Tetanus antibodies as a marker of potential efficacy of killed polio immunization

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Summary

The use of antibodies to tetanus toxin as a marker of efficacy of parenteral immunization was examined in a randomized sample of 1212 sera representative of the total black infant population of the RSA between 24 and 35 months. All but one of these sera had protective levels of antibodies measured by enzyme-linked immunosorbent assay. In contrast, in a previous study only 59-80% had tritypic immunity to polio and 70-84% monotypic immunity. Thus, this serological marker was found to be unreliable and some possibilities for this remarkably high level of antitetanus antibodies are considered.

Collection of blood specimens

From 2 to 5 ml of clotted blood was collected from each of 1212 black infants between the ages of 24 and 35 months. Samples were drawn from throughout the country reflecting urban, semi-urban and rural communities. Random and cluster techniques were used to obtain a representative randomized sample and the 1212 specimens comprised 0.23% of the black 2-year-old population of the RSA at that time. The design of the sampling methodology used is described in detail elsewhere.

Measurement of antitetanus toxin levels

Antitetanus toxin antibodies in sera were assayed by an enzyme immunoassay technique using Dynatech (M129B) polystyrene...
micro-titre plates coated with purified tetanus toxoid at 5 LF U/ml. The technique, described elsewhere, was for routine screening of plasma for the preparation of human hyperimmune tetanus globulin for therapy. In this study, however, the limit of testing was lowered by further dilution from 1 IU down to 0,01 IU, the lowest level described as being protective. For determination of neutralizing antibody prevalence in the urban and semi-urban strata, 15 of 377 (4%) versus 41 of 538 (8%) respectively, was significant at P < 0,05 > 0,02 (chi-square test) but the difference between urban and rural strata — 36 of 277 (15%) — was highly significant at P < 0,001 (chi-square test). In contrast, this same sample of sera tested for neutralizing antibodies to polio virus in the previous study displayed considerably lower levels of immunity — 59 - 80% for trivalent immunity and 70 - 84% for mono- or bitypic immunity. 13

Vaccine distribution figures published by the Department of National Health expressed as a coverage percentage of target population of children under 1 year of age revealed figures of 90%, 72%, 66% and 62% for polio vaccine for 1 - 4 doses respectively, and 78%, 66%, 58% and 32% for DPT vaccine for 1 - 4 doses respectively. 12

Results

Of the total of the 1212 sera examined only 1 had a value of less than 0,01 IU, the minimal published protective level, indicating a virtual 100% level of immunity in the black 24 - 35-month-old community. Using a cut-off level of 0,1 IU, maintained by others to be a minimal protective level, 1 1,120 of the 1212 specimens (92%) had protective levels of specific immunity. The difference in antibody prevalence between the urban and semi-urban strata, 15 of 377 (4%) versus 41 of 538 (8%) respectively, was significant at P < 0,05 > 0,02 (chi-square test) but the difference between urban and rural strata — 36 of 277 (15%) — was highly significant at P < 0,001 (chi-square test). In contrast, this same sample of sera tested for neutralizing antibodies to polio virus in the previous study displayed considerably lower levels of immunity — 59 - 80% for trivalent immunity and 70 - 84% for mono- or bitypic immunity. 13

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Discussion

During 1983/1984 a comprehensive nation-wide serological survey to evaluate the prevalence of neutralizing antibodies to poliomyelitis virus was carried out in the RSA. Over 1200 sera were collected from black infants between the ages of 24 and 35 months. The sample was designed to be representative of black 2-year-olds in urban, semi-urban and rural communities. This survey was planned to reassess immunity to polio in the black infant population after the severe polio outbreak in Gazankulu in 1982; although immunity levels for the urban and semi-urban strata were reasonably satisfactory (80% and 71% respectively), the figure of 59% for the rural stratum gave rise to some concern. Although breaks in the cold chain were found on examination of recalled vaccine samples, a major contributing factor in the Gazankulu outbreak was inadequate vaccination. 1 Similarly, in the extensive outbreaks in Taiwan and Paraguay in 1982, the primary cause was also ascribed to vaccination rather than vaccine failure. 19,20 The valuable sample of sera collected for this survey thus became available to investigate the efficacy of reach of parenteral immunization with a view to assessing the feasibility of replacing oral polio vaccine by parenteral immunization in developing countries, as suggested by some to overcome the problem with live vaccine of viral interference. 3 The possibility of incorporating killed polio vaccine together with DPT into a tetravalent injectable vaccine has been widely suggested as an option for routine immunization in developing countries, and indeed commercial tetravalent vaccines are available for this purpose. 21,22

In the RSA routine parenterally administered trivalent DPT vaccine is given at 3 months, 4½ months and 6 months, usually together with live polio vaccine, with a booster of diphtheria and tetanus at 18 months. A booster dose of live oral polio vaccine is given at varying times, often also at 18 months. Of these three bacterial vaccines, antibodies to tetanus are the most reliably produced at higher titres and are also the easiest technically to measure 11 and for this reason were chosen as a serological marker of efficacy of parenteral immunization.

The gold standard for determining antibodies to tetanus toxin is the mouse neutralization test. However, as this test is far too cumbersome for large-scale serological testing an alternative technique had to be used. The ELISA has been shown by various workers to give excellent correlation with the mouse neutralization test and to have similar sensitivity (down to 0,01 IU). 23,24 All the tests were carried out together with a reference serum calibrated against mouse protection studies.

The serological response to tetanus immunization may be affected by various factors often present in developing countries. Low rates of seroconversion are found associated with heavy parasitic infections, especially infantile ascites. 25 Whereas some workers have found that malnutrition lowers the serological response to tetanus toxoid 26 others have found no statistically significant effect. 27 On the other hand, chronic infection of the bowel with Clostridium tetani has been shown to be responsible for prevalent natural antitoxin levels in India. 29 In the RSA tetanus is a notifiable disease, although the annual notifications to the Department of National Health are low — 271 (1980), 338 (1981), 243 (1982) and 285 (1983) (personal communication). The extent of natural infection with Cl. tetani, both clinically apparent and asymptomatic, has not been determined in the RSA, although the results of this survey suggest that it is indeed very high. Undoubtedly a substantial proportion of the subjects with antibodies to tetanus toxin developed them from natural infection rather than from immunization, since the vaccine distribution figures for tetanus vaccine are, if anything, lower than those for polio.

Although detection of antibodies to diphtheria toxoid could also possibly be evaluated for serological determination of the efficacy of parenteral immunization, it is now also doubtful whether this would give a reliable indication and alternative techniques would have to be devised to assess the feasibility of replacing oral polio vaccine with a killed vaccine. However, the important factor to be reckoned with is that the levels of immunity with killed vaccine would have to be considerably higher than for live oral vaccine because of the prominence of faecal-oral transmission of enteric pathogens under overcrowded and deprived socio-economic conditions in the developing world. Thus, while killed vaccine could provide a measure of herd immunity in developed countries because of its effect in reducing pharyngeal spread of the virus, due to its insignificant effect on faecal excretion of the virus this vaccine would provide very little in the way of herd immunity against the introduction of wild-type virus. Significantly even in a country like Finland with a high level of socio-economic development, where polio had been controlled for many years with killed vaccine, 27 introduction of wild-type 3 polio virus was able to 'ferret out' the susceptible individuals, resulting in a minor outbreak in January 1985. 28

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REFERENCES

Evaluation of child health services at Gelukspan Community Hospital, Radithuso, Bophuthatswana, 1976 - 1984

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Summary
Since the independence of Bophuthatswana in 1977 many new services have been established. The policy of the Department of Health and Social Welfare to practise primary health care has been implemented step by step and special attention has been given to the outreach to the rural and preschoo1 children. During this period several parameters of child health have been monitored, such as mortality rates, nutritional status and immunization status. In a few years significant changes have taken place.

Implementation of primary health care in Gelukspan health area
Before 1977 Gelukspan Community Hospital was a mission hospital and the health services were mainly curative. There were two paediatric wards and sick children were also treated in the outpatient department and in the 3 outside clinics. Clinics for children under 5 years old had not been developed then and little time and money was spent on prevention, for example of infectious diseases. Whooping cough, measles and advanced tuberculosis were regularly seen.

In 1978 'under-5' clinics were organized at the existing mission hospitals and one outside clinic and a mobile clinic service was started for 5 other villages. Later in the same year a new approach began. After discussions with all population under 5 years was reached (about 75% of children under 5 years never attended the under-5 clinics). In 1980 a new approach began. After discussions with all village and community leaders, it was decided to screen all children under 5 years because it was realized that many of the children seen for immunization were malnourished. Until then no record had been kept and little was known about the extent of the problem. A survey was done to establish the nutritional status of preschool children; their immunization status and socio-economic and environmental factors were also investigated.

In 1979 road-to-health clinics were introduced and a start was made with measles vaccination. At first the mothers had to buy the vaccine but it soon became freely available. The road-to-health clinics were kept and completed by the clinic sisters and only a small proportion of the population under 5 years was reached (about 75% of children under 5 years never attended the under-5 clinics). In 1980 a new approach began. After discussions with all village and community leaders, it was decided to screen all children under 5 years because it was realized that many of the children seen for immunization were malnourished. Until then no record had been kept and little was known about the extent of the problem. A survey was done to establish the nutritional status of preschool children; their immunization status and socio-economic and environmental factors were also investigated.