IMMUNIZATION

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If a list of the notifiable diseases in the Republic of South Africa is considered, the outstanding impression is that a great deal can be done for all of them by way of prevention or cure by the immunological or chemotherapeutic approach. For several diseases there is the potential of eradication. This has actually been achieved in some countries for diseases like smallpox, poliomyelitis and malaria. Diseases like typhoid and diphtheria have been reduced to negligible proportions in a number of the highly developed countries.

Phenomenal progress has been made in the virus diseases in the past 15 years. The chemotherapeutic approach that has made such a dramatic difference to bacterial diseases, has until recently, been unsuccessful against the smaller viruses, but some very successful vaccines have been developed. There is the promise of more to come.

Current knowledge and available immunizing agents are well ahead of their practical application and exploitation to the full. If all accepted techniques could be applied on a nation-wide scale in this country an impressive number of communicable diseases would disappear or be reduced to very small proportions. It is, therefore, pertinent to evaluate some of the immunizing agents at present available against the bacterial and virus diseases that occupy the attention of medical practitioners and particularly of state health officers in this part of the world.

From a practical point of view the notification of diseases for 1963 in the Northern and Eastern Transvaal region serves as a guide to the relative importance of the diseases that affect the Bantu.

TABLE I. NOTIFIED DISEASES FOR NORTH-EASTERN TRANSVAAL REGION 1963

	Cases	*Deaths*
Tuberculosis (Resp.)	6,042 (25)	116
Typhoid	980 (10)	13
Diphtheria	249 (26)	7
Smallpox	96 (2)	0
Leprosy	19	0
Trachoma	16	0
Poliomyelitis	13 (2)	0
Rabies	1	1
Measles	? *	? *
Whooping cough	? *	? *

Figures for Whites in brackets
*Not known

Diseases with dramatic clinical features like poliomyelitis and rabies will naturally be much better reported than brucellosis, typhoid and early tuberculosis. Smallpox, in its variola minor form, presents diagnostic problems. Measles and whooping cough, notorious killers of infants and young children, are not notifiable. In general, it is reasonable to regard the figures as an understatement of the true situation. This makes the figures for tuberculosis even more startling.

IMMUNIZATION

From the point of view of maximum protection by *active* immunization, the following approaches are customarily used:

1. General practitioner immunization.
2. Routine vaccination at clinics.
3. Epidemic control and peripheral vaccination.
4. Mass vaccination with follow-up vaccination of new arrivals owing to population increase.

General practitioners are inclined to leave routine immunization to local authority and state health services. This is unfortunate since their help would be of great value in obtaining adequate coverage. Routine clinic type of vaccination alone has had varying degrees of success in urban areas. In the under-developed areas it has limited application and epidemic control with peripheral vaccination has been the method applied.

As an illustration of the fourth type of immunization, mass vaccination, the anti-poliomyelitis vaccination campaign of 1961,[1-5] serves as a near perfect model. It has inaugurated in this country the mass approach to communicable disease and was a good starting point because of its safety, efficacy and ease of administration. As the figures in Table I indicate, poliomyelitis is not the most important disease in the area concerned but, in the absence of immunization, paralytic poliomyelitis must be expected to increase in incidence as living standards improve. However, it has set a precedent for the type of

approach to a communicable disease that could be attempted with very good results in a number of other diseases. As a first attempt at mass vaccination in this country it showed how efficiently the health department and other departments concerned with the administration of the country, could cooperate and achieve remarkable results. It also shows clearly what happens when the follow-up phase is not closely controlled, owing mainly to the general apathy of the population to preventive medicine. The incidence of notified cases of poliomyelitis is shown graphically in Figs. 1, 2 and 3.

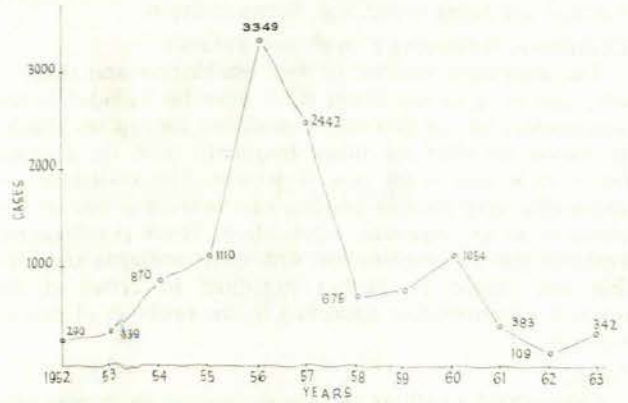

Fig. 1. Cases of poliomyelitis notified in Republic (1952 - 63).

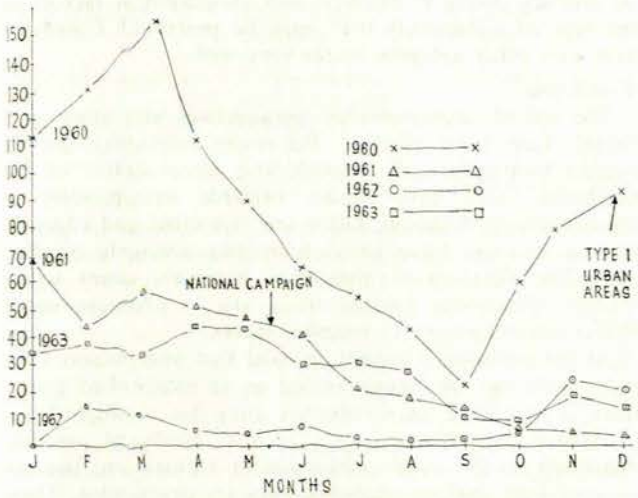

Fig. 2. Notified cases of poliomyelitis in all races in Republic (1960 - 62).

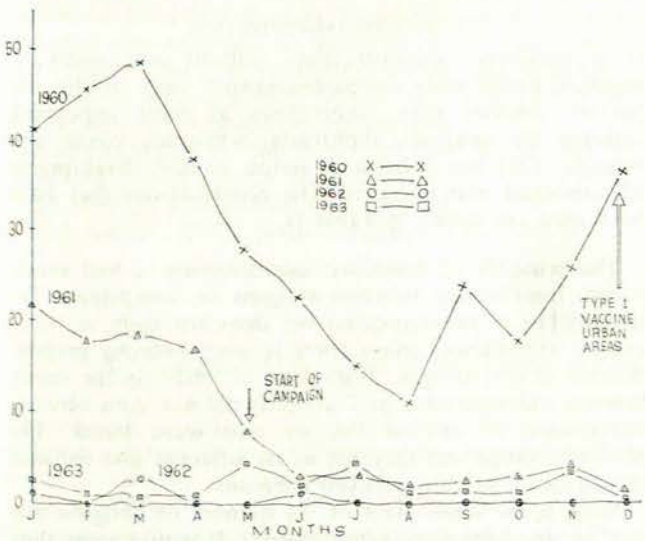

Fig. 3. Notified cases of poliomyelitis in Whites in Republic (1960 - 62).

The anti-poliomyelitis campaign has set a pattern in keeping with the concept of striving for eradication rather than control. With the available, adequately tested and relatively inexpensive vaccines, this can be attempted for diseases like tuberculosis, diphtheria, measles and smallpox. For these diseases with the target set at eradication, and possibly for some of the others, mass campaigns followed by sustained routine vaccination are the ideal approach to the immunization problem. From an economic point of view the investment of funds in the correct application of tested immunizing agents can be most profitable. It has been mentioned by the Minister for Health at this conference[6] that state expenditure on poliomyelitis for 1960 was R 1,200,000. The cost of the campaign was R410,000. The relatively low cost of immunization against tuberculosis compared with the very costly curative services that have to be subsidized at present should result in an even more favourable margin of saving in state funds.

Tuberculosis

Immunization against tuberculosis with BCG is rapidly becoming established practice. It is compulsory in France, Denmark, Norway, Brazil and Japan. But it must very clearly be considered as only a part of the approach to the problem. Improvement in the standard of living alone and particularly in nutrition leads to a decline in the incidence. The roles of the agriculturalist, sociologist, health educator and economist, etc., are of very great importance. These agencies have their difficulties, of which not the least is the traditional apathy of those that stand to gain from the application of modern knowledge.

In BCG vaccination the health administrator has a technique that can be immediately and rapidly applied, is relatively inexpensive and increases resistance to the disease within weeks. It allows the much-needed time for other important measures to receive attention.

Exposure to tubercle baccilli is unavoidable in any community. The introduction of harmless living BCG bacilli gives the body an opportunity to build up a resistance to the virulent organism—a process that is normally achieved at the risk of serious illness.

Ever since the first use of the Calmette and Guerin culture in 1921, the vaccine has been a matter of controversy. This was to be expected in a chronic disease where evaluation of effectiveness is complicated by factors such as race, age, social and living conditions, nutrition, wars, famine, etc. The Lübeck disaster in 1930 when 73 out of 249 children died as a result of receiving a wrong culture put back the clock in Europe for many years. However, the Scandinavian countries, among others, persisted with the development of the vaccine. The post-war increase of tuberculosis in Europe stimulated the use of BCG particularly through the WHO. Up to date over 200 million

inoculations have been given. This has certainly established safety. Its effectiveness is more difficult to evaluate. A favourable 8-year study from India,[7] some careful studies in the USA,[8, 9] a 10-year study reported on in 1958 by the British Medical Council,[10] and a 3½-year study in Southern Rhodesia in 1962,[11] puts the protective action at roughly 70 - 80% with evidence of diminution of the incidence of miliary tuberculosis and tuberculous meningitis. The latter 2 complications are of some significance in this area.

The 4 different methods of application have to be studied in relation to the available personnel, etc. It is, however, clear that BCG vaccination lends itself to mass immunization. Good evidence of that is the fine work of Spencer[12] and his colleagues when they vaccinated over 160,000 individuals in 18 working days and more recently[13] over 63,000 in 10 days.

A good case can be made out for a vigorous effort to reduce the alarming figures for tuberculosis in the Bantu population of the Republic of South Africa.

Typhoid

The salmonella bacteria that cause the typhoid group of infections and a number of other salmonella organisms have been a formidable public health problem for a long time. The relationship between the incidence of these infections and the standard of hygiene of food and water and sanitation in a community is well established, and typhoid is often taken as an index disease for evaluation of public health standards. The advent of effective drugs has reduced mortality. Morbidity is still high: 980 cases were notified in the North-Eastern Transvaal in 1963.

Prophylactic immunization has been attempted for 67 years. TAB immunization given to British troops fighting in the Anglo-Boer War has been described as useless by Bruce[14] and it has been stated that more British troops were killed by *S. typhi* than by the accurately aimed bullets. But it is generally held by Archer 1963[15] that the effectiveness of vaccination against enteric fever was demonstrated in the First World War and confirmed in the Second World War, though within the last 15 years claims for the degree of protection have been more modest.[15, 16] In a 1957 Yugoslavian field trial Cvjetanovic[17, 18] indicated 65% protection. In a 1962 report from Germany by Edwards,[19] 62 cases of typhoid occurred among 407 immunized individuals.

At present the indications for antityphoid mass vaccination as a preventive measure in the Bantu are not clearcut. Its inclusion in a combined immunization increases the hazard of reaction and resultant failure to complete the course. If this can be overcome or the reaction is accepted, its inclusion in combined vaccination should be considered.

Measles

Live virus measles vaccine mainly of the Edmonston strain of Enders has come through its testing stage and plans are afoot to use it on a multimillion scale in the developing areas of Africa and elsewhere.

As the trials by Spencer[20] have indicated in this country, the fairly severe reactions are accepted by the Bantu. It has the advantage of being a single-injection vaccination and can be safely combined with diphtheria-whooping cough-tetanus immunization. Vaccine virus strains with good immunological properties and with a less severe reaction are being tested, e.g. Schwarz strain.

Diphtheria, Whooping Cough and Tetanus

The combined vaccine is well established and there is only one thing to say about it: it must be included in the armamentarium of preventive medicine among the Bantu. It should be used far more frequently and on a much larger scale than is the case at present. The availability of disposable syringes and needles can overcome one of the obstacles to its large-scale application. There is substantial evidence that its combination with other antigens are feasible and should be further exploited to arrive at the optimal administrative approach to the problem of immunization.

Smallpox

Freeze-dried smallpox vaccine is used on an increasingly large scale[21] and is a useful development because of loss of potency owing to climatic and geographical factors in the type of community that must be protected. Combination with other antigens works very well.

Trachoma

The use of sulphonamides, tetracyclines and other antibiotics, have been effective. But many individuals do not receive treatment early enough and some strains of the trachoma virus have shown variable susceptibility to chemotherapy. Aqueous, killed and live virus and adjuvant treated vaccines have given promising antibody production. The duration of immunity, however, seems to be limited. Trachoma control trials are in progress under WHO supervision in 15 member states.[21]

At the moment it cannot be said that vaccination on a mass scale can be recommended as an established procedure. Large-scale pilot schemes may be attempted for evaluation of efficacy of a locally produced vaccine. Attention to the usual public health factors and the use of antibiotics and/or sulphonamides are practicable. These should be considered for inclusion in vaccination and health educational tours.

COMBINED IMMUNIZATION

It is obviously administratively difficult and costly to organize nation-wide campaigns against each of the important diseases with tuberculosis as most important, followed by smallpox, diphtheria, whooping cough and measles. This has focused attention on the development of combined immunization. The combinations that have been used are shown in Table II.

The principle of combined immunization is well established. Interference between antigens or competition for antigen has to be considered but does not seem to be of critical importance, unless there is overwhelming preponderance of one antigen. Tests done in 1962[24] on the simultaneous administration of 7 antigens did not show obvious suppression of any of the six that were tested. The pertussis component may act as an adjuvant and enhance the antigenic stimuli in mixed injections.

What is the upper limit of the number of antigens that can be simultaneously administered? It would seem that, from a practical point of view, the limiting factor is not an immunological one but the very important one of

TABLE II. COMBINED IMMUNIZATION SCHEMES

Antigens	*Description*	*Used*
DWT	Triple antigen: diphtheria, whooping cough, tetanus	General use
DWT + polio (Salk)	Quadrigen	USA, Canada, Britain
DWT + polio (Oral)	Triple antigen and oral polio	Yugoslavia, Johannesburg
DWT, TAB, polio	Diphtheria, tetanus, typhoid, inj. polio	French army[22]
DWT, measles	Triple antigen, live measles (Enders), no gamma globulin	Spencer[13]
DWT, smallpox	DWT plus smallpox	Spencer[23] Swaak
DWT, polio, smallpox	Triple antigen, oral polio and smallpox	Winter *et al.*[24]
BCG, smallpox	Concurrent immunization	Moodie *et al.*[25] Baltazaid *et al.*[26]

gaining the confidence of the population. Reactions must not be such that the child is withheld or hidden when the second series are due to be given. In the abovementioned study where 7 antigens were used on over 1,500 individuals, reactions were negligible and the confidence of parents of both White and non-White groups was gained. Maritz[27] in 1963 used the same combination of 7 antigens DWT, polio, vaccinia on 15,000 Ovambos. There was 1 untoward reaction when a child developed convulsions immediately after the immunization. There is clearly great scope for pilot schemes to test out combinations that will suit the administrative conditions applying to given areas.

Tuberculosis immunization obviously needs the most attention in the North Eastern Transvaal area. It has been combined with smallpox by Baltazaid *et al.*[26] and Moodie and Ching.[25] The oral poliovirus vaccine can apparently be combined with any form of vaccination because it has no reaction and is painlessly administered.

Ideal combinations that have not been tested, but on theoretical grounds may be successful and, of course, would simplify administrative problems are:

First Round: DWT, polio., smallpox, BCG.

Second Round: DWT, polio., measles, ?TAB.

Third Round: DWT, polio., ?trachoma, ?TAB.

A campaign must be planned on a yearly 3-tour basis at intervals not exceeding 2 months. The principle of taking the vaccine to the people is proving more successful than expecting people to travel long distances for procedures they do not always fully understand. Three planned tours will ensure a high proportion of the susceptible population receiving at least 2 antigenic stimuli that are essential for minimal DWT immunization. The necessary field staff, transport and equipment must be available to cover the area in the limited time available.

There is enough evidence available on combinations of antigens to plan pilot field trials. If they prove successful there is no reason why the mass immunization approach to the key diseases of tuberculosis, smallpox, diphtheria, whooping cough and measles should not dramatically change the incidence of these diseases among the Bantu in the North Eastern Transvaal. The inclusion of typhoid immunization in such a scheme is possible and new vaccines at present being developed against brucellosis and trachoma may be available in the not too far distant future.

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