were serologically confirmed—in our laboratory at University of California, Davis (UCD)—developed in the maximum number of cases (22); this was 12 days after the dust storm. In the ensuing days there was a sustained incidence of new cases, for example, 18 cases on January 5 and 17 cases on January 10—16 and 21 days, respectively, after the dust

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storm. After this the number of new cases began to fall off to 1 or 2 cases per day to yield a total of 216 cases (10 with onset of symptoms in December) through the end of January. Most of these detected at UCD were drawn from nonendemic areas of Northern California.

In Kern County 98 new cases were detected in January 1978 and 36 in February, compared with 3 and 14 cases, respectively, for these months in 1977. New cases had fallen off by March, eight being recorded compared with five in March 1977.

Cases of coccidioidomycosis with onset of symptoms in January but with belated diagnosis were still being diagnosed serologically or by culture late into May.* By the end of the first 12 weeks of 1978, a total of 379 new cases of coccidioidomycosis resulting from the dust storm were confirmed serologically at UCD, most from nonendemic areas of Northern California, and 142 were noted in Kern County. At this time, 359 new cases had been reported to the California State Department of Health (CSDH). These figures can be compared with the totals reported to the CSDH for the years 1977 (375), 1976 (500), 1975 (442) and 1974 (526). By the end of May the number (greater than 532) reported had exceeded those in any previously reported entire year in California.

Because of imperfect reporting to the County or State Health Departments, the tallies will be incomplete. At UCD we have detected 116 dust storm-related infections in Sacramento, 15 in Salinas and 51 in Stockton, but we realize that these and the 7 from San Francisco and 10 in Oakland represent incomplete figures.

The fiscal impact of coccidioidomycosis can only be crudely and incompletely estimated. Based on two studies[1,3] an *average* hospital stay for each case of coccidioidomycosis was placed at 35 days. Assuming $100 per day for hospital room costs, the 521 new cases recognized through UCD and in Kern county during the first three months of the year would have accounted for expenses of $1,823,500 for room costs alone. The seasonal recurrence of coccidioidomycosis in the southwestern United States (more than 500 cases per year are reported in Arizona) requires, therefore, a continuing substantial medical expenditure.

Additional cases in other species (canines and nonhuman primates) resulting from the dust storm were recognized in customarily nonendemic areas (for example, a gorilla in the San Francisco Zoo died from the effect of infection and attempted therapy).

The question whether the deposition of arthrospores by the dust storm in nonendemic sites, in northern and coastal areas, will have established new endemic foci will be answered by findings in the summer coccidioidal season or seasons. Inasmuch as small foci of endemicity in inland Northern California have been recognized,[17] it is conceivable that these regions could become more broadly endemic. Whether the regular agricultural tillage and cultivation of these areas and the particular circumstances of weather (rainfall is normally much heavier in the Sacramento Valley than in the recognized coccidioidal areas of the San Joaquin Valley), enhance a competitive microflora of the soil that may inhibit proliferation of C. immitis remains to be seen. It is not likely that Marin County, San Francisco, Oakland, Salinas and Monterey will provide hospitable circumstances for C. immitis to grow and persist. The near coastal area of Pacific Beach (San Diego County) did provide a source of coccidioidal infection[7] but the more northern coastal areas probably provide sufficiently different weather and soil to avert permanent establishment of C. immitis. (While Pacific Beach appeared to be the closest to a contemporary marine environment harboring C. immitis, recently a sea otter infected with C. immitis was found at Morro Bay, San Luis Obispo County [Kent Osborn—personal communication]; and the Swateks[16] have reported on the growth of C immitis in a medium containing sea water.)

The confinement of onset of new cases essentially to the end of December and the month of January was a fortunate result of the advent of the drought-ending rains. In Northern California this occurred on December 21 in the San Francisco Bay Area. In Sacramento, there were 0.45 inches of rain on December 21 and 1.10 inches on December 22. Usually such rains arrive in November or early December to end the annual increase in cases of coccidioidomycosis occurring in California during the late summer and fall. The latter was depicted clearly by Smith in his studies of Valley Fever in the 1930's and during World War II.[10,11] Small numbers of cases of acute coccidioidomycosis are encountered throughout the year both in California[10,11] and

*Sharon Beall, Sue Lindsey and Mary Toulson of UCD, and Jack Leonard of Kern County shared the burden of the tremendous increase in serologic testing.

in Arizona.[1,9] Interestingly, Arizona which has (in its coccidioidal endemic areas) less rainfall than California, has a short period of decreased cases of coccidioidomycosis in humans immediately following the summer rain showers, but seems to lack the pronounced diminution of cases during the winter months that characterizes California. Canine coccidioidomycosis is increased in Arizona during the winter months[8] possibly as a result of increased digging in soil by dogs during the cooler months of the year.

The immediate consequence of the rain following the dust storm was the salutary cessation of infections, but the abundant rainfall through the winter may set the stage for an additional substantial increase in cases during the customary summer and fall endemic season. This is based on the observations of Smith and co-workers[11] that following a heavy winter's rainfall a proportionate increase in cases of coccidioidomycosis can be expected in the summer-fall season. Physicians should be alert to this when encountering febrile respiratory illnesses.

With respect to diagnosis, many of the dust storm-related cases of coccidioidomycosis conformed to the expected clinical features: fever, pleuritic chest pain, malaise, myalgia and arthralgia. Erythema nodosum was observed in many patients. The resemblance of coccidioidomycosis to other febrile respiratory illnesses led to a delay in diagnosis of several cases in which there was persistence of malaise and low grade fever for four months or more. However, once again the unusual characterized some of the cases of coccidioidomycosis beclouding the diagnosis. This was the case, for example, in a woman in Sacramento in whom in the early stages of disease (in January) tenderness in the neck developed, the result of suppurative coccidioidal thyroiditis.

Recognizable extrapulmonary spread (dissemination) occurred relatively early after onset of the primary infections. Therefore, of the 379 dust storm-related primary infections recognized through our UCD studies during the first 12 weeks of 1978, in 16 (4.2 percent) recognizable dissemination developed. In 9 of these 16 (2.4 percent of the primary infections) meningitis developed. Most disseminations occurred in one to two months, fewer at two to three months, one at four months after onset of illness. Some few additional disseminations can be anticipated later. Some fatalities were associated with these coccidioidal infections, including four deaths from meningitis, two in Kern County; however, the precise numbers are not yet available. There was an apparent difference in age of patients infected during the dust storm in Kern County and those infected from the fallout north of Kern County in that the latter were virtually all adults whereas a large proportion of Kern County patients were under 12 years of age. The latter group released from school during the great turbulence apparently spent more time out of doors than the adults of Kern County who ensconced themselves indoors during the dust storm. Furthermore, a sizable proportion of adults of Kern County have already had their coccidioidal contact. (It is possible that pediatricians in northern California did not pursue the serologic or culture diagnosis of coccidioidomycosis as vigorously as did the physicians with adult patients.) The proportion of asymptomatic infections has not and probably could not now be determined in view of the lack of baseline studies. T. Larwood and co-workers, however, carried out skin tests in school children in Kern County four months after the dust storm and found a decrease in coccidioidin reactivity from that which they had previously determined in 1964 (T. Larwood—personal communication).

In a few instances biopsy studies yielded the diagnosis promptly by histopathologic means. In most of the other cases, serologic confirmation supported the diagnosis. The serologic studies showed once again the usefulness, indeed the necessity, of testing for the early precipitin type antibody.[13] This antibody precedes development of the complement fixing (CF) antibody by several days to weeks and may provide the only clue to early, primary acute coccidioidomycosis. This early antibody can be detected by the original tube precipitin text (used by very few laboratories), by the commercial coccidioidal latex particle agglutination, or by agar gel immunodiffusion provided the serum has been concentrated to enhance detection of the precipitins. Nevertheless, the CF test should also be carried out because the precipitins are relatively transient, and particularly if the diagnosis is delayed. While *conversion* of the skin test reactivity to coccidioidin or spherulin may itself be an early clue, a positive skin test finding per se can only suggest further diagnostic studies.

The problem of appropriate and effective therapy is still with us. Treatment of primary acute

coccidioidomycosis with the hope of forestalling dissemination has not been evaluated. The toxicity of and difficulty in administering amphotericin B has usually prompted reserving it for frankly disseminated cases or those with serious threat of dissemination. However, in these cases it remains the agent of first choice. Miconazole, the effectiveness of which is unequivocal only in some cases, also is difficult to administer.[15] The water soluble methyl ester of amphotericin B while apparently less toxic than the parent polyene[2] must also be given intravenously and its efficacy in man has not yet been fully assessed. The advent of two compounds—ketoconazole, an imidazole (Janssen Pharmaceuticals), and ambruticin (Warner-Lambert)[5]—that are effective when given by mouth in murine coccidioidomycosis gives some hope that perhaps humans may be treated early, before coccidioidal infections have disseminated. It should be recalled, however, that even amphotericin B was effective when given by mouth in mice infected with C. immitis,[14] so much work remains to determine if these newer compounds will be effective when given by mouth in man.

However, what remains a challenge is the cases of coccidioidomycosis that disseminate without an obvious or typical primary acute coccidioidal infection. Prevention of coccidioidomycosis through immunization offers promise.[4,6]

The challenge of all forms of coccidioidomycosis continues with an anticipated greater problem than usual confronting us with the advent of the 1978 summer and fall months. Such awareness must extend to physicians outside the endemic areas of the southwest as even those transiently present in these areas may return to other states and countries in which coccidioidomycosis is not the familiar word that it is in California.

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