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**EUROPEAN TECHNICAL CONFERENCE  
ON THE CONTROL OF INFECTIOUS DISEASES  
THROUGH VACCINATION PROGRAMMES**

**Rabat, Morocco, 23-31 October 1959**

**Report**

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**WORLD HEALTH ORGANIZATION**

PALAIS DES NATIONS

GENEVA

1960

EUROPEAN TECHNICAL CONFERENCE ON THE CONTROL OF  
INFECTIOUS DISEASES THROUGH VACCINATION PROGRAMMES

Rabat, Morocco, 23-31 October 1959

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**EUROPEAN TECHNICAL CONFERENCE  
ON THE CONTROL OF INFECTIOUS DISEASES  
THROUGH VACCINATION PROGRAMMES**

**Report**

The European Technical Conference on the Control of Infectious Diseases through Vaccination Programmes took place in Rabat from 23 to 31 October 1959. His Royal Highness, Prince Moulay Hassan, presided over the opening session, during which speeches were made by Dr Youssef Ben Abbès, Minister of Health of Morocco, and Dr P. van de Calseyde, Director of the Regional Office for Europe of the World Health Organization.

Professor V. M. Zhdanov was elected Chairman of the Conference, Professor P. Melnotte, Vice-Chairman, and Dr S. Tulinius and Dr B. Cvjetanovic, Rapporteurs.

Participants and discussion leaders were present from Austria, Belgium, Bulgaria, Czechoslovakia, Denmark, Finland, France, the Federal Republic of Germany, Greece, Ireland, Italy, Morocco, the Netherlands, Norway, Poland, Portugal, Spain, Sweden, Switzerland, Turkey, the Union of Soviet Socialist Republics, the United Kingdom of Great Britain and Northern Ireland, and Yugoslavia.

**1. Present Practice and Problems**

The participants reviewed the present practices relating to the control of infectious diseases through vaccination programmes in various countries of Europe. These are briefly summarized in Tables 1 and 2.

Immunization of the population is considered to be one measure in the comprehensive system of communicable disease control, itself an integral part of health services.

**1.1 Health legislation**

In all European countries, health legislation includes laws and/or regulations on the immunization of the population. It rests with the national authorities to develop this legislation further according to the needs and resources of the various countries. It is customary for the central health authorities to be responsible at least for the over-all planning and control of immunization programmes, and for local authorities to execute them.

TABLE 1. GENERAL INFORMATION ON VACCINATION \*

	Austria	Belgium	Bulgaria	Czechoslovakia	Denmark	Finland	France	Germany	Greece	Iceland	Ireland	Italy	Morocco	Netherlands	Norway	Poland	Portugal	Spain	Sweden	Switzerland	Turkey	USSR	United Kingdom	Yugoslavia
<b>Laws and regulations</b>	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Responsibility of central health services:																								
laboratory control of vaccines	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
overall planning of immunization programmes	-	+	+	+	+	+	+	-	+	.	+	+	+	+	+	+	+	+	+	-	+	+	+	+
control of vaccination programmes	-	+	+	+	+	+	+	+	+	.	+	+	+	+	+	+	+	+	+	-	+	+	-	+
execution of vaccination programmes	-	-	-	+	+	+	+	-	+	.	-	-	+	+	+	+	+	+	-	-	+	+	-	+
Responsibility of local health authority:																								
planning of vaccination programmes	+	+	+	+	+	+	+	+	+	.	+	+	+	+	+	+	-	-	+	+	+	+	+	+
control of vaccination programmes	+	+	+	+	+	+	+	+	+	.	+	+	+	+	+	+	+	+	+	+	+	+	+	+
execution of vaccination programmes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Planning of vaccination based on:																								
serological surveys and other laboratory tests	+	+	+	+	+	+	-	+	(+)	.	+	+	-	+	+	+	-	-	+	+	+	+	+	-
epidemiological evidence (morbidity, mortality statistics)	+	+	+	+	+	-	+	+	+	.	+	+	-	+	+	+	+	+	+	+	+	+	+	+
Instructions or manual	-	+	+	+	+	+	+	+	+	-	+	.	+	+	+	+	+	+	+	+	+	+	+	+
Vaccination performed by:																								
health services as a part of the regular activity of local health units	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
mass campaigns at certain seasons carried out by special teams responsible to central authorities	+	+	-	-	-	-	-	-	+	.	+	+	+	+	+	+	+	+	+	-	-	+	+	-
various arrangements according to local conditions	-	+	-	-	-	-	-	-	-	.	+	+	+	+	+	+	+	+	+	+	+	+	-	-
Recording:																								
individual	+	+	-	+	+	+	+	+	(+)	.	+	+	+	+	+	+	+	+	+	+	+	(+)	+	(+)
collective	-	-	+	-	-	+	+	+	+	+	-	-	-	-	-	-	-	-	-	-	(+)	+	+	+
Reporting on vaccination	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Vaccination recorded on notification form for communicable diseases	+	-	-	+	-	+	+	-	+	-	-	-	-	+	+	+	-	+	-	-	-	-	+	-
Control of execution of vaccination programmes:																								
by central authorities	+	+	-	+	+	+	+	+	+	.	+	+	+	+	+	+	+	+	+	-	-	+	+	+
by local authorities	+	+	+	+	+	+	+	+	+	.	+	+	+	+	+	+	+	+	+	+	+	+	+	+
by use of laboratory methods	(+)	(+)	+	+	+	+	+	-	-	.	.	+	-	+	+	+	-	-	+	-	-	+	+	+
Evaluation of the effectiveness of vaccination programmes:																								
by statistical and epidemiological evaluation of the data from the field	+	+	+	+	+	+	+	+	+	.	+	+	+	+	+	+	+	+	+	+	+	+	+	+
by field trials	-	+	+	+	+	+	+	+	+	-	-	-	-	+	+	+	-	-	+	-	-	+	+	+
Any penalties?	-	+	(+)	+	-	-	+	-	+	.	-	-	+	+	+	+	-	+	-	(+)	+	+	-	+
Cost of vaccination paid by:																								
state or local authority	Po Sm Tb Di Pe Te	All	All	All	Rb Tb Sm Di Te	AB Po Tb Sm Di Re Te	Sm Di Tb Sm Di Re Te Po SF	AB Tb Sm Di Tb Sm	AB Re Tb Sm	Di Re Tb In	Di Re Tb Po AB Lp	Tb Sm	Sm Di Tb Te Po Tb Ty	Sm Di Tb Te Po Tb Ty	All	Po Sm Di Tb Te Pe AB	Sm Di Re Tb Te Ty	Sm Di Re Tb Te	Tb Sm Di Te Te	All	Sm Di Re Tb Te Tb	AB Sm Di Re Tb Te Tb	AB Sm Di Re Tb Te Tb	
citizen	+	-	-	-	+	+	+	+	+	+	+	+	+	+	+	-	-	+	+	+	+	-	+	+

+ = yes, exists, is done

- = does not exist, is not done

. = not known

Di diphtheria

Pe pertussis

Te tetanus

AB typhoid para-

typhoid AB

Sm smallpox

Tb tuberculosis

Ty typhus

In influenza

SF scarlet fever

Po poliomyelitis

Lp leptospirosis

\* Teams responsible to local authorities

TABLE 2. GENERAL INFORMATION ON VACCINATION AGAINST SPECIFIC DISEASES \*

Vaccination against these diseases as practised in:	Austria	Belgium	Bulgaria	Czechoslovakia	Denmark	Finland	France	Germany	Greece	Iceland	Ireland	Italy	Morocco	Netherlands	Norway	Poland	Portugal	Spain	Sweden	Switzerland	Turkey	USSR	United Kingdom	Yugoslavia
Tuberculosis (BCG)	V	V	C	C	V	V	C	V	V	V	V	V	V	V	C	C	C	V	V	V	V	V	V	C
Smallpox	C	C	C	C	C	(C)	C	C	C	C	V	C	(C)	C	C	C	C	C	C	(C)	(C)	C	V	C
Diphtheria	V	V	C	C	V	V	C	(C)	C	V	V	C	(C)	V	(C)	C	V	V	V	(C)	(C)	V	V	C
Pertussis	V	V	C	C	V	V	V	V	-	V	V	V	V	V	V	V	V	V	V	V	V	V	V	C
Tetanus	V	(C)	(C)	C	V	V	C	V	V	V	V	(C)	(C)	V	(C)	V	(C)	V	V	(C)	(C)	V	V	C
Poliomylitis	V	V	V	C	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	-	V	V
Influenza	.	V	V	(C)	V	V	V	V	V	V	V	V	-	V	-	V	V	.	V	V	V	V	V	-
Typhoid	.	(C)	(C)	(C)	V	(C)	(C)	V	(C)	V	V	(C)	(C)	(C)	(C)	(C)	(C)	(C)	V	V	V	V	(C)	
Paratyphoid	.	(C)	(C)	(C)	V	(C)	(C)	V	(C)	-	V	(C)	(C)	(C)	(C)	V	(C)	(C)	V	V	V	V	(C)	
Cholera	.	V	V	(C)	V	-	V	V	(C)	-	-	.	V	(C)	V	V	V	.	-	-	V	V	V	V
Dysentery	.	V	(C)	-	V	-	-	-	-	-	-	.	V	-	-	V	V	.	-	-	-	-	-	-
Leptospirosis	.	-	.	-	V	-	-	-	-	-	-	V	-	-	-	-	-	-	-	-	-	-	-	-
Plague	.	-	.	(C)	V	-	-	-	(C)	-	-	.	-	-	-	-	V	.	-	-	-	V	-	-
Yellow fever	.	V	.	(C)	V	V	V	V	(C)	-	V	.	V	V	V	V	V	.	-	-	V	V	V	(C)
Typhus	.	V	.	(C)	V	-	(C)	-	V	-	-	.	(C)	V	-	V	V	.	-	-	V	-	V	-

\* Scarlet fever in Austria ; measles experimentally in USSR and Yugoslavia ; mumps experimentally in Finland and USSR ; adenovirus experimentally in Switzerland ; tick-borne encephalitis experimentally in USSR ; brucellosis experimentally in Poland and USSR ; tularemia experimentally in Poland and USSR ; Q-fever experimentally in Poland. Rabies : information on vaccination not included in this table.

V = voluntary  
 - = no vaccination performed  
 . = not known  
 C = compulsory  
 (C) = compulsory for certain groups (defined geographically, professionally, etc.)

This, naturally, will depend on the conditions prevailing in individual countries. The participation of general practitioners and paediatricians in immunization programmes is increasing in certain countries and is to be encouraged, since it is most important that the family doctor and child specialist should be active advocates of prophylactic immunization.

Many countries have adopted compulsory immunization against some diseases with voluntary vaccination against others. It has been pointed out that in some countries voluntary immunization has given results as good as, and even better than, compulsory vaccination. The general tendency to abandon compulsory vaccination was noted as reflecting the growing educational level of the population. Successful immunization of the population cannot be achieved merely by imposing compulsory vaccination. However, compulsion may still be necessary in certain countries, and its removal might be misunderstood by the population. In conclusion, no hasty steps should be taken to modify present laws, but health education activities should be carried on as though vaccination were not compulsory. Health education was considered a powerful instrument for the successful accomplishment of mass vaccination.

### 1.2 *The organization of vaccination programmes*

The organization of immunization of the population in Europe varies according to local facilities, prevailing conditions, and the system of health services available in the country. Lack of proper organization in vaccination programmes inevitably results in failure to control some diseases which can be controlled by vaccination, such as diphtheria. It is gratifying to note that some countries in Europe have achieved virtually complete control of diphtheria, which proves that this can be accomplished by well-organized programmes. It is therefore stressed that the proper organization of mass immunization programmes is a major public health problem which merits high priority in European countries.

Whatever may be considered the most suitable and useful arrangements for implementing such vaccination programmes, active and skilful work is required of the health personnel performing the inoculations. In some countries this work falls mainly on physicians, while in others it has been found that auxiliary personnel, when adequately trained, may be used with success. Since some European countries have a shortage of highly-trained personnel and it has been shown that many types of vaccination can be carried out satisfactorily by auxiliary (medical) personnel after an adequate period of special training, the role of auxiliary personnel should not be underestimated.

### 1.3 *The recording of immunization*

Individual cards for the use of health services and individuals, and the recording of immunization on collective lists for the use of health author-

ities, are considered useful as they permit the results of vaccination programmes to be controlled and evaluated. This recording should therefore be encouraged wherever practicable. Easily available individual record cards or other methods of identification are essential if large-scale active immunization against tetanus is undertaken.

#### 1.4 *Costs*

The cost of mass vaccination is borne mainly by central or local health authorities, according to their responsibility, but in some instances part of the cost is met by the individual, particularly when a costly antigen such as poliomyelitis vaccine is involved. This may adversely affect the success of mass vaccination, particularly in the groups with relatively low incomes.

Although it may be thought that the immunization of the population is a costly procedure, analyses of prophylactic versus curative procedures show that prevention is much cheaper than cure.

#### 1.5 *The role of health education*

In discussing the role of health education in vaccination programmes the Conference emphasized the need :

(a) for integrating health education into public health programmes and, consequently, for the adequate training of health personnel ;

(b) for adapting health education to local beliefs, and undertaking health-opinion surveys when needed ;

(c) for considering health education as a continuous process ; and

(d) for undertaking the systematic evaluation of health education efforts.

Health education is an essential preliminary to vaccination programmes. It should be an integral part of vaccination activities and all persons concerned should take an active part in this educational work. It is felt that the advice of a specialist in health education is valuable in the early planning stages of a campaign. Such a specialist may also act in an advisory or even an executive capacity throughout the campaign.

In most cases personnel need special training in health education. This ought to be provided for in the over-all planning of vaccination programmes. It is desirable for the basic training programmes of doctors, nurses and others concerned to include general courses on health education principles and methods, as well as practical work. Regular in-service training courses should also be organized, emphasizing whenever necessary the problems connected with vaccination programmes.

Health education, in addition to being an essential preliminary to vaccination programmes, should be a continuous process starting in childhood, continuing in the school and later in the community.

With regard to the contribution that the community itself can make to the success of health education, mention was made of the role which can be played by sports organizations, press and radio, voluntary organizations, political leaders, teachers, religious groups, administrative officers, and other key people. It was suggested that the creation of national and local health education committees, grouping these various personalities and organizations, might be a good way to stimulate and coordinate their efforts.

With regard to the possible hazards and limitations of immunization programmes, it is felt that the public should be fully informed. One reason for doing this is that they may otherwise sooner or later lose confidence in vaccination. Information should, however, be conveyed with tact. Undue emphasis on hazards should be avoided, while the real dangers associated with the disease in question should be explained. Where controlled field trials are being conducted, the community should be informed as fully as possible of what is being done and why.

Communities have their beliefs and superstitions about diseases and it is most important that these be discovered, if need be by special surveys, so that health education can be adapted to these beliefs and vaccination programmes become acceptable to the community. It is suggested that such surveys could be carried out as part of the in-service training of the vaccination team; this should only be done, however, under expert leadership, as such surveys are a very delicate matter.

One practical point that should be stressed is the need to make provision for health education for vaccination campaigns in central or local budgets.

Finally, if progress in health education is to be achieved, then an objective assessment must be made—preferably by someone outside the vaccination team and qualified for this work—of the receptiveness of the community to the various methods used and their practical results. The participation of the public in vaccination campaigns could be used as a yardstick.

## **2. Immunizations used in the Control of Infectious Diseases**

### *2.1 Immunizations in childhood commonly used in public health practice*

The Conference discussed the fundamental factors of importance in immunization in childhood, such as the role of maternal antibodies present in the child at the time of immunization, and the stage of development for active immunization of the young infant. It was pointed out that the newborn infant, until after the second month of life, could only partially synthesize gamma and beta-2 globulins. However, knowledge in this field is still incomplete.

There was agreement that with sufficiently potent antigens, such as diphtheria and tetanus toxoids, it was possible to overcome the difficulties encountered. However, not all of the antigens in use were of sufficient potency—as, for example, the inactivated poliomyelitis vaccine—though the situation was different with regard to live polio vaccine.

### 2.2 *Smallpox vaccination*

The Conference considered smallpox vaccination in relation to the European region, where smallpox does not exist as an endemic disease. There was general agreement that it was still necessary to maintain a relatively high level of immunity in the population. Reference was made to outbreaks during recent years caused by imported cases of smallpox, and it was agreed that strict quarantine measures alone could not afford protection against importation and that co-operation through education of the people, particularly international travellers, was of importance. Prompt notification and good laboratory facilities for diagnosis were considered essential. The necessity for hospital staffs to be properly vaccinated was also stressed. The question of post-vaccinal encephalitis and the possibilities of diminishing this risk, especially by early vaccination, were discussed. Data were presented from the United Kingdom suggesting that the risk of encephalitis was less in children vaccinated between 2 and 5 years of age. However, experience in Norway showed that the more traditional custom of vaccinating children in the first year of life was associated with the least risk of encephalitis.

Further studies by all countries on the age for primary vaccination are indicated. Investigations using the simultaneous administration of vaccine and gamma globulin in connexion with the prevention of encephalitis have so far met with encouraging results.

### 2.3 *Vaccination against tuberculosis*

The vaccine most widely used is a suspension of live BCG, administered either as freshly prepared, or after re-suspension of the lyophilized product. Lyophilized vaccine has obvious advantages, especially in countries where transport is difficult, and in hot climates. It appears to give satisfactory post-vaccination allergy; as yet, however, insufficient information is available on the duration of allergy after vaccination with lyophilized vaccine.

No biological standard has yet been established for BCG vaccine, but it is commonly accepted that a good vaccine should produce tuberculin allergy in 95% to 98% of persons vaccinated, and should not give rise to a significant incidence of local or regional complications. While a small ulcer at the site of the vaccination, lasting several weeks and with a slight secretion, should be considered a normal local reaction, regional suppurative adenitis should as far as possible be avoided; its incidence is very low when a correct technique is employed.

BCG vaccination should be preceded by a tuberculin test, except in the first two months of life, as unpleasant Koch phenomena are avoided by exclusion of persons already tuberculin-positive. Further, the pre-vaccination tuberculin test provides an important index of tuberculous infection in the community, useful for the planning of continued tuberculosis control. For this purpose, a uniform tuberculin-testing technique should be employed, as well as a standard tuberculin which will also permit international comparison of tuberculosis infection-rates in various age-groups.

Several different methods of BCG vaccination are employed in Europe, the most common being the intradermal injection. This technique has been used in nearly all the controlled trials in which the efficacy of BCG vaccination has been proved, and has been employed exclusively in the worldwide BCG campaigns (assisted by the International Tuberculosis Campaign, WHO and UNICEF) in which more than 100 million persons have so far been vaccinated. Vaccination by mouth is used in several European countries, especially for children. No controlled field trials have been carried out to demonstrate the value of this method which, in general, gives lower conversion rates than the intradermal-injection, multiple-puncture, or scarification techniques.

Routine post-vaccination tuberculin testing is not considered necessary, but it is essential that the potency of each batch of vaccine, as well as the technique of the vaccinators, be checked by careful observation of local reactions and post-vaccination tuberculin allergy in a sample of the persons vaccinated.

It is emphasized that both tuberculin testing and BCG vaccination can be carried out satisfactorily by medical auxiliary personnel after a period of special training.

The efficacy of BCG vaccination in producing a relative immunity against tuberculosis is considered to be proved beyond doubt by the carefully controlled studies which have been carried out, especially those in Canada, the United Kingdom and the USA, which were referred to at the Conference. The protection, after successful vaccination, has been shown to last through observation periods of from 5 to 11 years. It would seem that the vaccination protects against post-primary pulmonary disease as well as against the primary manifestation. One reservation should be made, inasmuch as the possibility has been indicated that BCG vaccination is less effective in areas with a high prevalence of the low-grade tuberculin sensitivity, probably not related to tuberculous infection.

The participants agreed that BCG vaccination should be considered as part of the over-all tuberculosis control programme of any country and should supplement, rather than take the place of, other control methods. The role of BCG vaccination will depend on the local epidemiological characteristics of tuberculosis, as well as on the availability of personnel and funds. In general, vaccination should be carried out at the age when

the individual passes from a lower to a considerably higher infection risk. In countries with a high prevalence of tuberculosis this age is at birth; in other countries it might be at the age when the individual leaves school or enters a particularly exposed occupation. It was felt that those vaccinated early should be periodically re-tested and, if necessary, re-vaccinated.

#### 2.4 *Poliomyelitis*

The Conference discussed at length the use of inactivated virus vaccine (Salk) and live virus vaccine (Sabin, Koprowski, Cox). Information was provided from a number of countries, and the effectiveness of the inactivated vaccine was recorded at from 70% to 80% or even higher. There was one report from outside the region of rather poor results where, in spite of extensive vaccination, epidemics had occurred with large numbers of paralytic cases, especially in children insufficiently vaccinated. The relatively rapid fall in titre of measurable antibodies within a few years of the primary course and booster dose was noted, and the question of giving further booster doses was raised. In some countries a fourth injection is already being given. The Conference recognized the weak points in the use of inactivated vaccine and especially the need for potent type-I antigens.

Information on small-scale trials of live vaccines in several countries and on some very large-scale trials was presented. In particular, the information given by the participant from the USSR, supported by a report from a WHO Consultant, on the successful application of the Sabin-type vaccine to more than 12 million persons, was received with great interest. In the USSR, by gradually expanding programmes under the supervision of various workers, carefully conducted trials have been performed during recent years with good results, both with regard to antibody response and protection against paralytic disease, as far as can be estimated at present, and without causing any cases of paralytic poliomyelitis among those vaccinated or their contacts. The results have been encouraging and justify optimism as to use of this vaccine in public health practice.

The capacity of the live vaccine to induce both circulating antibody and intestinal immunity was discussed. The difficulties of determining paralytogenic properties, except by human field trials, and the need for more information concerning the identification of wild virus and vaccine strains, were touched upon.

Minimum safety requirements must be laid down before live virus vaccine can be generally used, especially as many viruses can be present in monkey-kidney tissue-culture. One of these, the B virus, has proved fatal on several occasions.

The legal and ethical aspects of the use of live virus which spreads to contacts were in some degree touched on, and it was agreed that the use of the live polio vaccine represents a deviation from usual medical practice.

Various questions in connexion with the use of Salk vaccine, such as hypersensitivity and reactions, were discussed. It was generally agreed that there was very low frequency of reactions when using inactivated vaccine.

### 2.5 *Diphtheria, tetanus, pertussis : combined vaccines*

In many European countries diphtheria is still a considerable problem, and in some of them pertussis and tetanus are perhaps greater problems than poliomyelitis. Pertussis, even in a mild form, affects a high proportion of children, is incapacitating, and often causes severe complications.

Potent antigens for immunization against diphtheria and tetanus have long been known and should be used adsorbed, either onto pertussis vaccine or onto an alum preparation. If the right antigens are used in the right age-groups and a sufficient proportion of the population is vaccinated, these diseases can be brought under control. For diphtheria this has been clearly demonstrated in several countries.

Good pertussis vaccines give protection for several years to 80% or 90% of those exposed to infection. The pertussis vaccine should be used early as a particularly high percentage of deaths—up to 70%—occurs within the first year of life. Great attention must be paid to the preparation and standardization of the antigen. Immunization should not be continued when school age has been reached because of the severe reactions.

Active immunization against tetanus should replace the prophylactic administration of antitoxin. The vaccine is cheap, potent, and can be combined with other antigens. The importance of proper individual records was stressed. Neonatal tetanus may be combated by immunization of the pregnant mother, but further investigations in this field are required.

Combined diphtheria-tetanus-pertussis vaccine can advantageously be used for immunizing early in childhood. The Conference agreed unanimously that the use of such combined vaccines should be promoted. It was agreed that the use of a quadruple vaccine (DPT + polio) could not be recommended because :

(a) if used in the first six months of life there would be little antibody response to the polio vaccine, and

(b) the potency of some polio vaccines is not yet sufficient and is likely to deteriorate when mixed with vaccines containing formol.

### 2.6 *Immizations used occasionally or regularly in selected population groups*

The Conference considered the use of vaccines against virus infections of the upper respiratory tract : influenza, adenovirus, mumps and measles. The relative merits of killed and live *influenza* virus vaccines were discussed,

as was the necessity of using vaccines produced from strains antigenically related to the type causing the epidemic. The difficulties arising from these problems were recognized, but results from the last influenza pandemic were found quite satisfactory, with the range of protection covering from 60% to 70% of those vaccinated, both with live and killed virus vaccines. Evaluation had been possible because of the pronounced epidemic occurrence of the infection. The vaccine has been very helpful in the protection of key personnel in medical, transport, certain administrative and other services. The use of either polyvalent vaccine in non-epidemic periods or vaccines containing the specific virus type of an epidemic, was considered of great value in securing against the breakdown of certain vital functions of the community. The use of freshly isolated strains was recommended. In applying live-virus vaccine the technique is especially important (fine-droplet spraying). Normally, such live influenza vaccine should not be administered to children.

Vaccination against *adenovirus* infection is not considered of great practical value.

Vaccination against *mumps* with killed or live virus vaccine is considered important in various circumstances—for instance, the occurrence of an epidemic with a high attack rate followed by complications, as seen among young men entering military service.

Vaccination against *measles* was considered. Good results have been obtained using an attenuated live virus, with a subsequent mild course of the disease when the child was exposed to infection. The vaccine is still under trial. The question is of importance for some European countries where measles causes frequent complications and some deaths.

### 2.7 Vaccination against enteric fevers

The control of enteric diseases by vaccination against typhoid, paratyphoid and dysentery should be considered only as an activity supplementary to sanitation programmes and the raising of the general standard of hygiene.

The only definite proof of the effectiveness of typhoid vaccine was obtained in the controlled field trial carried out by the Yugoslav Typhoid Commission, showing that heat-killed, phenol-preserved typhoid vaccine gives protection to between two-thirds and three-quarters of those vaccinated. Two injections give sufficient protection and there are strong indications that there is no need to repeat booster doses more often than every 3-5 years. The vaccine seems to be particularly effective in school-children, and the vaccination of young children, who stand the injection perfectly well, is to be encouraged where typhoid fever is prevalent. Alcohol-killed, alcohol-preserved vaccine proved to have little or no prophylactic value. Other vaccines, such as acetone-dried and formol-killed vaccines,

may prove satisfactory but have not yet been subjected to controlled field trials.

It was noted with satisfaction that WHO has sponsored further field and laboratory studies of typhoid vaccines in order to find out whether some other vaccine than the phenolized is more effective, and to develop laboratory tests which could be satisfactorily used to measure the potency of various vaccines against typhoid fever.

There is no adequate evidence that oral typhoid vaccine is effective.

There is not enough evidence that paratyphoid antigens afford protection. It is known at least that they are not effective to the same extent as typhoid antigen. However, in countries where paratyphoid fevers are prevalent, the inclusion of paratyphoid A and paratyphoid B antigens in the vaccine is justified.

There is no proof that the dysentery vaccines so far developed are of any value at all. The use of these vaccines does not seem to be justified, except for research purposes.

At this stage, the control of enteric diseases cannot be achieved by vaccination. However, vaccination, primarily against typhoid, can be recommended where this condition is prevalent and where the improvement of sanitation and standards of hygiene cannot be expected in the near future. It may also be justified in emergencies when sanitation breaks down and no other effective measures can be applied. It might also be recommended, in addition to proper health education and proper sanitation, for persons living in close contact with carriers.

#### 2.8 *Leptospirosis, tick-borne encephalitis*

Vaccination against leptospirosis and tick-borne encephalitis can be used in some areas where natural foci of these diseases exist for those groups of the population that are particularly exposed (geologists, geographers, veterinarians, workers in rice-fields, etc.).

Immunization against leptospirosis can be performed with a heated or formol-vaccine which must contain the serotypes of *Leptospira* prevalent in the area where vaccination is required.

Immunization against tick-borne encephalitis can be done with a formol-vaccine prepared from the brains of infected mice or with a monkey-kidney tissue-culture vaccine. There is some risk of severe reaction (in particular, injury to the central nervous system) when using brain-tissue vaccine; for this reason monkey-kidney tissue-culture vaccine is preferable.

Both vaccines are used subcutaneously.

#### 2.9 *Tularaemia*

Vaccination against tularaemia is desirable in areas where natural foci of the disease exist. Hunters and other occupational groups and, in some

instances, the whole rural population of an area can be protected against tularaemia by the use of live tularaemia vaccine prepared from attenuated strains of the agent. The protective value of this vaccine is very high. It is given by scarification.

#### 2.10 *Brucellosis*

Vaccination against brucellosis with live vaccine can protect the population, especially certain groups (veterinarians, shepherds, zootechnicians, etc.). The vaccine can be used both subcutaneously and cutaneously (by scarification), the latter method being preferable because of the lesser risk of provoking severe allergic reactions in persons already infected with brucellosis.

However, the control of brucellosis must in the main depend upon the eradication of brucellosis foci in cattle, sheep and goats. This can be achieved both by veterinary measures and by the immunization of cattle, sheep and goats. Pasteurization of milk gives the population good protection against alimentary infection.

#### 2.11 *Rabies*

Rabies is still a problem in several European countries. The use of hyper-immune serum and the vaccination of persons who have been exposed to infection is a specific form of prophylaxis, but is without influence on the prevalence of rabies. The control and eradication of rabies must be achieved by reducing the numbers of the most dangerous wild animals—foxes, jackals and wolves—the elimination of stray dogs, and the vaccination of domestic dogs.

The Conference took note of the Report of the Expert Committee on Rabies.<sup>1</sup>

#### 2.12 *Other vaccinations*

*Scarlet fever and other streptococcal infections.* Over the past thirty years scarlet fever has not been the serious disease it once was; in addition, it is susceptible to chemotherapy. Vaccination has been abandoned by countries which used it in the past. Chemoprophylaxis is sufficient for contacts. The same is true of other types of streptococcal infection, and in particular of erysipelas.

*Staphylococcal infections.* Vaccination, either by means of antimicrobial or antitoxic vaccines, is of little help against the pathogenic staphylococci.

*Q fever.* Vaccination is restricted to workers in rickettsial laboratories who are particularly exposed to infection. The vaccine, which is very effective, may sometimes produce serious side effects.

<sup>1</sup> *Wld Hlth Org. techn. Rep. Ser.*, 1957, **121**

*Epidemic hepatitis.* There is so far no active immunization method. However, passive immunization through gamma globulin has given some results, but there are obstacles to its widespread use.

### 2.13 *Immunization against quarantinable diseases*

*Yellow fever.* The Conference recognized the importance of vaccination—both with the 17D-strain vaccine and the “Dakar” neurotropic-strain vaccine—in the control of yellow fever in endemic zones, and as one of the measures to prevent the introduction of yellow fever into receptive areas.

*Typhus.* The Conference recognized the value of using typhus fever vaccine as a partial safeguard for medical and similar personnel particularly exposed to risk of typhus infection. For the control of the disease, general sanitation and delousing procedures are the methods of choice.

*Cholera.* The vaccines against this disease are of minor interest to countries of the European region.

## 3. Risks of Immunization Procedures

While proper precautions are taken to ensure that prophylactic biological substances are free of contaminating germs and free from toxicity, there are certain hazards associated with the actual injection of such substances and with the host's reactions to them.

### 3.1 *The syringe and needle*

Absolute sterility of syringe and needle can be guaranteed if they are heated in a hot-air oven at 160°C for 1 hour, or in a high pressure steam sterilizer at 120°C for 20 minutes. In certain countries, a centralized syringe-sterilization service is available for immunization programmes. The more usual procedure is to boil the syringe and needle for 10 minutes immediately before use. It is essential that both syringe and needle be freshly sterilized for each injection if the risk of serum hepatitis is to be avoided. If not feasible, the needle must be sterilized by flaming or immersion in boiling water or hot oil. Alternative procedures are the use of the Gispén valve, which prevents reflux of tissue fluids into the syringe on changing the needle, the use of the needleless high-pressure injector, or the use of cheap disposable syringes. The procedure used in vaccination programmes should be applied on the basis of the incidence of hepatitis in the community concerned.

### 3.2 *Reactions and complications after vaccination*

*Pertussis vaccine.* The occurrence of local and/or systemic reactions in 50% to 70% of children receiving injections of pertussis vaccine has not affected the acceptability of this vaccine in large-scale immunization

programmes. A rare hazard is the occurrence of convulsions within 2-3 days after an injection, and a much rarer risk (perhaps less than one in 1 million) is encephalopathy with symptoms appearing within 6-24 hours after inoculation. To minimize these admittedly rare risks, pertussis vaccine should not be given to a child with a history of recent convulsions; any reaction of a neurological nature after an injection should be a contra-indication to further injections.

*Alum-containing prophylactics.* Experience in different countries has shown that there is a slight risk of post-inoculation paralytic poliomyelitis (provocation poliomyelitis) in children, following the injection of certain prophylactics. This risk is greatest with alum-containing combined antigens (pertussis vaccine plus diphtheria toxoid)—one in 15 000 inoculations among children aged between 1 and 3 years in one study—less with alum-adsorbed toxoids or mixed pertussis and diphtheria vaccine without alum, and negligible with pertussis vaccine or toxoids singly. The hazard may be minimized if inoculation of mixed or alum-containing antigens are given early in infancy under cover of maternally transferred polio antibody, or if the content of alum does not exceed 2 mg/ml. There is, however, no objective evidence on these points.

It should be noted here that other substances which cause local tissue reaction—e.g., procaine penicillin and quinine—may also be associated with provocation poliomyelitis.

*Smallpox vaccine.* Complications that may follow smallpox vaccination include generalized vaccinia (particularly in infants with eczema), encephalitis, and possibly provocation poliomyelitis. The risk of post-vaccinal encephalitis is greater after primary vaccination in schoolchildren and adults.

*Polio virus vaccine.* Injections of inactivated polio virus vaccine are remarkably free of reactions. Occasionally reactions, characterized by headache, soreness of the arm and skin rash, have occurred in penicillin-sensitive individuals, but this risk should disappear when a less commonly used antibiotic is substituted for penicillin during preparation of the vaccine.

*BCG vaccine.* Regional suppurative adenitis is a rare complication after BCG vaccination.

*Influenza virus vaccine.* If vaccines prepared in the chick embryo are to be used, inquiry should first be made about hypersensitivity to egg.

#### **4. Immunization Programmes in the Control and Possible Eradication of Infectious Diseases**

Immunization programmes are effective only when an adequate dose of an effective antigen is administered to a large enough proportion of the susceptible population to create herd immunity.

The evaluation of the effectiveness of the various antigens, of dosage, timing, immunization technique, and so on, is essential. In many instances insufficient attention is paid to strict scientific evaluation of the effectiveness of vaccines, while circumstantial evidence—which is often misleading, being based only on animal experiments, on serology or observations in the field—is accepted without due consideration.

It is stressed that the technique of strictly controlled field trials in human beings should be applied whenever necessary and feasible, as only in this way can unbiased and accurate data be obtained. Although such trials are difficult to organize and expensive to carry out, it is still considered that this is the quickest and cheapest way of solving the problem of which antigens should be used, of how and when they should be used, and of what results may be expected.

Such trials should be carried out on a large scale on volunteers, according to the usual principles laid down for strictly controlled field trials. The population should be allocated at random to groups, one of which should receive a placebo and serve as a control. Non-immunized individuals should not, in principle, serve as a control group. There should be a strict assessment of morbidity, and clinical and laboratory diagnosis should be adopted. In order to avoid any possibility of bias on the part of the observers, the vaccines and placebos should be coded. It is, however, to be noted that a field trial will only measure the effectiveness of the vaccine actually used. Steps must, therefore, be taken to ensure that this vaccine can be reproduced in future, for example, by establishing a portion of vaccine used as an international reference preparation.

Laboratory studies of vaccines are considered essential in order to establish good standards and keep the quality of the antigens at a high level. Close co-operation between the laboratories producing the vaccines, those controlling them, and the public health authorities is most important for the development of better vaccines and for the achievement of better results in vaccination programmes.

*The control of vaccination programmes.* This is one of the most important means of keeping health authorities informed of the status of immunity of the population. In addition to administrative methods and statistical evaluation of data on the immunizations performed, serological investigation of the immune status of the population can yield data which go beyond those obtained by recording clinical disease, since they will reveal not only the effectiveness of the antigen used, but also the prevalence of the infection itself. The information collected in this way may guide the health services in the planning of future activities and prevent epidemics which might occur as a result of a decline in the immunity of the population.

*The effectiveness of vaccination programmes in the control of communicable diseases.* Effectiveness of control will depend on the effectiveness of the vaccine and on the epidemiological features of the disease. Eradication,

in the sense of the eradication both of the germs and of the disease, can be achieved in the case of smallpox, and has been achieved in Europe. However, as this is not the case in other regions, vaccination against smallpox cannot be discontinued in the European region.

Complete control, leading to the extirpation of the disease but not of the germs, can be accomplished in diphtheria. It is felt that the complete control of diphtheria is feasible and that efforts should be made to wipe out this disease in Europe in the near future. Heavy responsibility lies on governments and parents where this preventable disease has not been controlled.

The control of most other diseases can be greatly improved by properly organized vaccination programmes supplemented by other public health measures.

### **5. Recommendations on Immunization Programmes**

The aim of immunization programmes is the control of infection in the community rather than individual protection. A lower level of immunity than is necessary for solid individual protection can effectively reduce the incidence of communicable disease if a high proportion of the susceptible community is immunized. Thus, in diphtheria, there is a rapid reduction in both morbidity and mortality when some 70% of the pre-school and schoolchildren are effectively immunized. Smallpox is controlled when approximately 80% of the whole community has been successfully vaccinated. Tetanus is an exception to this general rule in that protection of a proportion of the population does not reduce the risk to the non-immunized individual.

An immunization campaign carried out without provision for its continuation as a routine procedure will not give satisfactory results—except where complete eradication is achieved. Therefore, in planning immunization schedules, provision must be made to ensure receptivity by the public and, particularly, to secure the co-operation of parents who have to bring their children to the doctor or clinic for repeated inoculations. These measures are essential for the successful execution of the programme.

Difficulties in enlisting continued co-operation of the community, limited health budgets, and shortage of trained staff make it necessary to devise different immunization programmes according to the facilities available in each country or community. A number of communicable diseases that vital statistics have shown to be important public health problems are known to be controllable to a significant extent by specific prophylaxis. Where this is so, the general aim must be to immunize regularly and economically, with the minimum number of visits and injections, a sufficiently high proportion of the susceptible population.

Knowledge about the duration of immunity following the primary course of immunization and after booster (or recall) injections is not yet sufficiently precise in a number of communicable diseases. The number and timetable of booster doses must, therefore, be left rather elastic. The need to use efficient prophylactics and, wherever possible, ones that can be standardized, cannot be over-emphasized since the continuance of immunization programmes with the co-operation and confidence of the public depends on the successful results of these procedures.

The two schedules set out below are suggested models (*a*) for areas with well-developed medical services, and (*b*) for areas with inadequate medical services. They cover five diseases: smallpox, diphtheria, pertussis, tetanus and poliomyelitis. Tuberculosis and typhoid are considered separately. The indications and procedures for immunization in other communicable diseases are considered elsewhere in this report (see pages 12-16).

SUGGESTED SCHEDULE OF IMMUNIZATION IN AREAS WITH ADEQUATE PUBLIC HEALTH MEDICAL SERVICES: TO BE MODIFIED AS REQUIRED TO SUIT LOCAL CONDITIONS \*

Age	Proposed schedule
2-6 months	Diphtheria-pertussis-tetanus triple vaccine: 3 doses with 1 month's interval between each dose
6-7 months	Smallpox vaccination
7-10 months	Poliomyelitis vaccine (inactivated): 2 doses with 1 month's interval
15-18 months	Booster dose of triple vaccine; simultaneously, third dose of poliomyelitis vaccine
2-4 years	Fourth dose of poliomyelitis vaccine
5-6 years	Booster dose of diphtheria-tetanus vaccine; simultaneously, smallpox re-vaccination
10-15 years	Booster dose of diphtheria-tetanus vaccine if Schick test positive; no injection of diphtheria prophylactic in Schick pseudo-reactors

\* *Tetanus*: An individual who has been effectively immunized with a primary course of tetanus toxoid followed by 1 or 2 booster doses should be given a further dose of tetanus toxoid if exposed to the risk of tetanus. If the injury is extensive, a dose of tetanus antitoxin should also be given. If tetanus antitoxin is given to a non-immunized individual, active immunization with tetanus toxoid should be begun 4 to 6 weeks later.

*Poliomyelitis*: The use of live attenuated polio virus vaccine is not included in this schedule because of the still limited knowledge about its efficacy when given orally to infants. This procedure may become the method of choice in countries where there is a high incidence of clinical disease in early infancy. In these countries immunization with inactivated vaccine may have to be begun earlier than suggested in the schedule, but in such circumstances the antibody response will be negligible in a considerable proportion of infants because of the presence of maternal antibody.

It is suggested that the fourth dose of polio virus vaccine be given within 1 to 2 years after the third dose of the primary course since (*a*) antibody titres may have fallen to low levels by that time and (*b*) clinical disease has occurred in children after 3 doses. If the polio antigens, particularly types I and III, are improved, it may be possible to postpone the fourth dose until school entry.

*Quadruple vaccine* (DPT and polio) is not recommended at present.

SUGGESTED SCHEDULE OF IMMUNIZATION IN AREAS WITH INADEQUATE MEDICAL SERVICES :  
TO BE MODIFIED AS REQUIRED TO SUIT LOCAL CONDITIONS \*

<i>Age</i>	<i>Proposed schedule</i>
3-6 months	Smallpox vaccination and simultaneously first dose of triple vaccine <i>with alum</i> Second dose of triple vaccine 1 to 3 months after first dose
5-6 years	Booster dose of diphtheria-tetanus vaccine ; simultaneously smallpox re-vaccination

\* It is envisaged that this schedule will be used in countries with a low incidence of clinical poliomyelitis. In such areas poliomyelitis vaccine should not be employed routinely, but should be available to those at special risk of clinical disease.

Smallpox and triple vaccine should not be given simultaneously either to infants with a history of convulsions or other evidence of central nervous system disease or to those convalescent from an acute infection.

The injection of an alum-containing mixed vaccine carries a slight risk of provocation poliomyelitis in young children. It is recommended that the content of aluminium hydroxide or phosphate should not exceed 2 mg/ml and that the mixture should not be given to infants over 6 months of age.

#### *Tuberculosis : BCG vaccination*

High prevalence areas : first vaccination within first four weeks of life, or, where the modified vaccination schedule is used, BCG vaccine may be given at the same time as the second dose of triple vaccine at between 4 and 8 months of age. Routine pre-vaccination tuberculin testing may have to be done at this age, dependent upon the prevailing infection risk during the first year of life. Re-vaccination at school entry and at school leaving age, after tuberculin test.

Low prevalence areas : first vaccination—in school, or before leaving school after tuberculin test. Re-vaccination may be performed on military recruits and students, and on the occasion of routine examination of other occupational groups.

#### *Typhoid vaccine*

In areas where the incidence of typhoid fever justifies the use of this vaccine it may be given at school entry (5-6 years) : two doses of a phenolized vaccine, with 1 month's interval, will give a reasonable degree of protection for from 3 to 5 years. Booster doses may be given after this time.





