the importance of subtype specificity in the bactericidal response to meningococcal colonization.

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References

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Coccidioides immitis Antigen

To the Editor—The article by Peng et al. [1] provides evidence that an antigen of Coccidioides immitis referred to as the proline-rich antigen is shared by genetically and geographically diverse isolates.

Prior studies have demonstrated phenotypic differences among isolates of C. immitis, including differences in virulence for laboratory mice [2]. However, no clinically significant differences in serologic or skin-test antigenic reactivity were recognized among different isolates [2].

Recent genetic studies utilizing single-strand conformational polymorphism analysis have also demonstrated genetic diversity among isolates (strains), including differences associated with geographic origin [3, 4]. This led the authors to speculate that such diverse strains account for the varied clinical presentations of coccidioidomycosis and may be important in the development of (protective) vaccine coverage and effective antifungal therapy against coccidioidomycosis acquired in different geographic loci. However, both clinical and epidemiologic information and experimental vaccine studies already completed provide no support for such speculation. The broad clinical spectrum and response to antifungal agents is similar in patients in California, Arizona, and elsewhere. The clinical and epidemiologic information strongly indicate that infection of humans by 1 strain of C. immitis followed by clinical recovery provides durable immunity against different (geographic) strains of C. immitis. Thus, among 7000 cases of primary coccidioidomycosis proved serologically (and in some cases by culture), acquired in several states, including Arizona and California, no instance of a second primary infection was detected among those infections acquired in nature [2]. The number of such cases serologically and culturally confirmed has now exceeded 20,000 such patients in our own experience since 1967, a fraction of the total detected in the United States. The rarity of second primary (reinfection) is illustrated in table 1. Only 4 persons with evidence of a prior coccidioidal infection have had a documented second primary coccidioidal infection, three of which were laboratory-acquired (cited in [5]). The fourth patient had had a confirmed primary coccidioidal infection in Arizona in 1963. Several years later, he developed chronic lymphocytic leukemia, and 30 years after his initial coccidioidal infection, he developed, while still in Arizona, what was clinically and serologically a new primary coccidioidal infection [6].

This paucity of second primary infections among the thousands of new cases in Arizona, Texas, and California despite peregrinating populations provides evidence that infection with a single strain, regardless of geographic or genetic derivation, protects humans against infection with different strains.

Experimental studies have confirmed that a single strain of C. immitis, as a living or killed vaccine, provides protection against respiratory challenge with a phenotypically or genotypically different C. immitis. Strain Silveira, isolated in 1951 from a human in the San Joaquin Valley, California, is virulent for mice by intraperitoneal or respiratory intranasal challenge. Strain 46 was isolated from a human in California. Its morphology differs from that of strain Silveira, and it is relatively avirulent for mice by the intraperitoneal route but virulent by the intranasal route [7]. Zimmermann et al. [8] demonstrated that DNA from strain Silveira (and 1 other California isolate, K-727) yielded a restriction fragment length polymorphism

| Table 1. Exogenous reinfection coccidioidomycosis—rarity of occurrence in humans in 60 years (1938–1998). |
|--------------------------------------------------------|------------------|------------------|------------------|------------------|
| Acquisition, case no. | History | Route of second infection | References |
| Lab-acquired |
| 1 | + skin test | Respiratory | Smith et al., 1957, 1961a |
| 2 | + skin test | Injection, osteomyelitis | Overholt, Hornick, 1964a |
| 3 | + skin test | Injection | Sorensen, Cheu, 1964a |
| Acquired in nature |
| 4 | Biopsy-proven 30 years earlier, (+) skin and serologic tests, then chronic lymphocytic leukemia | Respiratory | [6] |

NOTE. +, positive.

a Cited in [5].
(RFLP) pattern different from that of 13 other isolates (including strain 46) from various geographic sites, including Venezuela, South America. Also, by a different method, single-strand conformational polymorphism analysis, strains Silveira and K-727 were shown to be different from several other California isolates and more akin to Arizona isolates ([3], Fisher M, personal communication).

Immunization with viable arthroconidia of strain 46 administered intranasally or intraperitoneally resulted in marked reduction in mortality of mice challenged intranasally with strain Silveira [7]. Vaccination with killed spherules of strain Silveira or those of an isolate from soil designated as Woodville protected against lethal intranasal challenge with strain 46 and against challenge with homologous Silveira or Woodville [9]. Killed spherules of strain Silveira protected against intranasal challenge with strain 46, strain Woodville, and 5 other phenotypically atypical strains of *C. immitis* [10]. Three auxotrophic avirulent mutants (1 of which was identical to strain 46 by RFLP [8]) protected against intranasal challenge with the virulent parental strain [11].

Therefore, the available information indicates that immunoprotective vaccines from a single strain of *C. immitis*, for example, Silveira [7, 9, 10], would provide protection against genetically and geographically diverse strains. The report of Peng et al. provides evidence of the universality of at least one antigen with potential immunoprotective properties among isolates of *C. immitis*.

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