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Maternally derived measles immunity in children of naturally infected and vaccinated mothers

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SUMMARY

Measles antibody titres were established in three groups of infants: children of vaccinated mothers, children of unvaccinated mothers and neonates born after different gestational periods.

Lower measles antibody titres were observed in children whose mothers had been vaccinated, and these decayed to undetectable values earlier than in children whose mothers had not been vaccinated, and were assumed to have had natural measles. Lower measles antibody titres were observed in premature neonates than in full term babies, and these lower antibody levels will presumably decay to undetectable values earlier than in full term neonates.

These results, if confirmed by larger studies, would indicate an earlier optimum age for vaccination against measles than the currently recommended 13–15 months for two groups in order to reduce the risk of natural infection before immunization. These groups are children in a highly vaccinated population whose mothers have a low measles antibody titre and premature children (defined as having a gestational period of less than 37 weeks).

Routine immunization against measles began in Great Britain in May 1968 for children aged 2–15 years, and in the following year for infants between 1 and 2 years (Miller, 1982). Trials have shown the live attenuated measles vaccine to have a high efficacy (Measles Vaccination Committee, 1965), mild and acceptable side effects (Measles Vaccination Committee, 1968), and to give effective protection for at least 21 years (Miller, 1987). Despite this, vaccine uptake has only been about 50%, although in recent years it has risen to 68% (Department of Health and Social Security, 1987).

One reason for low uptake is the inconvenience of an isolated clinic visit for vaccination in the second year of life (Sherrod *et al.* 1983). Immunization is carried out at 12–15 months because at earlier ages vaccination failures occur due to interference by maternal antibodies. Maternal antibodies begin to cross the placenta from the fourth month of gestation, and the majority of transfer occurs in the final trimester (Toivanen, Mantygorvi & Hirvonen, 1968). Albrecht *et al.* (1977) have shown that maternal antibodies can persist for more than 12 months, and this has been borne out by vaccination failures in children older than this (Yeager *et al.* 1983).

However, the optimum age for immunization was determined at a time when the majority of adult immunity was due to natural infection. It is known that live

attenuated vaccine induces lower antibody titres than natural infection (Krugman, 1977), and this can be predicted to result in lower levels of maternally derived antibody in the newborn of vaccinated mothers (Wilkins, Wehrle & Portnoy, 1972). These lower levels would be expected to decline more rapidly, with infants becoming susceptible to measles and responsive to immunization at an earlier age. Lennon & Black (1986) confirmed that mothers young enough to have been vaccinated had lower titres than older women, and predicted from this that 95% of the children of the younger mothers would have lost maternal antibody protection by 8 months, as compared to 11 months for those of older mothers.

We have tried to establish whether lower levels of maternal antibodies are found in children of vaccinated mothers, and whether premature babies have lower levels of maternal antibodies, as would be expected if the majority of transfer occurs in the final trimester.

Serological studies were carried out on routine blood samples collected at the Bristol Maternity Hospital and the Public Health Laboratory, Bristol. These samples were divided into three groups: 18 children aged 1–14 months born to vaccinated mothers; 34 children aged 1–14 months born to non-vaccinated mothers; and 41 neonates of various gestational ages. The measles vaccination history of the mothers of all the children aged 1–14 months was obtained from a questionnaire completed by their General Practitioners.

Haemagglutination-inhibiting (HI) antibody was detected by a modification of the method of Rosen (1961), using 0·25% *Cercopithecus aethiops* (Baboon) red blood cells. Antibody was detected by indirect immunofluorescence (IFAT) using the method of Gershon & Krugman (1979). Acute, convalescent and reference sera were set up as controls in each series. The end-point was taken as the last dilution showing weak but distinct immunofluorescence.

From Fig. 1 it can be seen that the HI titres of children of vaccinated mothers are lower in most age groups and decline to undetectable levels more rapidly than those of non-vaccinated, naturally immune mothers. The IFAT results gave higher titres, but were similarly distributed between the age groups.

Fig. 2 shows an increase in HI titre with length of gestational period from undetectable values at 24 weeks to full-term values at 37 weeks and over. Again a similar distribution was observed with IFAT titres.

The problem of delaying immunization until the second year may become a thing of the past in a highly vaccinated population if maternal antibody protection is lost earlier in children of vaccinated mothers. If this is the case, children will become susceptible both to natural infection and to successful vaccination earlier, and hence the age of immunization could be brought forward to the first year of life when clinic attendance is better. This would be expected to lead to a higher vaccine uptake.

Our results, though limited by small sample size, seem to confirm this, and also support the prediction by Lennon & Black (1986) that maternal antibody protection is lost in the majority of such children by 8 months. The one case of a 14-month-old child with a maximum titre was assumed to be due to natural infection occurring after maternal antibody protection had waned, and before immunization had occurred.

Further studies with larger sample sizes are needed to confirm our results before

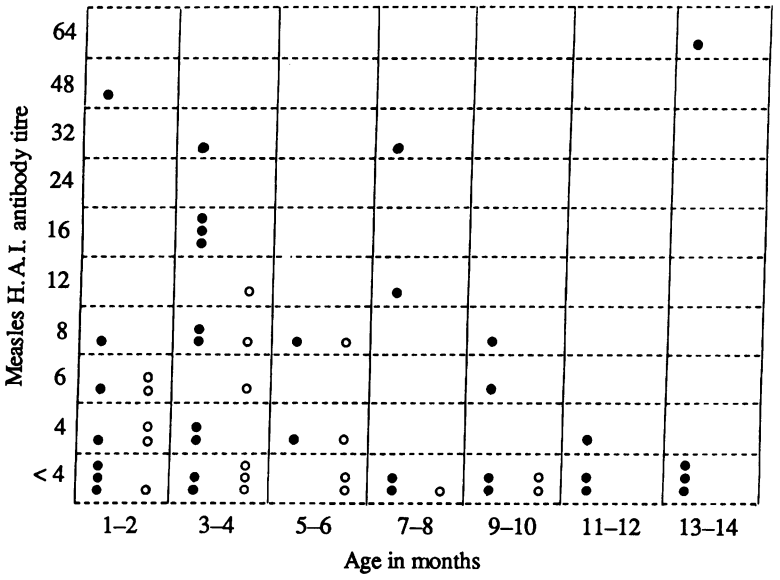

Fig. 1. HI antibody titres for children of non-vaccinated mothers (●) and vaccinated mothers (○).

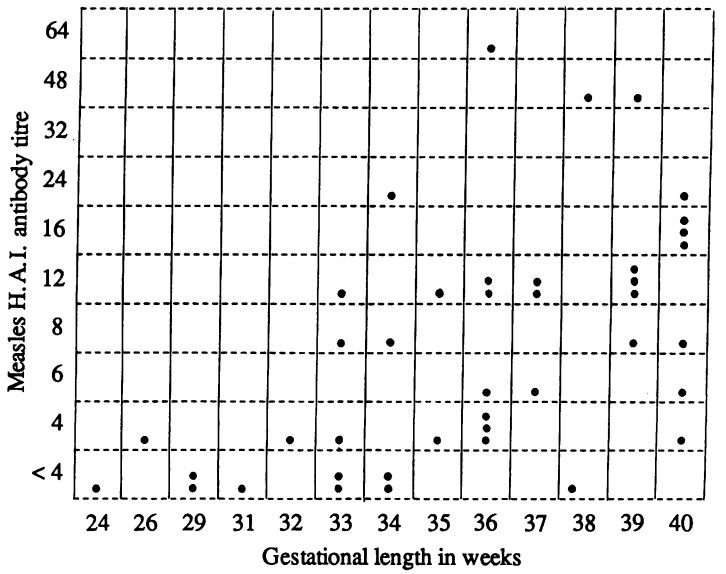

Fig. 2. HI titres for neonates of different gestational length.

any policy recommendeations can be made. It is also important to determine whether some children of vaccinated mothers have protection which does last up to 12 months. Again our sample size is too small for us to draw conclusions on this, but Lennon & Black (1986) predicted from their figures that 2% of children would fall into this category. If this is the case, selective early immunization of children of vaccinated mothers with low antibody titres would be successful, but

immunization of those whose mothers have high titres would need to be delayed until after 12 months to avoid vaccine failure.

The antibody levels of neonates of different gestational periods confirm that most maternal antibody is transferred across the placenta in the final trimester of pregnancy, and that babies born prematurely have lower levels of antibody, which becomes undetectable more rapidly. Again, policy recommendation cannot be based on such small numbers, but it would appear that vaccination at an earlier age is indicated in premature babies.

In conclusion, further studies are indicated to confirm these preliminary observations using a larger sample size to determine if an earlier age of vaccination is indicated in children in a highly immunized population whose mothers have a low measles antibody titre and in premature children (defined as having a gestational period of less than 37 weeks).

REFERENCES

ALBRECHT, P., ENNIS, F. A., SALTZMAN, E. J. & KRUGMAN, S. (1977). Persistence of maternal antibodies in infants beyond 12 months. *Journal of Pediatrics* **91**, 715–718.

DEPARTMENT OF HEALTH AND SOCIAL SECURITY (1987). *Health and Personal Social Services Statistics for England.* London; Her Majesty's Stationery Office.

GERSHON, A. & KRUGMAN, S. (1979). Measles virus. In *Diagnostic Procedures for Viral, Rickettsial and Chlamydial Infections* (ed. E. H. Lennette and N. J. Schmidt) 5th edition. pp. 665–693.

KRUGMAN, S. (1977). Present status of measles and rubella immunization in the U.S....a medical progress report. *Journal of Pediatrics* **90**, 1–12.

LENNON, J. L. & BLACK, F. L. (1986). Maternally derived measles immunity in the era of vaccine-protected mothers. *Journal of Pediatrics* **108**, 671–676.

MEASLES VACCINATION COMMITTEE (1965). Vaccination against measles: a study of clinical reactions and serological responses of young children. *British Medical Journal* i, 817–823.

MEASLES VACCINATION COMMITTEE (1968). A clinical trial of live measles vaccine given alone and live vaccine preceded by killed vaccine: second report. *British Medical Journal* ii, 449–452.

MILLER, C. L. (1982). Surveillance after measles vaccination in children. *Practitioner* **226**, 535–537.

MILLER, C. L. (1987). Live measles vaccine: a 21 year follow up. *British Medical Journal* **295**, 22–24.

ROSEN, L. (1961). Haemagglutination and haemagglutination-inhibition with measles virus. *Virology* **13**, 139–141.

SHERROD, J., KANE, R., CHERRY, J., FRICKER, J. & MARPLES, K. (1983). 'Timing of measles vaccination.' *Journal of Pediatrics* **102**, 186–190.

TOIVANEN, P., MANTYGORVI, R. & HIRVONEN, M. (1968). Maternal antibodies in human foetal sera at different stages of gestation. *Immunology* **15**, 395–403.

WILKINS, J., WEHRLE, P. & PORTNOY, B. (1972). Live, further attenuated rubeola vaccination. *American Journal of Research of Children* **123**, 190–192.

YEAGER, A., HONVEY, B., CROSSAN, F., DAVIES, J., ROSEN, L. & HALONEN, P. (1983). Need for measles revaccination in adolescence: correlation with birth date prior to 1972. *Journal of Pediatrics* **102**, 191–195.