range 0-75 nmol/l). She was treated with penicillamine 62.5 mg three times a day for 14 days; during this time her urine mercury concentrations fluctuated between 548 and 848 nmol/l. As expected this concentration fell very gradually and two months later (aged 1 year) it was 75 nmol/l. By this time her weight had increased to 6030 g. Her subsequent development was that of a normal healthy girl who was difficult to feed initially.

In Martinadale (1982) we are reminded that 'mercury or mercurial preparations should not be given to infants or applied to their skin as they may cause acrodynia'. Meyler's Side Effects of Drugs indicates that 'the use of mercury in dermatological therapy should be abandoned'.

Although no mercury preparations are listed in MIMS, I note that ammoniated mercury powder and mercuric chloride are listed in the Drug Tariff (1987) (DHSS), the American Hospital Formulary Service Book (1988); formulations are also found in the Pharmaceutical Codex (1977), which is still current.

References


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Correspondence

Protective effect of BCG vaccination in infant Asians

Sir,

I read the article by Packe and Innes with special interest because I have been involved in BCG vaccination of Asian children both in this country and in India.1 I am really surprised with their findings that BCG has a significant protective effect on Asian children as my own experience has been very disappointing.

In Patna, India, I followed up 90 children of the age group 1–12 who were found to be negative on prevaccination tuberculin testing and who did not show an accelerated reaction to BCG in the first seven days (BCG negative). All children were vaccinated by intradermal injection of 0.1 ml of reconstituted BCG vaccine supplied by BCG Laboratory, Madras, India, which uses the Danish 1331 strain of BCG. On serial tuberculin testing with 1 tuberculin unit (purified protein derivative, RT23 with Tween 80) every six months, I found that postvaccination tuberculin sensitivity appreciably decreased over an 18 month period (table).

Out of these 90 children six had developed tuberculous disease by 18 months. The criteria for diagnosis of tuberculosis in BCG vaccinated children were: (1) conversion of tuberculin negative child to positive; (2) increasing gradation of tuberculin reaction to greater than 10 mm; and (3) enlarged parahilar lymph nodes with or without parenchymal lesion on a chest radiograph. These findings made me think that immunity conferred by BCG is transient and probably does not last more than 18 months. Two years later (1982) while vaccinating school children in Blackburn I was not surprised to see that many school age Asian children had more than two BCG scars on their left deltoids and were still tine test negative. Other workers with BCG in developing countries have also had similar experience. Murtagh in Papua New Guinea found that 73–7% of the bacteriologically and histologically proved cases had already had BCG—some of them more than once.2 The largest controlled field trial ever done on BCG in Southern India did not show any protective effect.3

References

2 Murtagh K. Efficacy of BCG. Lancet 1980;i:423.

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Drs Packe and Innes comment:

In his letter, Dr Singh raises a number of important issues regarding the efficacy of BCG vaccination. It is noteworthy that the results of studies on BCG vaccination in the newborn and in infants are more encouraging and consistent than are the results of BCG studies in older children and young adults (of which the South India study was a prime example).1 This view is reinforced by the results of several recent studies sponsored by the World Health Organisation and by the results of our own study on infant

Table

<table>
<thead>
<tr>
<th>Tuberculin reaction</th>
<th>No (%) of cases after six months</th>
<th>No (%) of cases after 12 months</th>
<th>No (%) of cases after 15 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>More than 10 mm (positive cases)</td>
<td>54 (60)</td>
<td>33 (37)</td>
<td>19 (21)</td>
</tr>
<tr>
<td>Less than 10 mm (negative cases)</td>
<td>36 (40)</td>
<td>57 (63)</td>
<td>71 (79)</td>
</tr>
</tbody>
</table>
Asians in Birmingham, which show that BCG vaccination confers useful protection against tuberculous disease.

A discussion about why BCG in the newborn should be more effective than vaccination in older children and adults is outside the scope of this letter. One possibility, however, is that children given BCG vaccination soon after birth or at birth are not exposed sufficiently long to environmental factors which might mitigate the effect of BCG vaccination. For example, in areas where infection with atypical mycobacteria is common, such an infection before vaccination might provide a level of immunity comparable with that provided by BCG. This naturally acquired immunity might nullify or even oppose the effect of BCG vaccination.

Dr Singh’s results are in accordance with previous studies showing that tuberculin skin sensitivity induced by BCG vaccination diminishes with time. However, his interpretation of the results may be at fault because he makes the commonly made but erroneous assumption that tuberculin sensitivity equates with immunity against tuberculous disease. Indeed, there is evidence suggesting the absence of an association between tuberculin sensitivity and immunity. Although it is likely that the protection conferred by BCG wanes with time after vaccination, it does not necessarily diminish at the same rate as tuberculin sensitivity.

In his study, Dr Singh found that 6·7% (690) of his vaccinated subjects developed tuberculous disease by 18 months after vaccination. These results presented in isolation do not argue against the efficacy of BCG vaccination. If, for example, the incidence of tuberculosis in unvaccinated subjects in the same community over a comparable period was significantly higher than that in the vaccinated group it would strongly suggest that BCG was exerting a protective effect.

Similarly Dr Singh quotes a study in which 73·7% of proved cases of tuberculosis in a population had received BCG vaccination, and cites this as evidence against the efficacy of the vaccine. Again, this information alone is inadequate to reach any conclusion about the efficacy of BCG. In his quoted example, if 90% of the total population had been vaccinated, the estimated protective efficacy of the vaccine would still be 68·9%—a level sufficient to justify its continued use. This result is difficult to grasp intuitively but can be better understood by reference to the paper by Smith.

We firmly believe that routine BCG vaccination of the newborn and infants is a valuable preventive measure in communities where there is a high incidence of tuberculous disease.

References


Incidence of zinc and copper deficiency in Japan

Sir,

This correspondence is concerned with the report by Shaw, in which copper concentrations of infant formulas were cited from data by Lönnerdal et al as being 60 μg/l in Japan and 120–680 μg/l in other countries.

In 1983, we sent questionnaires to 662 hospitals concerning zinc and copper deficiency from 1978–83. Three hundred and thirty five (51%) replied, of which 86 had treated children with these deficiencies. Further detailed answers were obtained from 40 out of these 86 hospitals (47%); deficiency for zinc was recorded in 76 cases and for copper, 11 cases. For those with zinc deficiency, 43 were under 6 months of age and 14 were aged 6 months to 1 year. Thus most of the patients (57/76, 75%) were under 1 year of age. Of the 76 patients, 17 were premature infants, 33 had intractable diarrhoea, 12 were on parenteral nutrition, two had inherited acrodermatitis enteropathica, and 12 had other complaints. Only two premature infants and none with intractable diarrhoea were fed breast milk. Of those with copper deficiency, two were below 6 months of age and seven were aged 6 months to 1 year. Like the infants with zinc deficiency these infants were mostly (9/11, 82%) under 1 year of age. At the time of this survey, the contents of zinc and copper in commercial formulas were 0–81–1–82 mg/l and 30–80 μg/l, respectively, as reported by Lönnerdal et al. Since 1984, when the Japanese government accepted the addition of zinc and copper to infant formulas up to the concentrations recommended by the Food and Agricultural Organisation/World Health Organisation (3·2 mg/l zinc, 300 μg/l copper), the number of cases of zinc and copper deficiency has been dramatically reduced. Only five cases of zinc deficiency and no cases of copper deficiency have been recorded in the last three years among the same 40 hospitals concerned with the first survey.

References