the importance of subtype specificity in the bactericidal re-
ter action to meningococcal colonization.

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Coccioides immitis Antigen

To the Editor—The article by Peng et al. [1] provides evidence
that an antigen of Coccioides immitis referred to as the pro-
line-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 dif-
fences in serologic or skin-test antigenic reactivity were rec-
ognized among different isolates [2].

Recent genetic studies utilizing single-strand conformational
polymorphism analysis have also demonstrated genetic diver-
sity 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 pres-
etations of coccidioidomycosis and may be important in the
development of (protective) vaccine coverage and effective an-
tifungal therapy against coccidioidomycosis acquired in differ-
ent geographic loci. However, both clinical and epidemiologic
information and experimental vaccine studies already com-
pleted provide no support for such speculation. The broad clin-
cal 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 coc-
cidioidomycosis proved serologically (and in some cases by cul-
ture), acquired in several states, including Arizona and Cali-
ifornia, 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 ex-
ceeded 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 de-
spite peregrinating populations provides evidence that infection
with a single strain, regardless of geographic or genetic deri-
vation, 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 geno-
typically 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 mor-
phology 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).

<table>
<thead>
<tr>
<th>Acquisition, case no.</th>
<th>History</th>
<th>Route of second infection</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lab-acquired</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>+ skin test</td>
<td>Respiratory</td>
<td>Smith et al., 1957, 1961a</td>
</tr>
<tr>
<td>2</td>
<td>+ skin test</td>
<td>Injection, osteomyelitis</td>
<td>Overholt, Hornick, 1964a</td>
</tr>
<tr>
<td>3</td>
<td>+ skin test</td>
<td>Injection</td>
<td>Sorensen, Cheu, 1964a</td>
</tr>
<tr>
<td>Acquired in nature</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Biopsy-proven 30 years earlier, (+) skin and serologic tests, then chronic lymphocytic leukemia</td>
<td>Respiratory</td>
<td>[6]</td>
</tr>
</tbody>
</table>

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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