Komentar

THE ROLE OF SECONDARY VACCINE FAILURE IN MEASLES OUTBREAKS

G. Richard, Mathia, G. William, Meekison, Teri A. Arcand, & M T. Schechter. American Journal of Public Health. April 1989.

An outbreak of measles in 1985-1986 in a community where measles vaccine trials had been carried out from 1974-1976 allowed the assessment of the role of secondary vaccine failures in previously immunized children. A total of 188 children from the vaccine trial were followed. Of these, 175 seroconverted initially while 13 (6 percent) required re-immunization (primary failure). A total of 13 cases of measles, eight of which were laboratory and/or physician-confirmed, were reported in this cohort. Of these, nine cases occurred in the 175 subjects who had hemagglutination inhibition (HI) and neutralizing antibody responses following the initial immunization. These nine cases represent secondary vaccine failures. An additional four cases occured in the 13 subjects with primary vaccine failure. We conclude that secondary vaccine failures occur and that while primary failures account for most cases, secondary vaccine failures contribute to the occurrence of measles cases in an epidemic. A booster dose of measles vaccine may be necessary to reduce susceptibility to a sufficiently low level to allow the goal of measles elimination to be achieved.

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Background.

There are two kinds of vaccine failure: (1) Primary vaccine failure means that patients after immunization do not make the appropriate and expected antibodies; (2) Secondary vaccine failure means that patients contract the disease against which they were vaccinated despite the fact that they produced an initial antibody response to the immunization.

Primary vaccine failure after measles immunization under reasonably good conditions is about 5%.

Secondary vaccine failure may mean that there is a fall of antibody titre and revaccination may be necessary. This is the reason for the booster doses given, for instance, with DPT immunization.

For measles vaccine the need and timing of booster doses is not yet clear.

Recapitulation

The reported study makes a careful analysis of children who were part of a trial of two measles vaccines from 1974-1976.

The vaccine trial included 382 volunteers out of 6000 possible one-year olds. Two vaccines were compared. Serum for antibodies was drawn before and after vaccination. Repeat samples were done on children that could be located at 3 and 5 years.

A measles outbreak occurred in the area in 1985/86 7479 cases were reported. In the vaccine trial area there were 744 cases.

Near the end of the epidemic period all children taking part in the vaccine trial were identified in the records: 225 of 382 families were contacted and blood was drawn from 188 subjects. IgM estimation was included.

The results report the details of primary vaccine failures, who were reimmunised later (13), 12 other children reimmunised as part of outbreak control and 13 cases of the vaccine trial cohort, who contracted "measles", 8 of which were confirmed by a doctor. Four cases occurred among the 13 initial vaccine failures (31%); 9 cases amongst the other 175 trial children were secondary vaccine failures (5%).

Mean neutralizing antibody titres were lower in the group with antibodies who later developed measles, than in those who did not. Children who required reimmunization for initial vaccine failure were 6 times more vulnerable to measles later. IgM was negative all 188 participants, even in those with recent infection, but neutralising antibodies showed a rise overtime as expected in the measles cases. There was no significant difference between the two vaccine trial groups on any parameter.

The authors comment that the literature and this study suggest that measles epidemics will continue due to both primary and secondary vaccine failures and that the search for a still better vaccine must continue.

Reader's Comment

The article is important because it draws attention to reasons why measles continues even in areas with careful immunization programmes. The authors are very explicit in exposing the weaknesses of the study, most of which could not be avoided, and show that, with due care, imperfect studies can yield important thoughts.

What was wrong with the study?	Comment
1. The cohort consisted of volunteers	Provided children were healthy, this should not influence serocon-version. Therefore of no importance in a vaccine trial.
2. The sample was very small 382 out of 6000	This did prove a problem in drawing conclusions from the follow up study.
3. The vaccine trial was unbalanced: 265 vs 117, but! a bit of luck !	Fortunately no differences were found between seroconversion titres in the two groups. The vaccine used in the smaller group is widely used in some countries today.
4. Out of the original 382 only 188 were located: 129/265 and 59/117.	After 11 years this is not surprising. The study was not planned for a 10 year follow-up. The measles epidemic gave unexpected opportunities.
5. The diagnosis of measles was by parent report, doctor. diagnosis or antibody rise but not in all cases.	The article is as explicitas possible about the diagnosis of the cases and their prevous immunization status. Five of the cases occurred during the recent epidemic. Morever neutralizing antibodies were higher in those who were reported to have had measles. The authors state that measles may have bee nover-diagnosed.

	However, the authors' reasoning on validation seems acceptable.
6. IgM was negative in all	The authors indicate their surprise that this was so. They expected 5 positives onrecent cases. IgM responses may occur only in primary vaccine failure The very small numbers did not allow the authors to confirm this.

In the discussion the authors point at the possible predictors of subsequent measles:

- Primary vaccine failures that required reimmunization, sometimes again with relatively low titres.
- Low (*relatively low*) titres predict vulnerability in secondary vaccine failures.
- Those who are not protected by their immunization appear very often to contact measles eventually (31% in children old enough to have been through two epidemics, 1980 and 1986 in primary vaccine failures and 5% of secondary vaccine failures).

Therefore the authors conclude that the vaccines used at present still do not mimick natural infection well enough to protect all children.

The authors warn that secondary vaccine failure indeed constitutes a health hazard.

CONCLUSION

How does this reasoning affect developing countries?

1. Measles immunization undoubtedly saves numerous lives by primary conversion.
2. The proportion of primary failures is likely to be higher than in developed countries and will insure the survival of measles virus in epidemics for sometime to come, be it on a lesser scale.
3. The continued (small) epidemics will also infect children whose antibodies have waned (secondary vaccine failure) and ensure natural immunity in them, as well as in the primary vaccine failures.
4. Antibody checks after immunization with reimmunization, and rechecks of antibody again, will not become necessary for sometime, except perhaps for a small proportion of the affluent whose children are shielded from exposure to ordinary life. It is also far too expensive for large scale use.

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