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Measles Vaccination with Reduced Dosage*

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INTRODUCTION

Widespread immunisation against measles is currently being undertaken in many developing countries with outside financial assistance. The health authorities in these countries will eventually be faced with the problem of maintaining the immunity status of their child populations once the assisted schemes come to an end.

Measles vaccine is expensive even when administered to relatively large groups of children and multidose containers are used. Containers for single or small numbers of doses are relatively more expensive, since a fairly large proportion of the total cost is absorbed in ampouling. This high cost of measles vaccine is likely to present serious problems in many areas and may deter authorities from using the vaccine (Cooper et al., 1966). If adequate immunization was achieved with a lower dose of vaccine than is currently being used, there could be a significant reduction in the cost.

It is well known that small doses of attenuated or "further attenuated" measles virus can produce infection in susceptible individuals. Karelitz et al. (1961) showed that 100 $TCID_{50}$ of attenuated virus, as assayed in tissue culture, would infect human subjects. Rey et al. (1965) obtained 95% sero-conversion rate with 100 $TCID_{50}$ of Schwarz further-attenuated vaccine, and Cooper et al. (1966) quote a personal communication from Dr. Schwarz indicating that as little as 10 $TCID_{50}$ of this vaccine, given by syringe and needle, will infect.

Hendrickse et al. (1966) noted that doses of approximately 30 $TCID_{50}$ of Leningrad 16 measles vaccines, as titrated in Hep-2 cells, produced a 78% sero-conversion rate when given by syringe and needle to a small group of children. The same group of workers (Hendrickse et al., 1967) reported promising results when small doses of further-attenuated vaccine were given by Dermojet; the disadvantage of this apparatus is that only about 0.07 ml. is delivered, and sometimes it is obvious that a substantial proportion of the dose remains on the skin. A similar observation was made by Calafiore et al. (1968), who showed that the efficacy of Schwarz vaccine was dependent not only on the dose administered in terms of $TCID_{50}$ content but also on the volume of fluid in which the virus was injected. These workers suggested that small infective doses might be satisfactory when given in a relatively large volume, but that until this had been demonstrated 1,000 $TCID_{50}$ should be retained as the standard dose.

It seemed worthwhile, therefore, to investigate the immunizing potential of reduced doses of measles vaccine administered by the same technique and under similar field conditions to those obtaining in most countries where mass vaccination campaigns are currently in progress.

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CLINICAL TRIAL

Vaccination was offered for children aged 6 months to 3 years living in a rural area of Kwara State, Nigeria. A small number who were younger than these also attended, and there were also a few who were up to 4 years old.

After registration the first 191 children had pre-vaccination blood samples taken: these were obtained by finger-prick, and the sample was absorbed on to numbered filter-paper discs which contained 0.2 ml. of blood when fully saturated. The rest of the children attending were vaccinated(see below) but no pre-vaccination blood samples were taken.

After vaccination each child was given a suitable dose of pyrimethamine to prevent any attack of malaria during the period when vaccination reactions might be expected, and was told to return to the clinic in four weeks' time, bringing the duplicate registration card. Post-vaccination finger-prick blood samples were taken from all children who had been bled initially and who returned for the second visit. Some additional post-vaccination blood samples were obtained from children who were not bled initially.

VACCINE AND ADMINISTRATION

Beckenham 31 strain measles vaccine (Wellcovax) was used. This was supplied as a lyophilized material of known viral content, which was reconstituted with distilled water immediately before the vaccination session began. Initial reconstitution yielded a suspension containing 1,000 $TCID_{50}$ virus per 0.5 ml. Further dilutions were made in distilled water to yield suspensions containing 330 $TCID_{50}$ and 200 $TCID_{50}$ per 0.5 ml. These dilutions were stored in a vacuum flask at 4°C. until used. Bleeding and vaccinating the children took a little over four hours: at the end of the session the remaining vaccine dilutions were returned, at 4°C., to the laboratory for check titration. They reached the laboratory about seven hours later, and were then frozen at -40°C. until titrated; the titration values obtained showed that there had been no loss in potency from the calculated values as a result of these procedures.

RESULTS

Over half the children were already immune to measles by the age of 3 years, and over half the children under 8 months old were also immune, in this case probably largely due to the presence of maternal antibodies. (The best age for measles vaccination in this community would therefore appear to be between 8 and 24 months of age.)

POST-VACCINATION IMMUNITY

Satisfactory paired blood samples were obtained from a total of 129 children.

There was an apparently low sero-conversion rate among the children aged 3 to 7 months given 200 $TCID_{50}$ virus. This was most probably due to a number of "non-converters" who appeared to be initially non-immune in fact, possessing titres of maternal antibodies which were too low to be detected by the laboratory methods used, but which were sufficient to inhibit multiplication of the vaccine virus. The % immune after vaccination was 94.8%.

The numbers of children in the 330 and 1,000 $TCID_{50}$ groups are very small, but when all age groups, with the exception of those aged 3 to 7 months were combined, little difference was apparent in the serological responses to the differing dose levels. The percentage immune was 95% and 100% respectively.

Post-vaccination blood samples only were only available from 37 of the children given 160 $TCID_{50}$ vaccine. The percentage immune was 87%. Though the numbers were small

there appeared to be no significant difference in the proportion of children serologically immune four weeks after receiving any of the doses of vaccine used. This would suggest that serological conversion rates are satisfactory even with the lowest doses of vaccine used, and would thus indicate that there is a reasonable margin of safety with 200 $TCID_{50}$.

CONCLUSION

While it may be desirable to confirm these results with other vaccine preparations, it would seem that the way is open for a considerable reduction in the cost per dose of measles vaccine, especially when used on a scale large enough to justify the use of multidose containers.

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