Skin rash after triple vaccine

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SUMMARY
Skin rash after triple vaccine is rare. We describe a child who developed a generalised asymptomatic rash after the second and third triple vaccine. Little information of the pathogenesis of the rash is available. We argue that the development of a rash is not a contraindication to future immunisation.

Case report
A normal baby of atopic Iranian parents developed a rash five days after her second triple vaccine given with oral polio vaccine at 5 months of age. She had no systemic upset during this time. The first triple immunisation was uneventful. She was referred to the community immunisation advisory clinic by her health visitor, where she was advised to have the third triple vaccine and oral polio vaccine at the normal time. This she received at the local clinic and five days later a rash nearly identical to the first appeared. No concurrent medication was administered on either occasion. The rash was most prominent on the face (Figure), with two large macules on the trunk. The rash consisted of large (1 cm) and small (3 mm) macules. Those on the trunk were slightly raised. The lesions all appeared at the same time and faded over the next four days. The child did not scratch the lesions. There were no oral lesions. Again there was no systemic upset.

It was considered that the rash was probably due to the preservative thiomersal 0·01% present in triple vaccine. There have been several reports of skin hypersensitivity to this agent,1 and one of these reports detailed reactions to hypo-sensitisation therapy with thiomersal 0·01%. Patch testing and intradermal testing is unreliable in determining hypersensitivity.1 In view of this, the child was challenged with 0·5 ml thiomersal 0·01% by deep subcutaneous injection. No rash occurred.

Discussion
Rash after triple vaccine does occur (Table) and is not considered a contraindication to subsequent immunisation. Of these reports to the committee on safety of medicines, some reactions are probably reported under more than one component. It is not

Table Reports to the committee on safety of medicines of rash attributed to vaccines either in monovalent or combined forms. Inclusion of a particular reaction does not necessarily mean it was caused by that vaccine

<table>
<thead>
<tr>
<th>Rash types</th>
<th>Tetanus</th>
<th>Diphtheria</th>
<th>Pertussis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dermatitis</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Exfoliative dermatitis</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Eczema</td>
<td>2</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Erythema multiforme</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Pruritus</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Rash</td>
<td>7</td>
<td>45</td>
<td>30</td>
</tr>
<tr>
<td>Erythematous rash</td>
<td>4</td>
<td>17</td>
<td>4</td>
</tr>
<tr>
<td>Follicular rash</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maculopapular rash</td>
<td>3</td>
<td>9</td>
<td>3</td>
</tr>
<tr>
<td>Morbilliform rash</td>
<td>1</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Urticaria</td>
<td>17</td>
<td>31</td>
<td>26</td>
</tr>
<tr>
<td>Skin discoloration</td>
<td>1</td>
<td></td>
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</tr>
</tbody>
</table>

Data by kind permission of the committee on safety of medicines.
possible to find out why some reactions are attributed to only one component and not to the normal combinations used. Furthermore, some of these individuals will have suffered viral exanthemata and some will have been treated with pharmaceutical agents, including antibiotics, which can also cause rashes. Rash is probably genuinely rare as several reports reviewing adverse reactions to vaccines do not mention rashes at all, one giving an incidence of 5-2% among other adverse reactions and another recording urticaria and angio-oedema occurring in 29 of 158 230 airmen, an incidence of 0.018%. 

Was this child's rash due to thiomersal? It has been suggested that the degradation products of thiomersal that accumulate after storage in contact lens solution cause eye hypersensitivity. The accumulation of these degradation products is accelerated by storage in the light and at room temperature, but vaccines are stored in the dark and at +4°C. We do not believe thiomersal was responsible for this child's rash. We also do not believe aluminium hydroxide was responsible for the rash in the light of a complete absence of reports of hypersensitivity.

The question that must be addressed is, what recommendation should be given to parents for subsequent immunisation? In the case quoted above, the question centres around diphtheria and tetanus immunisation at school entry. Both these vaccines are given to protect the individual against a potentially lethal disease, made rare by immunisation. Without immunisation the child remains at considerable risk to either of these illnesses as protection wanes with time. These individuals should, therefore, be immunised if it is safe to do so. Does the five day period between immunisation and development of the rash give us any help? The rash of penicillin allergy typically occurs on the fifth day after administration and does not usually herald anaphylaxis. Perhaps the allergic mechanism involved is the same in both situations. The mechanisms of penicillin allergy are, however, poorly understood. An IgE response, together with positive immediate skin hypersensitivity to tetanus toxoid immunisation, is a normal response associated with rash. The IgE response has been dissected out, showing a wide range of responses, including heterogeneous IgE antibody production, basophil degranulation, and basophil IgG blocking antibodies, none of which correlate with skin test positivity. A report of adverse reactions to tetanus toxoid included 38 of 740 patients with generalised rash. All these patients had negative intradermal skin tests and did not react to subsequent challenge. Even the 95 patients with previous anaphylactoid responses did not suffer any reactions to a challenge. No additional data on allergic skin reactions to diphtheria or pertussis vaccine are available.

We are left, therefore, in a rather unsatisfactory state of knowledge and can make no scientifically validated recommendations about future immunisation in those who develop a rash. We believe that subsequent immunisation will be safe in the vast majority of cases and that it is in the patient's interest to be protected against diphtheria and tetanus. We advise that those immunised be observed for about an hour afterwards by a doctor to ensure that any anaphylactoid reaction that occurs is rapidly treated. We question the wisdom of continuing to use the preservative thiomersal in vaccine preparations.

References

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