

SPECIAL ARTICLE

Design of Immunization Programmes for Developing Countries

by

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Introduction

In areas, population groups or countries where health manpower and material resources are limited, the communicable diseases normally constitute a significant problem and immunization programmes are of special importance. Effective, alternative approaches for the prevention of most diseases are not at the moment available or economically possible, as, for example, the development of safe water supply systems to prevent typhoid. Health personnel and facilities are limited

which necessarily restricts what can be done in the isolation and treatment of patients, procedures which can be of considerable importance in the control of many diseases.

While programmes of immunization represent, by and large, one of the most productive public health investments which any country can make to improve the health of its people, immunization programmes in the developing countries have, to date, remained comparatively limited in scope and have generally been restricted to a few antigens. There

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are many reasons for this but a few of the major contributing factors should be noted as they have a bearing on the design of effective programmes.

Important limiting factors in the development of immunization programmes Relative development of health services.

In the developing countries, physicians and other health personnel are inadequate in number and often taxed to meet minimum demands of curative services; health centres are widely scattered.

Immunization programmes, such as those in the developed countries, which depend on individuals attending health centres, have generally produced disappointing results. Vaccination coverage, while sometimes satisfactory in the immediate area of a health centre, has been found to decline sharply in persons living no more than 2 to 3 miles away (Keja, 1970; Kimmance, 1970; Kreysler, 1970).

Facilities for the refrigerated storage of vaccine are usually limited, making it difficult to conduct effective programmes which employ such thermolabile vaccines as measles and poliomyelitis.

Costs of vaccines and their application.

Vaccine cost is a major concern. Since, in many countries, the expenditure for all health programmes does

not exceed \$ 2.00 per person per year (Charles, 1970) it is apparent that, however effective a vaccine, it must be comparatively inexpensive if it is to be widely employed. In general, when vaccine costs more than \$. 100 per dose, it is beyond the financial resources of most developing countries. Even for the less expensive vaccines, limitations of budget and foreign exchange may prelude purchase.

As vaccine cost a great deal more when packaged, for example, in vials of 2 or 5 doses than in vials of 25 doses or more, many health administrators, in an effort to economize, have purchased the larger containers for use in health centres. Frequently in the health centres, only a few persons are vaccinated each day and, with unsatisfactory facilities for refrigeration, the vaccine deteriorates, resulting in many being vaccinated with ineffective vaccine.

Vaccine quality has been a special problems. Most countries are not able to establish competent independent national testing centres. Many vaccines produced nationally and some which are imported are known to be sub-standard. On many occasions, considerable expense has been incurred in vaccination programmes in which the vaccine used has been imported.

The cost of instruments to administer vaccines may also be a problem, particularly as foreign exchange is usually required for purchase.

The cost of disposable syringes and satisfactory durable jet injectors is so great as to preclude their use in most developing countries. Continuing maintenance of the jet injectors has proved difficult. Single dose syringes are similarly a luxury which most cannot afford. Multiple-dose syringes, although undesirable because of the intrinsic risk of possible transmission of serum hepatitis, are frequently the only economically practicable and available instruments for subcutaneous or intramuscular administration of vaccines.

Other difficulties.

Transport, whether for distribution of vaccine or of vaccinators or of vaccinees, is frequently a problem due to lack of vehicles and/or fuel, as well as satisfactory roads. Illiteracy may be prevalent making it difficult to convince the population of the need for vaccination, at least by conventional methods of health education as practised in the developed countries. The possibilities for publicity through radio and other, conventional news media may be more limited and information provided may not reach beyond the already educated and persuaded. Thus, many techniques and approaches to immunization which are effective in the more developed countries are less applicable to the developing countries.

Design of immunization programmes for the developing countries.

The decision as to which vaccines should be administered, to whom and according to what schedule must be considered in relation to a number of factors including the relative importance of the disease; the effectiveness and cost or available vaccines; possibilities for the financing of vaccine purchase or production; resources for testing of vaccines to assure purity and potency; feasibility of vaccine administration by various alternative approaches such as in health centres, in mass campaigns or by individual vaccinators; methods for supervision and assessment of programmes; availability of central and peripheral refrigerated storage facilities; and the costs and financing of instruments to administer vaccines.

Selection of vaccines for immunization programmes.

Taking into account the various factors elaborated above, the available vaccines may be considered in four general categories. The rationale for the assignment of vaccines to each of these groups is set forth in Annex 1.

1. Vaccines recommended for general use in developing countries.

- Smallpox BCG Pertussis
- Diphtheria Tetanus Typhoid
- Measles (Rubeola)

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(Assuming substantial reductions in cost of measles vaccine or provision through international assistance).

2. Vaccines recommended for use under special circumstances:

Poliomyelitis and Yellow fever

3. Vaccines not recommended for routine use in the developing countries:

Rubella (German measles), Mumps, Influenza and other respirovirus vaccines, Cholera.

4. Vaccines in the development stage which may in the future be applicable for use among populations at special risk:

Arbovirus	Meningococci
Rickettsiae	Plague
Trachoma	Shigella

Procurement of vaccine

Vaccine cost is particularly important consideration in the developing countries, a consideration which is frequently complicated by restrictions in the availability of foreign exchange. These problems may, in part, be overcome if vaccines can be inexpensively produced locally or better, on some sort of cooperative regional basis. Production of bacterial vaccines (diphtheria, pertussis, tetanus, typhoid) involves a less complex technology than for live virus vaccines such as poliomyelitis and measles. These could be relatively inexpensively produced in mode-

rately well-equipped and staffed laboratories in developing countries. Smallpox vaccine is now produced in several developing countries and is available to most others through donations made to WHO or through bilateral assistance; BCG vaccine is being supplied to many countries through UNICEF.

Production of poliomyelitis and measles vaccines is technically far more difficult and their production in the developing countries, except in a few special cases, is not a practicable proposition. To reduce costs and foreign exchange requirements, a very few large regional production centres might be considered. Alternatively, both these vaccines as well as other vaccines might be purchased in bulk form from major producers and packaged locally.

Quality control of vaccine

Illustrative of the importance of the quality control of vaccines in the fact that, at the beginning of the global smallpox eradication programme, not more than 10 to 15% of vaccine in use in endemic countries met WHO recommended standards. The present status with respect to other vaccines in routine use in developing countries may not be different. Thus, provision must be made for routine testing of all vaccines at a competent independent national testing centre or at an international centre.

Packaging of vaccine

It is commonly believed that if vaccine is supplied in single dose containers for use in health centres, hospitals, etc., vaccine wastage may be sharply reduced. While wastage may, in fact, be reduced, the cost of preparing vaccine, for example, in 1, 2 or 5 dose containers, is considerable compared to the cost for each dose of vaccine prepared in 10, 20 or 100 dose containers. This fact alone recommends the design of immunization programmes which permit the use of larger multiple dose containers of vaccine.

Administration of vaccine

With the exception of smallpox vaccine which is administered by the bifurcated needle and polio vaccine which is administered by mouth, all vaccines in routine use are administered by syringe and needle or the jet injector. Presently available jet injectors are not fully satisfactory as they are expensive, difficult to maintain and repair and several are not sufficiently sturdy for routine field use. For efficient use of the injectors, large numbers are required to be immunized each day. Single dose glass or plastic disposable syringes are usually employed in the developed countries to ensure particularly that the virus of serum hepatitis is not, by chance, transmitted from one to the next. While technically sound, the cost of this approach has precluded its use in most

developing countries. Until a more effective and inexpensive means of vaccine administration can be found, the use of 5 or 10 dose glass or nylon syringes employing separate needles for each recipient, would seem at the point to be the only economically practical means of vaccine administration in most developing countries.

Possible schedules of immunization

In the developed countries, model vaccination schedules call for vaccination on as many as 10 to 15 different occasions between birth and 5 or 10 years. Such is not reasonable in the developing countries where visits to health centres are sporadic and touring vaccinators or vaccination teams may reach village or towns not more than once in one or two years.

Simultaneous administration of several antigens may in part, reduce the number of visits required. A considerable number of studies have now been done which indicate no impairment in vaccine efficacy or increased risk of adverse effects when a number of different inactivated and live antigens are simultaneously administered.

Reduction in the usually recommended number of injections of the killed antigens, such as diphtheria, pertussis, tetanus and typhoid, constitutes a second approach which may permit a reduction in the number of required visits. In the deve-

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veloped countries, 4, 5 or 6 injections of the inactivated antigens are usually recommended. However, each additional inoculation after the second or third improve only fractionally the level of protection. Where cost of vaccine and vaccine administration is a minor consideration, such additional inoculations may be justified. In the developing countries, however, the cost of each additional inoculation must be carefully weighed in terms of the additional protection conferred.

Finally, the inactivated vaccines (diphtheria, pertussis, tetanus, typhoid) may be combined in a single preparation thus reducing the cost of administration and of instruments. In most programmes, the single combined product could be administered to all children in an immunization programme.

However, other mixtures of vaccines, such as smallpox-measles, have proved to be of limited value in routine programmes. In the instance of a programme administering measles and smallpox vaccines for example, it is necessary to have smallpox vaccine as a separate preparation for vaccination of those younger than 6 months and older than four years.

Having the mixture available adds very little as, in either instance, two preparations are required in the programme and the added cost of preparation of a combined smallpox

measles vaccine, for example, is not justified by other savings. With other mixtures of live virus preparations, similar problems pertain and, in fact, a mixture of yellow fever and smallpox vaccines results in a lower proportion of seroconversions to the yellow fever vaccine (Meers, 1960; Meyer et al., 1964) although administration at the same time but at different sites produces a satisfactory response.

A virtually infinite number of vaccination schedules could be prepared, each with its relative merits and demerits. Taking into account the various factors bearing on the optimal time for vaccination, the relative risks of the diseases at various ages (Annex II) and the costs and benefits of multiple inoculations, three schedules are set forth below as illustrative of simplifications which might be achieved.

In Schedule A, quite acceptable levels of protection could be afforded against the seven diseases in Group I in four immunization sessions, one of which is timed to coincide with the time of school entry.

Schedule B might be considered for a programme of immunization in which mobile vaccination teams were able to visit each area only once in two years. It is recognized that protection against diphtheria, pertussis and tetanus would not approach satisfactory levels until after the se-

cond session and protection against poliomyelitis and, in some, against measles would not be optimum. However, such a programme would in fact, confer substantial protection to a considerable proportion of the children.

Schedule C — for countries which are non-endemic for smallpox, and thus where early vaccination is less critical, a simplified programme has been suggested in which the BCG vaccination scar could be used as one "maker" to indicate that a group of antigens had been given and the smallpox vaccination scar to indicate that the second group of antigens had been administered. The scars could serve effectively as vaccination certificates for administrative and assessment purposes. As in Schedule B, protection afforded is not opti-

mum, although one would anticipate that a very substantial reduction in incidence might be achieved in respect to each of the diseases.

Prevention of neonatal tetanus

Because of the importance of neonatal tetanus in all developing countries and the fact that it can be readily prevented if the mother has been protected by at least two injections of tetanus toxoid, special provisions should be made for administration of tetanus toxoid to adolescent girls and women in the child-bearing years.

Place of vaccination

While in the developed countries, vaccination is usually performed in a clinic or physician's office, satisfactory coverage cannot be achieved

Schedule A

1-3-months DPT ¹ -Typhoid	4-8 months DPT ¹ -Typhoid	9-12 months	5-6 years DPT ¹ -Typhoid
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Vaccines — Group I

Smallpox ² BCG ²		Measles	Smallpox
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Vaccines — Group II

Polio ³	Polio ³	Polio ³	
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Schedule B

0-24 months DPT ¹ -Typhoid	2-3 years DPT ¹ -Typhoid	4-5 years DPT ¹ -Typhoid	
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Vaccines — Group I

Smallpox ² BCG ²		Smallpox	
Measles (if 9 months of age or older)			

Vaccines — Group II

Polio ³	Polio ³		
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Schedule C

	1-9 months DPT ¹ -Typhoid	9 months-2 years DPT ¹ -Typhoid	
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Vaccines — Group I

	BCG (marker)	Smallpox (marker) Measles	
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Vaccines — Group II

	Polio ³	Polio ³	
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1. Diphtheria — Pertussis — Tetanus with adjuvant 2. These may be given from birth onwards
3. Oral trivalent

in the developing countries if vaccination is restricted to existing health installations. As shown in several studies, vaccination coverage rapidly diminished among persons living more than 2 to 3 miles from a vaccination centre. Even those health units which have been established are frequently without refrigeration and thus cannot serve as immunization centres for other than very thermostable vaccines. Further, even in developed countries, experience has shown that the immunization coverage of children in lower socioeconomic levels is generally inadequate unless immunization programmes are extended into the communities themselves.

In the developing countries, a dual approach to vaccination would seem most practicable: (1) vaccination in existing health centres which are equipped to undertake this; (2) vaccination by special vaccinators or vaccination teams moving from village to village, performing vaccinations at collecting points or on a house to house basis. Such an approach serves to strengthen the role and importance of the health centre for its overall programmes of health care while the special vaccination units, perhaps using the health centres as bases, would ensure adequate coverage.

Health centres which serve as vaccination centres should be equipped with necessary refrigeration and the

staff properly trained in vaccination technique. As certain of the vaccines (BCG, smallpox, measles) are freeze-dried in multiple-dose containers which must be discarded at the end of the day on which they are reconstituted, vaccination programmes should be designed to ensure that at least 25 to 50 persons (depending on size of vaccine container) are available for vaccination in order to avoid waste. In some areas, this has been achieved by designating one day in the week as "vaccination day". Attendance may sometimes be improved through provision at this time of powdered milk or other foods.

Schedules for vaccination by vaccinators or vaccination teams must similarly be arranged and proper supervision provided to ensure that large amounts of vaccine are not wasted through failure to vaccinate a sufficient number of persons each day. Experience in smallpox and BCG vaccination programmes has shown that upwards of 100 persons per day can readily be vaccinated daily by a single vaccinator even under very difficult circumstances of travel and terrain. Vaccination may, in some instances, be conducted at "collecting points" in villages; in other circumstances, vaccination on a house to house approach has produced better results. When thermostable vaccines are employed, particularly careful planning is required

in regard to refrigeration to ensure that the vaccine is still potent when it is administered.

Recording and registration of vaccinees.

Experience has shown that most immunization programmes, at their inception, have endeavoured to maintain far too complex and elaborate records which, almost inevitably, have had to be abandoned as they have served no useful purpose. Efforts to maintain complete registers of eligible children in a community have almost invariably failed except in isolated instances when very small numbers have been involved.

For programmes in which only BCG or smallpox vaccine is administered, the vaccination scar provides an indication of vaccination status. However, it is recognized that in the instance of BCG, this is subject to some error as inactivated BCG vaccine, for example, may induce the development of a small scar. Simple survey methods have been developed which, with minimal effort, permit an estimate to be made of the immunity level in a village, city or for a very large area.

For other vaccines, the problem is more difficult. The most workable system has involved a simple tabulation, by age, of numbers vaccinated by vaccinators and at health centres and, at the same time, the issuance of a simple vaccination card which is retained by the vaccinee. An imme-

diately report is thus available as to numbers of vaccinations being performed; vaccination coverage is determined by a simple survey in which vaccination cards are checked. While it has been assumed by many that vaccination cards would readily be lost, experience in several African and Asian countries has shown that a large proportion keep these cards. Instead of a vaccination card, some have proposed the use of a metal disc to be suspended around the neck.

Programme execution and assessment.

A very great deal could be and has been written regarding various administrative aspects of importance to the execution of immunization programmes. To discuss in detail the various approaches and contingencies in terms of different health service systems, resources and objectives is beyond the scope of these recommendations. A number of authors have discussed this subject at some length and reference may be made to these papers (WHO, 1967; Jelliffe and Cook, 1966; Moffatt, 1969; Ristori, 1969; Stanfield, 1967).

Certain principles in the development of an immunization programme should, however, be noted. The need for detailed planning prior to the inception of a programme cannot be over-emphasized; objectives must be established, specific time targets decided upon, the methodology of exe-

cution elaborated, lines of authority clearly demarcated, logistics of supply and transport elaborated, personnel recruited and trained mechanism for publicity and public education decided upon, etc.

Finally methods for assessment of the success of the programme must be decided upon and incorporated from the very beginning. Two general methods of assessment have proved most valuable; (1) appraisal by independent assessment teams of the extent of vaccination coverage and (2) surveillance for disease occurrence. In the past, most programmes have appraised the success of their efforts by counting the number vaccinated and comparing it with the population in the area. While this approach may be useful, it has often proved unsatisfactory and sometimes misleading. Health centres and vaccinators alike have frequently exaggerated or grossly over-estimated the numbers of vaccinations performed; census data have frequently proved to be highly unreliable. This problem may be countered by conducting regular simple surveys of the population by trained independent assessment to provide the necessary quality control for a programme. Experience has shown, in fact, that when it is known that assessment is being regularly conducted in this manner, vaccinators and health centres alike are more productive.

As the objective of an immunization programme is to control disease incidence, the ultimate test of the programme is whether or not a decrease occurs in the incidence of the disease for which vaccination is being given. Surprisingly, this has been the most neglected component in evaluation of immunization programmes and yet it is the most important and helpful. For example, persistence of disease in one area or segment of the population suggests the need for more intensive efforts in this area; the occurrence of cases of the disease in supposedly vaccinated persons raises questions as to the efficacy of the vaccine and/or closely following disease occurrence, technique of administration. By the overall programme may be monitored and appropriate adjustment made as required.

ANNEX I

Vaccine recommended for general use in developing countries.

— Smallpox, BCG, Diphtheria, Pertussis, Tetanus, Typhoid (preferably as a combined vaccine), Measles (Rubeola)

(Assuming substantial reductions in cost of measles vaccine or provision through international assistance).

For each of the diseases noted, vaccination is, in general, the preventive procedure of choice, taking into account the economic costs of possible alternative preventive mea-

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asures such as water supply development in the prevention of typhoid or case-finding and treatment in the instance of tuberculosis.

Tuberculosis, tetanus, pertussis and measles are generally acknowledged to be significant public health problems of real concern in all developing countries. Diphtheria is a problem in urban areas but is a less serious problem in rural areas, perhaps because of the frequency with which immunity develops as a result of cutaneous infection. Because diphtheria toxoid can be readily and inexpensively combined with pertussis and typhoid vaccines and tetanus toxoid and administered at essentially no additional cost, diphtheria toxoid is included in the "recommended" group. The extent and severity of typhoid infections is incompletely documented although in most areas where detailed studies of enteric infections have been conducted, it has been found to be a significant problem.

Lastly, the ever present threat of smallpox has, for a century or more made smallpox vaccination a primary component of public health programmes throughout the world.

Each of the vaccines induces effective and durable protection in a high proportion of recipients after not more than two or three injections. Two injections of diphtheria or more, will produce satisfactory immunity in 80% or more of recipients

and a third injection will increase the efficacy to more than 90 per cent. Effective protection against the disease itself may extend for a decade or more and protection against a fatal outcome for an even longer period. Pertussis vaccine, although usually regarded as a comparatively poor antigen, appears to induce a significant 'herd immunity' when used on a community-wide basis even when less than the "optimum" number of doses are administered (Morley, 1966; Ristori, 1969)

In studies in endemic areas, acetone-killed and dried typhoid vaccines has been found to provide protection to 80% after a single injection and to more than 90% after two injections for more than 7 years. Typhoid vaccine prepared by other means has been almost as effective (Hornick et al., 1970). BCG vaccine is generally acknowledged to afford a substantial and durable protection, particularly against the disseminated miliary and meningeal forms of the disease. Primary smallpox vaccination provides protection to more than 95% for more than 5 years; a single revaccination is believed to extend the duration of protection for at least two decades with only gradually waning immunity thereafter. Measles vaccine provides very long-term if not effectively life time immunity.

Except for measles vaccine, all of these vaccine are comparatively stable and their cost, comparatively are low. Most could be produced in

reasonably equipped national laboratories or may be obtained through international donation (BCG and smallpox vaccines for example).

Measles vaccine constitutes a special problem, however. While measles is recognized as one of the most serious health problems in infants and young children in all developing countries, the vaccine has two major drawbacks. It is much more thermolabile than other vaccines in this recommended group of vaccines and its cost is probably from 10 to 100 times greater than that of any of the other vaccines. Timing of immunization constitutes an additional problem.

Due to the presence of maternal antibody, the vaccine is in-effective if administered before the sixth month and its efficacy is somewhat diminished if administered before the ninth of age. As measles generally afflicts children at earlier age in developing countries, it must be administered before the third year of life if it is to be effective. The problem is to execute an immunization programme which assures vaccination in the comparatively narrow span between 6 or 9 months and 24 months of age.

The relative expense of a measles programme is illustrated by the experience of one African country (N'Dow, 1970) where a highly effective measles vaccination programme was conducted at the same time as a smallpox programme.

Three-fourths of the additional cost in the measles vaccination programme was for the vaccine itself which, at that time, cost \$.44 per dose, a cost not appreciably higher than at present. The cost to prevent one measles case was calculated to be \$ 3.69 and to prevent one measles death, \$ 73.85.

To reduce cost, some have advocated the administration of measles vaccine diluted two or three fold and have shown that a high proportion of those given the diluted vaccine exhibit satisfactory serological responses. Unfortunately, this is an unsatisfactory and hazardous approach. It is noted that standards for all live virus vaccines require that they contain substantially more than the minimum infective virus titre. Since all such vaccines lose titre in the process of normal storage and handling, an excess of virus is normally incorporated to assure that at the time of immunization, the vaccine is satisfactory; under conditions of routine field use, dilution is a hazardous procedure, particularly with presently available thermolabile vaccines.

Until vaccine costs are substantially reduced, most developing countries cannot consider the routine use of measles vaccine without international assistance to defray costs for vaccine and special refrigeration facilities.

Vaccines recommended for use under special circumstances.

Yellow fever and Poliomyelitis

Yellow fever vaccine — The considerable threat posed by yellow fever has generally recommended the use of this vaccine in threatened populations. While the vaccine is highly efficacious and affords very long-term protection after a single injection, it has the disadvantage of being very thermolabile, relatively expensive and impracticable to produce in most countries. The risk of the disease to particular populations during specific periods generally overrides other considerations and dictates the general use of this vaccine.

Poliomyelitis vaccine — In recent years poliomyelitis has become an increasingly serious problem in a number of the developing countries although far more complete reporting is required to assess fully the magnitude and extent of the problem. While in the past, naturally acquired subclinical infection protected most children at an early age, more cases of paralytic diseases are being observed today in many of the developing countries. However, until more information is available regarding the extent of the problem, the overall need for immunization programmes is difficult to assess.

The variable efficacy of the vaccine when used in tropical countries constitutes a second and a yet unresolved

problem. Interfering enteroviruses not infrequently prevent necessary growth of the vaccine virus in the intestine. These factors make it difficult at this time to appraise the probable benefits of a vaccination programme.

While a few developing countries may wish to include polio vaccination in routine programmes of immunization, it is probably more practicable at present to restrict vaccination to urban areas where costs of administration can be held to minimal levels and to provide vaccination to other areas only when outbreaks occur. The age distribution of cases should be used as a guide to determine what ages should receive the vaccine.

Vaccines not generally recommended for routine use in the developing countries.

Mumps

Rubella

Cholera

Influenza and other respirovirus vaccines

Mumps vaccine — Mumps is normally a mild disease with only rare and usually not severe complications while the vaccine is very expensive. Even if available at very low cost, the costs of administration of this very heat labile vaccine preclude its routine use in the developing countries.

Rubella vaccine — While a small number of rubella-induced malformations undoubtedly occur in all countries, the incidence even in the

developed countries is comparatively low. In developing countries, where most infections are usually far more widely disseminated in children, it would be reasonable to suppose that natural immunity among women reaching the childbearing years must be higher than in the developed countries. Thus, rubella induced congenital malformations in developing countries would be even less frequent. Use of this expensive heat labile vaccine is certainly not warranted.

Influenza and other available respirovirus vaccines — While extensive morbidity occurs in all countries as a result of infection with influenza and other respiroviruses, available vaccines confer only very transient, partial protection. None can at this time be recommended for immunization programmes in the developing countries.

Cholera vaccine — While cholera is a serious diseases in a number of endemic areas, presently available vaccines are regrettably unsatisfactory. One injection of vaccine provides, at best, equivocal protection while two injections, given a month or so apart, may provide protection to perhaps 50 to 55% for a period of 3 to 6 months (Azurin et al., 1967; Cvjetanovic, 1968). Repeat inoculations every 6 months are required to assure continuing protection. The costs of conducting repeat programmes of mass vaccination every 6 months are far too great for most

countries. It is believed that comparable expenditures diverted to the treatment and isolation of patients and contact and to control of waste disposal and water supplies, where possible, would produce more satisfactory result at far less cost (Morley, 1970).

Vaccines in the developmental stage which may, in the future, be applicable for general use among populations at special risk. Vaccines against the arboviruses, rickettsiae, trachoma, plague, shigella and meningococci.

All of these vaccines are considered to be in the "developmental" stage with, as yet, uncertain or unsatisfactory levels of protection and durations of immunity. None can be recommended for routine use at this time. However, the primary diseases against which they provide protection constitute major health problems in some areas. When further developed, the possible use of these vaccines would have to be weighed in regard to the cost of the vaccine, the duration and degree of protection afforded, the extent and severity of the diseases problem itself and the problems of administration of vaccine to large populations.

ANNEX II — VACCINE SCHEDULES

Pertinent considerations

Smallpox

Vaccination from the time of birth has been shown to be safe and ef-

fective. Revaccination at about the time of school entry should provide reasonably complete protection for several decades.

BCC

Vaccination from the time of birth (without antecedent tuberculin testing) has been shown to be safe and effective.

Diphtheria-pertussis-tetanus-typhoid

A vaccine combining these four antigens has been shown to be effective. As an adjuvant preparation, more effective antibody responses are induced. Immunization before one month of age may be less effective in the instance of diphtheria and pertussis vaccines because of maternal immunity and thus immunization at birth is not recommended. The most effective antibody responses are induced if 2 to 3 months or more are allowed to elapse between inoculations. However long the interval between inoculations, second and subsequent inoculations produce a booster response.

As few as two inoculations spaced two or more months apart is believed to provide protection against diphtheria and tetanus to more than 80% of vaccinees for periods of more than 5 years. A third inoculation should provide levels of protection of 90% or more for at least 10 years. In respect to typhoid, the vaccine has been found to confer protection to 80%

for 7 years, and perhaps longer, whereas two inoculations confer protection to more than 90%.

Polio

Vaccine given before one week of age is frequently ineffective in breastfed infants. If polio vaccine is to be used, at least two and preferably three feedings, at least one month apart, are recommended. No statement can be made regarding vaccine efficacy as frequently in the developing countries, other viruses in the intestinal tract interfere with the growth of the polio virus. As poliomyelitis in developing countries is a disease of children under 4 to 5 years, feeding of vaccine to older children is *not* recommended.

Measles

A single injection of vaccine confers long-lasting, perhaps lifetime immunity. Diluting the vaccine before administration, although recommended by some, is not advised since the vaccine is very thermolabile; the excess titre in the vaccine, as originally prepared, only serves to ensure that the requisite minimum titre is present in the vaccine at the time of administration. Vaccine given before 9 months of age is ineffective as there is interference by maternal antibody. Administration of vaccine to those older than 4 to 5 years is not recommended as natural infection in most areas rarely occurs beyond this age.

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