Effect of Pertussis Vaccination on the Sensitivity of Mice to Insulin, Bicarbonate, and CO₂

A. G. LANE

Commonwealth Serum Laboratories, Parkville, Victoria, 3052, Australia

Received for publication 19 March 1969

Prior pertussis vaccination increased the sensitivity of mice to intraperitoneal injections of insulin and of sodium bicarbonate, but it reduced their sensitivity to high levels of inhaled carbon dioxide.

In 1948 Parfentjev and Goodline discovered that prior pertussis vaccination greatly increased the sensitivity of mice to the effects of administered histamine (8). The component of the microorganism causing sensitization has been called "histamine-sensitizing factor" (HSF). However, it has become apparent that the sensitization is not specific to histamine; increased sensitivity has also been reported to serotonin, anaphylaxis, infection, endotoxins, X-irradiation, anoxia, cold, peptone shock, pollen extracts, bradykinin, Salmonella typhymurium neurotoxin, epidemic typhus toxin, and methacholine (7) and to extracts prepared from tissues of the central nervous system (4).

It is still not certain whether HSF causes a similar nonspecific hypersensitivity in a small proportion of humans vaccinated or infected with pertussis. Because of possible relevance to humans, it was of interest to see whether prior pertussis vaccination increased the sensitivity of mice to insulin, acidosis, or alkalosis.

Tests were carried out in groups of 10 male mice weighing 18 to 21 g. The HCO₃⁻/CO₂ imbalance of respiratory alkalosis was simulated by administering saturated sodium bicarbonate solution by intraperitoneal injection in doses of 1.0, 0.9, 0.8, 0.7, 0.6, or 0.5 ml; deaths were counted on the following day. Acidosis was simulated by holding the mice in an atmosphere of about 50% CO₂ in oxygen for about 2 hr; the deaths were counted on the following day. Sensitivity to insulin was tested by administering 0.02, 0.013, or 0.009 units of crystalline insulin by intraperitoneal injection while incubating the mice at 35 °C; mice dead or convulsing were counted 2 hr after challenge (Table 1).

The sensitivity of mice to insulin and to alkali was increased by prior pertussis vaccination, but contrary to expectation, their sensitivity to CO₂ was decreased. The test was repeated and the result was confirmed.

This is believed to be the first report of pertussis vaccination decreasing rather than increasing the sensitivity of mice to a form of stress.

At present it is thought that the HSF component of pertussis increases the sensitivity of mice to any form of shock or stress by blocking the effect of the adrenal medullary hormone, epinephrine (7). The significance of HSF for humans either suffering from or vaccinated against pertussis is not clear. There have been occasional reports of cerebral complications after the usual vaccination procedures and during infection with pertussis (1, 2, 4-6, 10). There is very little evidence that HSF might be the component responsible. Pittman drew attention to the apparent parallelism between the sensitization of infected mice to histamine and the onset and duration of coughing in the human (9). On the other hand, Stronk and Pittman (12) reported that HSF

**Table 1. Effect of prior pertussis vaccination on the sensitivity of mice to insulin, CO₂, bicarbonate, and histamine**

<table>
<thead>
<tr>
<th>Challenge material</th>
<th>Challenge dose per mouse</th>
<th>Deaths/10</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Vaccinated group</td>
</tr>
<tr>
<td>Saturated solution of NaHCO₃</td>
<td>1.0 (ml)</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>0.9</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>0.8</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>0.7</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>0.6</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>0.5</td>
<td>3</td>
</tr>
<tr>
<td>Insulin</td>
<td>0.02 (units)</td>
<td>7*</td>
</tr>
<tr>
<td></td>
<td>0.013</td>
<td>5*</td>
</tr>
<tr>
<td></td>
<td>0.009</td>
<td>1*</td>
</tr>
<tr>
<td>Histamine diphosphate CO₂</td>
<td>6.0 (mg)</td>
<td>9</td>
</tr>
</tbody>
</table>

- Test 1
- Held for about 2 hr
- in 50% CO₂
- in oxygen

* Mice (per 10) dead or convulsing.

938
did not sensitize either the rabbit or the guinea-pig; the sensitivity of these animals to histamine is normally comparable to that of humans and it was concluded that HSF would probably not sensitize humans. This may well be true for humans in general, but does not disprove that the occasional cerebral complication seen in humans may be due to HSF. The number of children showing severe reactions to infection or vaccination with pertussis is apparently very small (1, 3, 11), and therefore is presumably due to idiosyncrasy (13), which could possibly involve hypersensitization by HSF (2).

Until the role of HSF in the occasional encephalopathy is better understood, the significance for humans of the result reported here cannot be properly assessed.

LITERATURE CITED