A FIELD EXPERIENCE OF COMBINED MEASLES, DIPHTHERIA, WHOOPING COUGH AND TETANUS IMMUNIZATION

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The safety and efficacy of Enders' attenuated live measles-virus vaccine was accepted.[1,2] The objective was a trial of mass field application of the vaccine and its combined administration with other antigens in a selected community.

The Bantu residential complex of Johannesburg covers an area of 26 square miles and houses about half a million persons. The population structure varies from recently detribalized Bantu to professional levels with academic qualification. In varying degree there is retention of Bantu tradition and concept, which is greatest in the recently detribalized and least in the higher socio-intellectual strata where the European way of life is paramount. The socio-economic advancement of this community has been relatively rapid and is generally superior to that in the Bantu homelands. The complex has a network of polyclinics acting as an integrated system with a base hospital (Baragwanath Hospital). The polyclinics operated by the Johannesburg City Council are staffed by 520 Bantu and European medical officers, health visitors, nurses and others, and, of the total, 458 are Bantu and 62 are European. These clinics provide curative, midwifery, dental, health-visitor, child-welfare, tuberculosis and immunization services; are linked by radio communication with each other, and with their midwives operating in the district, ambulance services, and the base hospital; and conduct an extensive home-visiting service by doctors, nurses, health visitors and midwives. During 1961 there were 935,052 patient-attendances, 12,135 district confinements, and 72,299 ambulance removals. In addition, private practitioners have established practices in the area.

Certain advantages were inherent in the selection of this population group for the present trial. It represented a large static community resident in an area small enough for reasonable practical control, and served by an adequate medical service which formed part of the daily life of the people and to which any markedly untoward reaction to immunization could be reported and medical advice and care obtained if necessary.

There were further specific indications for undertaking here an extensive application of measles immunization in combination with other antigens. As in other parts of Africa, measles is a greater problem among Bantu than Europeans, though in the community selected it is very much less of a hazard than for example in Nigeria[3] or in the upper Volta.[4] Nevertheless epidemics of measles are frequent in South Africa and mortality statistics fail to reflect morbidity, and frequently mortality, resulting from complications. Further, varying degrees of malnutrition in the children contribute to the severity of the illness and to a higher incidence of complications. Katz *et al.*[3] consider that in Nigeria measles is the acute infection most likely to precipitate acute kwashiorkor.

In Table I comparative mortality rates are shown for Europeans, Coloured, Asiatics and Bantu in Johannesburg. In Table II comparison is made between deaths from diphtheria and measles in the Bantu. As a result of 3 basal phases of mass immunization the number of deaths from diphtheria in 1962 was reduced to 8 among the Bantu living in Johannesburg; none of these occurred among children living in the complex under discussion, which was the area where the immunization campaigns were carried out.

TABLE II. NUMBER OF DEATHS FROM DIPHTHERIA AND MEASLES IN THE BANTU

Year	Diphtheria	Measles
1957	20	33
1958	22	52
1959	14	15
1960	24	29
1961	23	42

On the basis of clinical experience and preliminary serological studies by other workers, it was estimated that by the age of 5 years most Bantu children in the selected community had contracted measles. On these grounds, and for technical reasons, it was thought practicable to combine measles vaccination with diphtheria, whooping-cough and tetanus immunization in the age group 3 months to 2 years, in a scheduled fourth (booster) phase of a diphtheria, whooping-cough and tetanus immunization campaign, in which 3 basal phases had already been completed. In selecting this age group, consideration was given to the effect of persistent maternal antibody in the younger infants. Reilly *et al.*[5] showed that infants with detectable measles antibody of maternal origin, whether under or over 5 months of age, failed to respond clinically and serologically to live attenuated measles-virus vaccine, and that later, when maternal antibody was lost, they became susceptible to infection with the virus given parenterally. In our mass field experience vaccine would inevitably be wasted if administered to children with protective antibody levels of maternal origin or, as Bantu medical histories are notoriously unreliable, from previous infection. Moreover, the vaccine would tend to be brought into disrepute if children vaccinated against measles while they still had protective maternal antibody titres subsequently contracted the disease on exposure to natural infection. However, it was felt that maternal antibody would be lost by 6 months of age, that infants of younger age who possessed it would do so in varying degree, and that in those with lower levels the result would be similar to the modifying effect of gamma-globulin when co-administered with measles vaccine. In a mass campaign involving thousands of inoculations of measles vaccine, antibody estimations were impracticable; and, apart from impracticability, our experience of rural and urban Bantu communities is that, though venipuncture is acceptable in small clinical trials, yet in pilot probes just before a mass campaign, or during a mass campaign, it should be rigorously avoided. This opinion was supported by Katz *et al.*[3] in their Nigerian experience, where they found

TABLE I. DEATHS FROM MEASLES (NUMBER AND RATE) FOR 5 YEARS

Year	Europeans		Coloured		Asiatics		Bantu		Total	
	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate
1957	1	0·003	2	0·06	1	0·04	33	0·07	37	0·04
1958	2	0·005	1	0·03	1	0·04	52	0·10	56	0·06
1959	Nil	Nil	2	0·05	Nil	Nil	15	0·03	17	0·02
1960	2	0·005	7	0·16	Nil	Nil	29	0·06	38	0·04
1961	Nil	Nil	3	0·07	Nil	Nil	42	0·08	45	0·05

that parents were quite unwilling to have blood taken from their children, and where in their later studies they ceased to urge bleedings on an unwilling population. It was thus essential in our undertaking to give measles vaccine to all children in the age group in which the most susceptibles were to be found.

Multiple immunization techniques are of especial significance in Africa, where communities are frequently in need of mass immunization, and where conditions often preclude a satisfactory return on numerous occasions for different inoculations. In South Africa, Spencer and Coster[6] showed that smallpox vaccination could safely be combined with triple vaccine in mass immunization, and Winter *et al.*[7] subsequently showed that immunization against poliomyelitis, diphtheria, whooping cough, tetanus and smallpox could be successfully combined. The combination of measles vaccine with triple antigen was therefore a further step in a necessary direction. Only one inoculation of live attenuated measles-virus vaccine is necessary for protection.

Taneja considers that mass trials are desirable in various parts of the world with different population groups and environmental and socio-economic conditions.[8] Weibel *et al.*[2] report that among susceptible children given Enders' attenuated live measles-virus vaccine, without gamma-globulin, 80% develop a temperature over 100°F. and 20% 103°F. or higher, and that 45% develop a rash. Similarly the Advisory Committee on Measles Control[1] states that when it is administered without gamma-globulin, although in the majority symptoms are minimal, pyrexia of 103°F. or higher may occur in 30 - 40%, beginning on the 6th day and lasting 2 - 5 days, and a rash in 30 - 60% beginning with or after the subsidence of fever. Observers comment on the striking lack of disability in children with reactions. If gamma-globulin in recommended dose is given at the same time as the vaccine, reactions are greatly reduced in incidence and intensity; but this addition was found to be impracticable in the present trial, in which live measles-virus vaccination was combined in a fourth (booster) triple-vaccine immunization campaign for which planning, organization and propaganda were already complete.

Consideration was given to the contraindications to measles vaccine. Though no reports were found in the literature describing concurrent immunization with live measles-virus vaccine and diphtheria, whooping-cough and tetanus antigens, there appeared no valid reason against it. Though difficult under field conditions, every effort was made in mass campaigns to exclude any child who was febrile or appeared ill or where any such history was obtainable. The following were considered to be specific contraindications to measles immunization in the selected age group 3 months to 2 years: marked egg sensitivity, neomycin sensitivity, depression of resistance by steroid therapy, and leukaemia or other malignancies. The hazard of egg sensitivity was slight. Children with antibiotic sensitivity, or undergoing steroid therapy by the hospital and clinic services, are given bracelets on which data are recorded, though they will not necessarily always wear them. In view of the medical services available the possibility that children with known leukaemia or malignant disease might present for immunization seemed minimal.

Broadly the procedure adopted was modified to the circumstance.

A PRELIMINARY EXPERIENCE OF MASS IMMUNIZATION

Routine diphtheria immunization services at clinics in 1960 resulted in only 5,537 completed courses in the Bantu residential complex. This and other unsatisfactory features necessitated a reassessment of established practice.

There were 2 primary observations: (a) However diligently routine immunization at clinics was pursued only a small fraction of the population was immunized. (b) Panic attendances during an outbreak of epidemic disease were of little value. Large, near-uncontrollable numbers presented at the immunization centres, and as the impetus of fear subsided numbers rapidly dwindled. The seemingly impressive number of inoculations tended to originate from localized areas near to the centres and was inadequate in comparison with the total population at risk.

Possible causes were considered. Distances, straitened family circumstances, and transport problems, made it difficult for mothers living far from immunization centres to abandon their homes, cover the distances involved with their children, stand in queues of hundreds in panic situations, and return late to their homes and domestic chores. Similar factors operated at clinics under non-panic conditions of routine immunization, and under panic conditions also affected adults who desired immunization, though to a lesser extent. It was evident that the willingness of the people to cooperate would permit of a more effective organization if these factors could be overcome.

We concluded that routine clinic immunization services would continue to form the foundation of immunization procedure and that an increased health-visitor service would expand clinic immunization on a domiciliary basis. However, in the threat of epidemic, or when boosting was necessary, mass immunization had to be brought to the people by teams operating on a street-to-street basis with an assurance that immunization would be available within a specified time to all who needed protection. Panic reaction and huge queues at isolated points had to be replaced by a calm community to whom immunization would be brought as near their homes as possible and to schools and crèches.

These principles were adopted in this Bantu complex in the administration of 3 feeds of trivalent oral poliomyelitis vaccine in 1961. The target age group was 3 months to 9 years. Nineteen mobile teams and 13 at other centres, were used. The totals of feeds given in the 3 phases were 83,958, 91,035 and 88,847, being 81%, 90% and 86% of the estimated target. (Oral poliomyelitis immunization of the newborn has since been maintained in this area.) The results were encouraging. A frustrating feature, however, was the overlapping of areas in practice, however carefully they were allocated to teams, and the flux of persons passing from one area to another in their desire to be immunized. It was obvious that to overcome these difficulties the allocation of areas to teams would, in addition, need the plotting of times and places of stops on individual team field-maps, together with the homes to be immunized at each stop during the whole operative period of a phase, and the people informed in advance of the scheduled date of arrival of a team in their environs. The areas and movement so defined would have to provide a single, uniform, advancing progression of teams through the entire area. People had to be persuaded to wait at their houses for teams to come to them.

Apart from determining the rate of operation of a team, the card record system used proved particularly valueless because it was almost impossible to relate any individual to a card for long periods after the campaign. Clearly, therefore, a system of simple record books for each team had to be devised whereby every individual inoculated could be easily related subsequently in each phase to his recorded entry. It required an address for each of the 70,000 houses in the area opposite which details of immunization and consent for each child and phase could be tabulated. These books could then later be issued to clinics serving the areas recorded in a specific set of books, and be retained for reference purposes.

There was need for fewer but more effective teams. Six mobile teams operating from vans equipped with public-address systems and 2 school and crèche teams were considered sufficient. In instances when children were not at home when teams called at their houses referral slips would be left with which they could report at clinics for inoculation.

There was increasing evidence that propaganda methods suitable for Europeans were not the best for our Bantu communities, and that posters and radio press and magazine announcements were not necessarily interpreted in the manner intended. Word of mouth by those who knew, notably Bantu medical, nursing and clinic personnel, and the families of those safely inoculated, remained the most powerful channel for the majority, coupled with a forthright, simple presentation of essential facts in brief circulars in Bantu languages to every householder and parents of school and crèche children, and in letters to school principals and crèche supervisors. Private practitioners and hospitals were to be kept informed.

These conclusions were precisely incorporated in a diphtheria, whooping-cough and tetanus immunization campaign, and proved completely satisfactory, especially since it was more complex than the oral poliomyelitis immunization campaign and required administration of antigens by hypodermic injection. The 3 basal phases were completed in 15 working days each, in December 1961, February 1962 and April 1962, when 80,657, 85,475 and 74,945 children, being 81%, 85% and 75% of the estimated possible target, were inoculated in the selected age group 3 months to 9 years. In addition, 158,964 persons of all ages were vaccinated against smallpox in the second phase. Children aged 3 months to 2 years received triple antigen and those in the age group 3 years to 9 years received only diphtheria and tetanus prophylactic. No untoward reactions were reported except 1 urticarial response and 3 abscesses at the site of injection. Observation during the ensuing year showed no detectable increase of serum hepatitis. Syringes were boiled at regular intervals only, but a sterile needle was used for each individual and operators were directed to avoid drawback into syringes after insertion of the needle. The obtaining and recording of consent in every case introduced an essential element of trust in the minds of an urbanized Bantu population.

The fourth (booster) phase of the campaign was scheduled for a year later, and combination of measles vaccination in this phase would therefore meet a population conditioned to mass immunization procedure. Thus the method evolved was an adaptation to meet the particular circumstances and epidemiological needs of a specific community that was similar to many others in Africa.

THE PILOT PROBE

It has been our custom before introducing any new undertaking to submit pertinent data to regularly held discussion groups attended by less senior medical field workers. Bantu participants have usually given a reflection of views or reactions to be expected from the community, thus stimulating confidence, or producing modification or withdrawal of the proposal. They thought that measles vaccination would be acceptable, notwithstanding moderately severe clinical reactions in a proportion of cases, but they emphasized that parental and community reaction to these clinical manifestations, and not the manifestations themselves, was the decisive factor. They recommended that a pilot survey of these attitudes should be completed, and that, if opinion was adverse, administration of the vaccine should be withheld. The purpose of the pilot project was therefore a preliminary assessment of (*a*) concurrent administration of measles vaccine, given without gamma-globulin, and diphtheria, whooping-cough and tetanus antigens, and (*b*) parental reaction to the procedure.

The measles vaccine was Enders' attenuated dried live virus (Edmonston strain), and the triple antigen was purified diphtheria and tetanus toxoids adsorbed on aluminium phosphate, with killed Bordetella pertussis organisms.

The random sample chosen consisted of 100 children in the age group 3 months to 2 years 11 months. It represented a sample of subjects expected in the mass phase, and included various nutritional states and social, economic and intellectual strata; it deliberately excluded any enquiry whether the subjects had suffered from measles or not. The undertaking was clearly explained to the mothers in their own language, and they were told that reactions of variable severity to the measles vaccine would occur in some children. Consent was requested in all cases and refused in none.

Clinical Reactions

Inevitably the clinical reaction survey was of limited accuracy owing to factors such as intercurrent infection, even if the excess were to be calculated above a 'norm'. Further, the incidence of intercurrent infection of a respiratory nature was high in the colder early months of winter, in which the pilot probe and mass phase took place. In addition, non-susceptibles with residual maternal or naturally acquired measles antibody were included. However it indicated what could be expected in the mass field experience to follow.

The measles vaccine was stored at —20°C. and reconstituted with sterile water immediately before use. Syringes and needles free of detergent and antiseptic were provided throughout, with complete separation in sterilization and use of equipment between measles vaccine and triple antigen, thus avoiding contamination of the virus with the formalin content of the antigen.

Each child received subcutaneously 0·25 ml. of measles vaccine in the left arm and 0·5 ml. of triple antigen in the right. Every mother was requested to advise the clinic of any untoward reaction in the ensuing week, as reaction to the triple antigen was likely to occur 48 hours after inoculation, and to bring their children to the clinic on the 7th postvaccinal day for assessment of clinical reaction to the measles vaccine. In cases where mothers failed to present with their children on the 7th day, the children were visited in their homes by two of us. All children in the sample who showed any clinical reaction were observed by the same two medical officers, assisted by the health-visitor service, during the 7th - 14th postvaccinal days at the clinic and in their homes. Clinical reactions in this period are summarized in Table III. The pattern of reaction to the measles vaccine appeared to fall within the range reported by other workers, and no indication was noted of adjuvant or adverse effect on reaction severity to measles vaccine or triple antigen caused by combination of the two.

TABLE III PILOT SURVEY: ANALYSIS OF REACTIONS TO COMBINED IMMUNIZATION

	3 – 6 m. %	*7 – 9 m.* %	*10 m. – 2 yr.* %
Pyrexia less than 102°F. ..	21	30	45
Pyrexia over 102°F.	11	10	4
Rash	18	20	17
Coryza	25	25	45
Conjunctivitis	2	5	33
Cough	48	40	67
Vomiting	16	5	8
Diarrhoea	18	5	29
Anorexia	9	10	4
Restlessness	9	20	8
Epistaxis	2	—	—
Local reaction	—	—	8

The percentile occurrence of a rash in the 3 age groups in Table III suggested that residual maternal antibody could be evaluated in terms referred to in the earlier part of this communication.

Parental Reactions

This part of the survey commenced after all clinical reaction had subsided and was limited by the few days available before the beginning of the mass phase. It comprised the parents of 25 children who had shown reac-

tions in the pilot probe and the parents of 25 who had not. As reactions had varied from mild coryza and minimal indisposition to pyrexia greater than 104°F., it was not possible to choose a random sample of parents of reactors, and selection was based on a median representation of reaction from the mildest to the most severe. The selection of parents of non-reactors was truly random.

Two health visitors, a European and a Bantu, carried out the assignment. The former was responsible for organization, while the latter, avoiding leading questions, obtained statements from parents and recorded them virtually *verbatim*. To obviate the naturally courteous desire of Bantu to give to non-Bantu persons answers most calculated to please the interrogator, the European health visitor did not enter homes to assist in interviewing parents.

Critical analysis of replies showed uniformity of opinion in the 4 main groups of Zulu-, Shangaan-, Xhosa- and Sesutho-speaking people. There was remarkable confidence in any injection or measure for protection, and recurrent comment that children were well and free from the diseases against which they had been immunized. In our opinion, the skein of protection against adverse influence woven into the fabric of African tribal medicine has facilitated acceptance of immunoprophylactic technique.

In both samples parents made it clear that a degree of indisposition after inoculation was to be anticipated, the view being held that immunization kills disease and 'nothing can die without a little struggle'. They thought that measles killed many children, and dreaded it and its complications more than they did diphtheria. There was an almost constant opinion that 'if the rash does not appear well on the body it remains inside, damages the lungs, and the child dies'. In some homes they still had the shrub used in their treatment of measles and believed to bring out the rash. They held it necessary that the measles should be driven out. Following this concept the whole propaganda approach to measles vaccination for the mass phase was based on the injection driving out the disease.

There was some confusion among mothers of reactors who did not develop a rash. Mothers whose babies had no reaction at all, in the main, considered that the dose of vaccine was so accurately measured for their particular children that it caused no reaction, that as their children did not become ill second doses might be necessary to make the vaccine effective, or that their babies were so strong that they did not seem ill after the vaccination.

In both groups of the total sample, even in cases of relatively severe clinical reaction, there was unshaken trust in straightforward immunization, and complete acceptance of the introduction of measles vaccination.

THE FIELD EXPERIENCE

Propaganda and organization were as outlined above. Routine immunization with diphtheria, whooping-cough and tetanus antigens, and smallpox and BCG vaccination, was discontinued 1 month before the phase in order to eliminate field problems related to multiple use of upper arms. All teams carried resuscitatory and antihistaminic drugs and equipment. Measles vaccine was given on the left arm, and triple or diphtheria and tetanus antigens on the right. Measles vaccine was administered entirely by medical officers, and diphtheria, whooping-cough and tetanus antigens by nursing staff under their surveillance. The precautions taken in the pilot probe were maintained in the mass phase. Dried measles-vaccine supplies were refrigerated at —20°C., and teams carried their issues for estimated 6-hourly periods of requirement in fibre-glass bags packed with 'dry ice'. As the vaccine contained no preservative other than residual neomycin, special caution was taken with multiple puncture arrangement of the multi-dose vials, which required reconstitution of the vaccine by the addition of 8 ml. of sterile water. In general, vaccine in a vial was not reconstituted until sufficient vaccinees had collected, and when this was impracticable the reconstituted vaccine was stored at about 4°C. in the fibre-glass containers and discarded if not used within 8 hours. A record relating vaccine batch numbers to vaccinees was kept. Detailed reaction survey forms to be completed by examining medical officers were issued to the clinic and hospital services of the area.

Each child in the age group 3 months to 2 years 11 months received 0·25 ml. of measles vaccine and 0·5 ml. of triple antigen, and in the age group 3 years to 9 years 11 months 0·5 ml. of diphtheria and of tetanus antigens.

The functioning of the organization, comprising 80 personnel and 16 transport vehicles, was uneventful. It completed its assignment in 14 working days between the scheduled dates 6 and 24 May 1963.

Statistical Results

105,636 inoculations were given. Details are tabulated in Table IV. The 21,947 children inoculated with triple antigen received measles vaccine at the same time, and

TABLE IV. IMMUNIZATION CAMPAIGN, FOURTH PHASE

	Antigens			*Measles vaccine*	*Total inoculations*
	DWT 3 mth. to 2 yr.	*DT 3 yr. to 9 yr.*	*Total*	*3 mth. to 2 yr.*	
Inoculations ..	21,947	61,400	83,347	22,289	105,636
Percentage of estimated target ..	73·2%	87·7%	83%	74·3%	

DWT = diphtheria, whooping cough and tetanus immunization
DT = diphtheria and tetanus immunization

342 more children received measles vaccine alone because they had inadvertently been given a booster injection of triple antigen at a clinic shortly before the phase began.

It was found usual in all phases of the campaign to achieve a higher percentage of the estimated target in the age group 3—9 years than that of 3 months — 2 years. Children of the older group were more easily reached in crèches and schools than those of the younger group, where mothers were often unwilling to bring their children to teams in inclement weather, and where the occupants were often found away from homes and failed to report at clinics for subsequent inoculation.

Reported Reactions

There was a fundamental difference in assessing clinical reaction in the pilot probe and in the mass phase. In the pilot probe all the vaccinees were examined for reaction.

whereas in the mass phase cases were brought for examination only when parents thought that the severity of reaction rendered it advisable to seek medical aid. Parental opinion in the pilot probe clearly indicated that a considerable degree of incapacitation would be accepted as a normal sequel to immunization. Thus the study of reactions in the mass phase merely indicated the degree of clinical reaction found in those who were brought for examination.

An analysis of symptoms in the 333 children whose parents considered this necessary is represented in Table V; 43 were aged 3 - 6 months, 38 7 - 9 months, and 252 10 months to 2 years 11 months. Generalized reaction attributable to triple antigen was insignificant, but 9

TABLE V. FIELD EXPERIENCE: ANALYSIS OF REACTIONS TO COMBINED IMMUNIZATION

	3–6 m. %	*7–9 m.* %	*10 m.–3 yr.* %
Pyrexia less than 102°F.	51	15	49
Pyrexia over 102°F.	14	24	25
Rash	37	45	52
Coryza	49	42	54
Conjunctivitis	14	32	38
Cough	60	76	81
Vomiting	2	21	11
Diarrhoea	26	34	21
Anorexia	19	24	27
Restlessness	33	28	31
Convulsions	—	8	4
Local reaction	16	—	6

local abscesses were reported, all on the right arms and related to triple antigen. The incidence of local infective reaction was thus higher than in the combined 3 basal phases of the campaign, but it was nevertheless thought to be low in view of the conditions of high wind and incessant dust which, with later cold and rain, dogged the 4th phase.

The reactions in Table V are broadly related to measles vaccine, within the limits of unassessable intercurrent infection and insignificant reaction to triple antigen, and the extent of occurrence in 3 age groups of symptoms is shown.

Of the 333 children brought for medical advice, 37 were found to have rectal temperatures over 102°F., 23 over 103°, 13 over 104°, and 3 over 105°. Further, 4% were reported to have had convulsions, apparently pyrexial in origin. No convulsions were reported in the pilot probe. Reference to pyrexial convulsion in measles vaccination was made by Goffe *et al.*[9] and Markham *et al.*[10] Tympanitis featured prominently in reaction survey reports by medical officers, among whom were several who considered reactions rather severe and approximating to natural measles. It was not thought possible to attempt an analysis on the basis of reaction severity, owing to the difficulty of determining suitable criteria and eliminating the variable of multiple examiners. However, in general, the degree of incapacitation was little in relation to the degree of clinical reaction, and only in 333 out of 22,289 vaccinees (i.e. 1·5%) did parents think symptoms sufficiently marked to seek medical advice. None of the classical complications of measles were reported after vaccination and there was no evidence of secondary cases. Combination of triple antigen and measles vaccine appeared to have no adverse effect on reaction.

In one instance an 11-months-old infant inoculated with triple antigen and measles vaccine the preceding afternoon died on the following morning. The mother stated the child was well when she took it for immunization. At autopsy the cause of death was lobar pneumonia in grey hepatization and gastroenteritis. Death was apparently not related to immunization. The result of virology studies was not available at the time of writing. The case emphasized the possibility in mass immunization that a child may be brought for immunization with established acute respiratory disease, where the symptoms are so masked by chemotherapy that the parent considers the child well enough for immunization and the history not significant enough to mention. One other child who received triple antigen and measles vaccine died in hospital of unrelated disease. Permission for an autopsy was refused.

Only 3 European children received measles vaccine in this study. The 15-months-old son of one of us received measles vaccine without gamma-globulin, and was a healthy, well-nourished infant, immunized against diphtheria, whooping-cough, tetanus, smallpox and poliomyelitis, and without any history of previous illness whatsoever. A maximum rectal temperature of 106·4°F. was recorded on the 8th postvaccinal day during 4 days of pyrexia, which was followed by a generalized morbilliform rash between the 10th and 12th postvaccinal days. Aspirin and sponging were necessary for pyrexial control on the 8th postvaccinal day, but no other therapy was required. Except at the time of maximum pyrexia, when the child was obviously incapacitated, the disability was relatively slight. Two children of one of the team medical officers—girls aged 1 year 9 months and 3 years 4 months—were also given measles vaccine without gamma-globulin. One developed a maximum rectal temperature of 104·8°F. on the 8th postvaccinal day during 4 days of pyrexia, and the other 102·6°F., with a generalized morbilliform rash.

Community Reaction

Immunization against measles in the mass phase appeared acceptable to the Bantu community, and parental reaction paralleled that obtained in the pilot probe.

CONCLUSIONS

The concurrent administration of live attenuated measles-virus vaccine with triple antigen proved safe in the study described.

Under the presenting conditions of mass inoculation the use of gamma-globulin was impracticable. In these circumstances, and in a proportion of cases, clinical reactions to the measles vaccine tended to be rather severe for a routine immunization procedure.

The incidence of intercurrent infection in winter months suggested the advisability of conducting mass measles immunization in months when these conditions are less prevalent.

The relatively slight incapacitation associated with high pyrexial levels found in instances after live measles-virus immunization may have produced insufficient maternal care of some poorly nourished and ill-clad children, with risk of exacerbation of existing disease or lowered resistance to other infection.

Maintenance measles immunization of the newborn, on their reaching the selected age group, will become neces-

sary if immunological advantage gained by mass immunization is to be retained.

While mass vaccination campaigns with live attenuated measles virus without gamma-globulin appear justified where measles is a critical problem, in communities at intermediate risk consideration should be given to combination schedules[1] of an inoculation of inactivated measles vaccine followed 2 months later by an injection of live attenuated measles-virus vaccine. Reactions would be minimal and, though the duration of antibody persistance is not yet definitely determined, protection would seem very satisfactory. Moreover, it would permit of combined administration in diphtheria, whooping-cough and tetanus immunization programmes. In other circumstances, where measles is a lesser health problem, there would appear to be no indication for mass immunization, and live attenuated measles-virus vaccine should be administered with gamma-globulin and possibly reserved, at this stage, for cases at high medical risk should they contract natural measles infection.

SUMMARY

1. Immunization with combined live attenuated measles-virus vaccine and diphtheria, whooping-cough and tetanus antigens in an urban Bantu community is described.

2. The development of immunization procedure to meet the epidemiological needs of the community is outlined.

3. A pilot survey and field campaign of combined immunization is discussed.

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REFERENCES

1. Advisory Committee on Measles Control (1963): J. Amer. Med. Assoc., **183**, 120.
2. Weibel, R., Halenda, R., Stokes, J., Hilleman, R. and Buynak, E. B. (1962): *Ibid.*, **180**, 1086.
3. Katz, S. L., Morley, D. C. and Krugman, S. (1962): Amer. J. Dis. Child., **103**, 402.
4. Medical News (1963): J. Amer. Med. Assoc., **184**, 44.
5. Reilly, C. M., Stokes, J., Buynak, E. B., Goldner, H. and Hilleman, M. R. (1961): New Engl. J. Med., **265**, 165.
6. Spencer, I. W. F. and Coster, M. E. E. (1962): S. Afr. Med. J., **36**, 881.
7. Winter, P. A. D., Mason, J. H., Kuhr, E., Schaafsma, A. W., Robinson, M., Saayman, L. R. and Spence, R. G. (1963): *Ibid.*, **37**, 513.
8. International Conference on Measles Immunization (1962): Amer. J. Dis. Child., **103**, 431.
9. Goffe, A. P., Woodall, J. T., Tuckman, E., Paulett, J. D., Manser, I. N., Franklin, L. M. and Chapple, P. A. L. (1963): Brit. Med. J., **1**, 26.
10. Markham, F. S., Cox, H. R. and Reugsegger, J. M. (1962): Amer. J. Publ. Hlth, **52**, suppl. 2, 57.