Immunoglobulin E Anti-\textit{Candida} Antibodies and Candidiasis$\dagger$

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Elevated levels of immunoglobulin E anti-\textit{Candida} antibodies were observed in the sera of patients with systemic and vaginal candidiasis and in cervicovaginal washings of the latter.

Since the discovery (4) and characterization (1, 2, 9) of immunoglobulin E (IgE), it has rapidly emerged as a significant reaginic antibody in patients with atopic diseases (8) such as asthma, hay fever (7), and atopic dermatitis (11). Parasitic infections by \textit{Ascaris lumbricoides} (10) and \textit{Toxocara canis} (3) are also associated with elevated serum IgE levels, as are chronic dermatological disorders (46). Since elevated IgE levels are usually found in mucosal secretions such as nasal secretions (5) and colostrum (2), the significance of IgE antibodies in mucosal infections is apparent. In the present study, levels of IgE were quantitated in the sera of seven patients with systemic candidiasis and 17 with vaginal candidiasis. Cervicovaginal washings of three patients with vaginal candidiasis were also studied. Levels of IgE anti-\textit{Candida} antibodies were evaluated by absorption of the sera and cervicovaginal washings with blastospores and germ tubes of \textit{Candida albicans}.

Sera were obtained from normals and from patients at the Medical University of South Carolina. Antibody titers to \textit{C. albicans} were evaluated by using passive hemagglutination and indirect fluorescent-antibody techniques described elsewhere (12). IgE levels were quantitated with Phadebas IgE radioimmunoassay kits (Pharmacia, Uppsala, Sweden).

Sera and cervicovaginal washings were carefully absorbed with an excess of lyophilized \textit{C. albicans} blastospores and germ tubes obtained from a 48-h culture in yeast nitrogen base (Difco, Detroit, Mich.) supplemented with 30% glucose. The extent of absorption was checked by passive hemagglutination and indirect fluorescent-antibody techniques. Differences in IgE levels between absorbed and unabsorbed sera gave a quantitative estimate of IgE anti-\textit{Candida} antibodies.

The normal levels of IgE in the sera of healthy controls, as reported in the assay kit, vary between 25 and 150 IU/ml. In the three normals studied, the arithmetic mean was 48.0 IU/ml (Table 1). The sera of systemic candidiasis patients, however, contained high levels of IgE (arithmetic mean, 1,941 IU/ml), about 82% of which were shown to be anti-\textit{Candida} antibodies. High titers of IgG and IgA anti-\textit{Candida} antibodies were also evident. Two of the patients with systemic candidiasis were deficient in serum IgA. These had significantly lower anti-\textit{Candida} antibody titers than the others with systemic candidiasis.

The sera as well as cervicovaginal washings of vaginal candidiasis patients (Table 1) also had high levels of IgE antibodies (arithmetic means, 745 and 1,467 IU/ml, respectively), 50 to 74% of which were anti-\textit{Candida} antibodies. Among these patients, three (J. Q., C. M., and R. S.) with long-standing and severe infection had IgG as well as IgM anti-\textit{Candida} antibodies, although IgA antibodies predominated. J. Q. and R. S. had low IgE levels as compared with the other vaginal candidiasis patients. We have arbitrarily termed this group as “intermediates” between the systemics and the vaginals. The other chronic vaginal candidiasis patients had predominantly elevated IgA antibody titers, along with elevated IgE anti-\textit{Candida} antibodies.

The finding of elevated levels of IgE in patients with various degrees of infection by \textit{C. albicans} and the finding that a large percentage of these antibodies are \textit{Candida} specific provide strong evidence for the involvement of IgE in mucosal infections, especially by fungi. Of special interest are the results for patients with systemic infections, showing significantly lower levels of IgE anti-\textit{Candida} antibodies in those who are IgA deficient than in those with normal immunoglobulin levels. That IgA-deficient people have a lower capacity to produce antibodies to \textit{C. albicans} (13) and lower IgE levels (2, 17) is already known.

The absorption of anti-\textit{Candida} antibodies from sera with \textit{C. albicans} was double-checked

\footnote{$\dagger$ Publication no. 139 from the Department of Basic and Clinical Immunology and Microbiology, Medical University of South Carolina.}
### TABLE 1. *IgE, IgG, IgA, and IgM anti-Candida antibodies in the sera of systemic and vaginal candidiasis patients*

<table>
<thead>
<tr>
<th>Patients</th>
<th>Passive hemagglutination antibody titer</th>
<th>Fluorescence titer (anti-Candida antibodies)</th>
<th>IgE levels</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Whole</td>
<td>Ab-</td>
<td>IgG</td>
</tr>
<tr>
<td>With systemic candidiasis IgA deficient</td>
<td></td>
<td>sorbed</td>
<td></td>
</tr>
<tr>
<td>K. L.</td>
<td>64</td>
<td>0</td>
<td>64</td>
</tr>
<tr>
<td>B. A.</td>
<td>32</td>
<td>0</td>
<td>64</td>
</tr>
<tr>
<td>With normal immunoglobulin levels</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>G. A.</td>
<td>128</td>
<td>0</td>
<td>256</td>
</tr>
<tr>
<td>B. R.</td>
<td>256</td>
<td>0</td>
<td>64</td>
</tr>
<tr>
<td>F. S.</td>
<td>256</td>
<td>0</td>
<td>64</td>
</tr>
<tr>
<td>M. D.</td>
<td>256</td>
<td>0</td>
<td>32</td>
</tr>
<tr>
<td>D. L. (child)</td>
<td>64</td>
<td>0</td>
<td>64</td>
</tr>
<tr>
<td>Mean ± SE</td>
<td>151</td>
<td>0</td>
<td>±29</td>
</tr>
<tr>
<td>Normal controls</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B. F.</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>E. O.</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>C. P.</td>
<td>16</td>
<td>0</td>
<td>16</td>
</tr>
<tr>
<td>Mean ± SE</td>
<td>7</td>
<td>±5</td>
<td>±5</td>
</tr>
<tr>
<td>With vaginal candidiasis Intermediates</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>J. Q. (1)</td>
<td>128</td>
<td>0</td>
<td>128</td>
</tr>
<tr>
<td>J. Q. (2)</td>
<td>128</td>
<td>0</td>
<td>128</td>
</tr>
<tr>
<td>C. M.</td>
<td>256</td>
<td>0</td>
<td>256</td>
</tr>
<tr>
<td>R. S.</td>
<td>64</td>
<td>0</td>
<td>64</td>
</tr>
<tr>
<td>Mean ± SE</td>
<td>144</td>
<td>±47</td>
<td>±47</td>
</tr>
<tr>
<td>Chronic vaginals</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P. A.</td>
<td>64</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>J. C.</td>
<td>256</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>D. T.</td>
<td>256</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>P. L.</td>
<td>512</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>L. P.</td>
<td>512</td>
<td>0</td>
<td>16</td>
</tr>
<tr>
<td>G. M.</td>
<td>64</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>N. R.</td>
<td>256</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>P. G.</td>
<td>128</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>D. A.</td>
<td>256</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>J. W.</td>
<td>128</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>S. R.</td>
<td>64</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>S. G.</td>
<td>256</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>L. Y.</td>
<td>64</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Mean ± SE</td>
<td>192</td>
<td>±38</td>
<td>±10</td>
</tr>
<tr>
<td>Cervicovaginal washings</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D. A.</td>
<td>60</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>C. M.</td>
<td>120</td>
<td>0</td>
<td>20</td>
</tr>
<tr>
<td>P. G.</td>
<td>120</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>Mean ± SE</td>
<td>100</td>
<td>±25</td>
<td>±8</td>
</tr>
</tbody>
</table>

* Student's t test: (i) antibody titers—patients > controls, P < 0.05; (ii) serum IgE levels—systemics with normal levels of immunoglobulins > controls, P < 0.005; IgA-deficient systemics < other systemics, P < 0.025. Linear regression correlation: (i) IgE levels versus percentage of IgE anti-Candida antibodies—chronic vaginals, P < 0.05. (ii) IgA anti-Candida antibodies versus whole IgE levels—systemics, P < 0.01. (iii) IgG versus IgA—systemics, P < 0.01. SE, Standard error.
by using passive hemagglutination and immuno-
nofluorescent-antibody tests. The range of IgE anti-
Candida antibodies in the majority of candidi-
sis patients was between 11 and 97.4%. A
significant linear regression correlation (P < 0.05)
between total IgE level and percentage of anti-
Candida antibodies was obtained in the case of
vaginal candidiasis patients. In one systemic
candidiasis patient and two intermediates, 100%
of the total IgE levels were anti-Candida in
specificity. Previous work on IgE antibodies
against Nippostrongylus brasiliensis in rats showed
that IgE antibody specific for worm antigen became detectable 3 to 4 weeks after
infection and increased steadily thereafter, even
though total IgE levels were at a minimal level
(6). Obviously, the kinetics of the IgE antibody
did not necessarily parallel the total IgE syn-
thesis during severe infections. Thus, it is entirely
possible that the IgE anti-Candida antibody
levels were at their peak in the case of the three
patients with severe and long-standing candidi-
asis.

The presence of elevated levels of anti-Can-
dida IgE antibodies in the cervicovaginal secre-
tions of the vaginal candidiasis patients implies
a possible synergistic role of IgE and secre-
tory IgA (12) in the local immune system of the
cervicovaginal area. The correlation of IgA and
IgE levels in the patients supports this concept.
Our results for the group of intermediate pa-
tients seem to indicate that IgE levels may re-
main elevated during the earlier stages of infec-
tion and decline in the later stages.

Does IgE at the mucous membrane play a
role in antimicrobial defense? The presence of
elevated IgE, especially anti-Candida antibo-
dies, during mucosal infection with C. albicans
suggests that it does; however, the mode of
action of IgE during candidiasis is still unknown.
The correlation between elevated IgE levels and
defective cell-mediated immunity, as indicated by
reduced leukocyte chemotaxis and lympho-
cyte responsiveness to phytohemagglutinin (15),
in patients with skin infections such as atopic
dermatitis, who also have low levels of T cells
22:159A, 1974), suggests a requirement for sup-
pressor T cells in controlling IgE production.
Studies are under way to evaluate the possibility
that increased production of IgE in patients
with candidiasis may indicate a subtle defect in cell-
mediated immunity—specifically, a reduction in
a "suppressor" T-cell population that would nor-
mally monitor IgE levels.

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