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SMUFD D/A ltr, 4 Feb 1972

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INTRADERMAL ALLERGY TEST FOR Q FEVER

TRANSLATION NO. 694

OCTOBER 1962

U.S. ARMY BIOLOGICAL LABORATORIES
FORT DETRICK, FREDERICK, MARYLAND
INTRADERMAL ALLERGY TEST FOR Q FEVER

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The possibility of using an intradermal test for Q fever was brought up by P. F. Zdrodovskiy in connection with efforts to improve and facilitate the diagnosis of this disease especially in the case of mass examinations.

An expedition led by S. M. Kulagin was sent by the Department of Rickettsia to one of the focal points of endemic Q fever in southern USSR. As a member of this expedition, I was assigned to make preliminary observations of the possibility of producing an allergic skin reaction and of the course of its development in patients with Q fever and in those who had had the disease.

Foreign literature contains some references to the successful use of allergy diagnosis for Q rickettsia (Mirri, 1951; Lopes, 1952; Onul and Rysalefe, 1953). Lopes thinks that an intradermal test is more sensitive than the complement reaction. Thus, in 76% of the 121 persons he examined, a positive skin test coincided with a complement reaction, in 20% a positive skin test was accompanied by a negative complement reaction, while in 3% the ratio was reversed. Onul and Rysalefe regard an allergy skin test as suitable even for early diagnosis of Q
fever because they noted positive reactions between the third and eighth days of the disease. The authors observed positive reactions at different periods of time thereafter (a maximum of about four years) in those who had had the disease. A positive reaction in the form of an infiltrative erythema appeared 10 to 12 hours after intradermal injection, became intensified during the next 12 hours, reached a maximum by the 40th hour, and then gradually disappeared. The infiltrative erythema was usually more than 3 cm in size (about 6 to 8 cm). There was a central induration which persisted somewhat longer. Some of those who recovered from the disease had a general reaction. In those who had never had Q fever, small white papules (about 0.5 cm in size) appeared in the area of the Q antigen injection. These turned red and disappeared 6 to 8 hours later. The redness occasionally remained longer.

In performing the intradermal allergy tests, we used the allergen (Golievich and Kazanskoy) prepared from carefully purified suspensions of killed, sterilized Rickettsia burnetii grown in egg cultures. A 0.25% solution of phenol was added as a preservative. The prepared allergen was tested for bacterial and specific sterility and standardized for the complement reaction with specific immune serum (allergen titer 1:2 ++++. The allergen's specific activity and harmlessness was tested on guinea pigs. In 1:10 and 1:50 dilutions the allergen, after intradermal injection into the guinea pigs, caused a distinct local reaction in those who had had Q rickettsia, whereas in 1:100 dilution the reaction was weak or absent.

We performed the test by intradermally injecting 0.1 ml of the allergen into the inner surface of the forearm starting with a 1:20 dilution (with physiological solution) and then 1:10 and 1:5 dilutions after we became convinced that it was safe and produced no reactions in healthy persons.

We observed the course of the reaction 6, 8, 12, 18, 20, 24, and 48 hours (sometimes up to 72 hours) after the test. The local reaction was measured by the extent of hyperemia and edema of the skin at the allergen injection site. At the same time we noted the reaction of the regional lymph nodes (enlargement and tenderness) as well as the systemic reaction (elevation of temperature, headache, etc.).

A positive reaction was the development of hyperemia and slight skin edema ranging from 1 to 3.5 cm in size. The hyperemia appeared 6 to 8 hours after the injection, became intensified, remained for 24 to 48 hours, and then gradually disappeared.

The development of a small more intensely hyperemic infiltrate in the center of the hyperemic area was a characteristic reaction. Sometimes this central infiltrate persisted longer.
The allergy test was given to those who had had Q fever 2 months, 1 year, and 3 years before. A positive reaction usually appeared 10 to 12 hours later, became intensified by the 24th hour, and generally persisted more than 48 hours. The hyperemic zone and edema were 1 to 3.5 cm in size (Table 2).

**TABLE 2**

<table>
<thead>
<tr>
<th>Time of onset</th>
<th>Number of cases</th>
<th>Positive reaction (number)</th>
<th>Titer of complement reaction</th>
<th>Duration of reaction in hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 months before</td>
<td>4</td>
<td>4</td>
<td>1:10</td>
<td>24</td>
</tr>
<tr>
<td>1 year before</td>
<td>13</td>
<td>12</td>
<td>1:5, 1:10</td>
<td>48</td>
</tr>
<tr>
<td>3 years before</td>
<td>3</td>
<td>3</td>
<td>1:5</td>
<td>48</td>
</tr>
</tbody>
</table>

After comparing the results of the allergy tests with the serological investigations, we found a discrepancy in three cases. In one person who had had Q fever 2 months before, a negative allergic reaction was accompanied by a positive complement reaction when a dilution of 1:10 was used; in one patient with Q fever on the 10th day of the disease and in one person who had had the disease a year ago, there was a marked allergic reaction with a negative complement reaction to the antigen from Rickettsia burnetii.

Allergy tests with the Q antigen given to 18 persons, healthy or sick with such diseases as rheumatism, heart disease, liver disease, or helminthiasis yielded completely negative results (no reaction at the injection site).

It will be noted that the extent of the allergic reactions was relatively small (an area of 1 to 1.5 to 3.5 cm) because we used very low doses of the allergen, fearing, on the basis of published reports, a general reaction. In view of the absence of any reaction in persons not suffering from Q fever and the absence of a general reaction with a positive skin test, we deem it quite possible to administer much larger doses of the allergen when making the test.
Our data suggest that the use of an allergy test for Q fever is highly promising and is probably especially valuable in mass examinations for retrospective diagnosis of the disease. As for an allergy test to diagnose an active case of Q fever, the problem is complicated by the possibility of finding a positive reaction as a result of a past occurrence of the disease. In such cases an allergy test may have diagnostic value if the serological reaction is negative, as may happen in the early stages of Q fever, because in this disease antibodies usually appear somewhat later.

Findings

1. An allergic skin reaction with the allergen from Rickettsia burnetii was noted in patients with Q fever starting with the ninth day of the disease (period of significant observations).

2. An allergic reaction with the same allergen was noted in those who had had Q fever one to three years before.

3. An allergic reaction in persons did not cause a general reaction.

4. A skin reaction with the Q allergen did not occur in healthy persons or in those with other diseases.

BIBLIOGRAPHY


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