

WORLD HEALTH
ORGANIZATION

ORGANISATION MONDIALE
DE LA SANTÉ

THIRTEENTH WORLD HEALTH ASSEMBLY

A13/Technical Discussions/4 ✓
3 May 1960

ORIGINAL: RUSSIAN

ADDRESS BY THE GENERAL CHAIRMAN
AT THE
OPENING OF THE TECHNICAL DISCUSSIONS
AT THE THIRTEENTH WORLD HEALTH ASSEMBLY

THE ROLE OF IMMUNIZATION IN COMMUNICABLE DISEASE CONTROL

by

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Ladies and Gentlemen:

At the suggestion of the Executive Board of the World Health Organization, confirmed by a resolution of the Twelfth World Health Assembly, the subject chosen for the Technical Discussions at this Assembly is "The Rôle of Immunization in Communicable Disease Control". The Executive Board and the Assembly undeniably acted with great wisdom when they chose so important a subject as the theme for the Technical Discussions.

In selecting me as General Chairman of the Technical Discussions, the World Health Organization did me a great honour. While expressing my deep gratitude and thanks, I cannot help, at the same time, feeling somewhat diffident since I understand clearly all the difficulties and responsibility which I incur in undertaking this important task. However, I am sustained in my belief that this discussion will be fruitful and extremely useful for the work of the World Health Organization by the presence at this Assembly of so many outstanding representatives of scientific medicine and the health services in various countries, whose erudition and experience will, I am sure, help me to overcome the difficulties with which I am faced and will make it possible for us to work together to draw up recommendations. In opening this discussion I wish, therefore, without becoming too deeply immersed in technical details, to try to give a short outline of the problem.

Although the first attempts to use immunization for the prophylaxis and control of infectious diseases were made in the distant past and the first important contribution to the solution of the problem was made by the great English physician, Edward Jenner, as long ago as the end of the eighteenth century, the real development of theoretical and applied immunology began at the time of the great discoveries of Pasteur and his followers, Robert Koch, I. Mechnikov, Joseph Lister and many other outstanding microbiologists and immunologists. The discovery of the virus by Dmitri Ivanovski at the end of the last century considerably broadened our conceptions of the causative agents of infectious diseases and promoted the further development of immunology. From the end of the last century onwards the work done on problems of microbiology and immunology has led to the production of many preparations for active and passive immunization against infectious diseases. The number of these preparations is increasing from year to year and their quality is being improved

pari passu with the development of our knowledge of the nature of infectious diseases and the properties of their causative agents. At the present time the number of these preparations is so great that the time has come to discuss which of them should be used, where, and under what conditions, and to settle the place of immunization in the system of measures for the prevention and control of infectious diseases. Perhaps this last question, i.e. the rôle and place of immunization in the prophylaxis and treatment of infectious diseases, should be the central theme of our discussion, since all the other questions, such as quality standards for vaccines, the scale of immunization programmes, the correct time for immunization in various age-groups, the actual methods employed and, finally, the legal questions raised by the use of vaccine, derive from and depend upon the solution of this central problem. In determining the rôle of immunization in the system of measures for the prevention and control of infectious diseases, the first thing to be clearly demonstrated is what can be achieved in the prophylaxis of a particular infectious disease by immunization of the population and whether immunization is a basic and decisive measure or only subsidiary. The answer to this question must, of course, be based primarily on the latest available data on the epidemiology of infectious diseases or, if I may be permitted to use the expression, the ecology of their causative agents in human society.

In the case of a large number of infectious diseases, immunization is the basic and principal measure of prophylaxis, owing to the nature of the mechanism of spread of the infection and the durability of post-infectious immunity. An example of such a disease is smallpox. Since this disease is transmitted by droplet infection, which quickly spreads it among the population, restrictive measures and quarantine, while they may prevent it spreading in a particular locality, will hardly be sufficient to eradicate it. The presence of marked post-infection immunity, reproducible to a large extent by means of artificial vaccination, makes vaccination the principal measure of smallpox prophylaxis. Half a century's experience in many countries has already shown that active immunization by means of high-quality vaccines has led to the complete eradication of smallpox in those countries and that if the immunity of the population is maintained by periodical revaccination, then even the importation of smallpox from other countries will not lead to any appreciable

spread of the disease. Furthermore, even if for various reasons a considerable proportion of the population is not immune when smallpox is imported, a speedy immunization campaign in conjunction with quarantine measures will make it possible to eliminate the focus in the shortest possible time. Striking proof of the correctness of these statements is afforded by experience in the speedy eradication of smallpox outbreaks in New York in 1947, in Brighton in 1951 and in Moscow in 1960. In particular, the swift suppression of the smallpox outbreak in Moscow in January this year was due not only to energetic anti-epidemic measures but also to the fact that more than nine million persons were immunized in that city in the course of a week, so that 10-12 days afterwards smallpox had no chance of spreading further.

The leading rôle of active immunization in the prevention and eradication of the disease was the basis for the decision taken by the World Health Organization in 1958 to eradicate smallpox throughout the world by means of large-scale vaccination of the public. In view of the high quality of smallpox vaccine and the simplicity of the vaccination methods used, the world-wide eradication of smallpox by mass vaccination, in the first instance in countries where the disease is endemic, is not a task of insuperable difficulty and therefore the decision taken by the World Health Organization is completely realistic. We may not only hope but can be quite certain that the next few years will bring victory over this dread infection and that its causative agents will be eliminated throughout the world.

A number of other infectious diseases could be listed, in the prophylaxis and eradication of which immunization plays a primary rôle. They include diphtheria, the epidemiological features of which are similar to those of smallpox, although it differs in that in addition to patients, carriers of the diphtheria microbe, who may themselves even be immune, act as a source of infection. Experience in many European countries, such as Britain, France and the Scandinavian countries, and in many cities and localities in the Soviet Union and the United States of America, shows that correctly organized and systematically carried out immunization and re-immunization of children against diphtheria leads to the practical eradication of this infection among the population. Here we have a distinctive conversion of quantity into quality: the high degree of immunity enjoyed by the bulk of the population not only prevents the contraction of diphtheria but also sharply reduces

the opportunities for its causative agent to circulate. It is, of course, both possible and necessary to discuss whether in these conditions the causative agent of diphtheria will disappear or maintain itself in existence, but for those of us working in the health services it is nevertheless much more important that in this way a practical start is being made towards the complete prevention of diphtheria cases among the population, not to speak of the fact that the odd cases of residual infection which do occur follow a very mild course and as a rule do not result in death.

Obviously poliomyelitis should also be included among those infectious diseases in which it is possible in principle, by mass immunization of the population, to achieve practical eradication to the same extent as in the case of diphtheria. The problem of the possible eradication of poliomyelitis has only recently come to the fore. It was still not realistic to hope for eradication a few years ago, when vaccination with the Salk vaccine prepared from the killed virus began to be more widely practised, because although the vaccine conferred individual immunity to the contraction of the paralytic form of poliomyelitis, it did not prevent the multiplication of poliovirus in the intestines and respiratory tract and consequently did not hinder its circulation in the population. The position changed when living poliovirus vaccine began to be used in practice, administration of which not only establishes insusceptibility to the paralytic forms of the disease but also increases the specific resistance of the cells in the intestines and respiratory passages, thus hindering multiplication of the virus in them. This cannot but lead to diminished circulation of the poliovirus and, consequently, if a large percentage of the population is immune, will bring about conditions similar to those observed where there exists a mass immunity to diphtheria. Experience of carrying out extensive immunization of the population in certain regions of the USSR, particularly in the Baltic Republics, has demonstrated the practical possibility of eradicating poliomyelitis morbidity among the population. We therefore await with impatience the results of the immense programme of immunization against poliomyelitis, in the course of which it is intended in six months or a year to administer the vaccine to not less than 80 million persons. If this experiment proves fully satisfactory, it will answer the question of whether it is possible to eradicate poliomyelitis, at any rate for practical purposes, by means of mass immunization of the population.

Obviously these infectious diseases do not exhaust the list of infections in which mass immunization is such a basic and important measure that its large-scale practice, while not ensuring complete eradication of the causative agents, at least results in the practical elimination of the disease. If our knowledge of the nature of measles and immunity to it is reliable, it can be presumed that the development of an improved vaccine against that disease will make it possible in practice to raise the question of eliminating measles in many countries at any rate, if not throughout the world. If considerable improvements are achieved in the development of a pertussis vaccine, particularly one which involves less risk to child health, then it is quite probable that the prophylaxis of whooping cough will approach diphtheria prophylaxis in effectiveness. I shall confine myself to this short list of infections in which immunization plays a basic and decisive rôle in the prophylaxis, or even elimination, of the disease concerned.

There is a sizeable group of infectious diseases for the prophylaxis of which vaccines have also been proposed which are sometimes quite effective but which cannot be assigned a primary rôle in solving the problem of the prevention or elimination of the disease in question. An example of this type of infection is tuberculosis. World-wide experience in the use of BCG vaccine since 1920 has shown that large-scale vaccination of the child population confers on the organism a relatively appreciable resistance to tuberculosis and reduces the probability of subsequently contracting the disease. At the same time, nowhere, even in countries where practically the whole child population is vaccinated against tuberculosis, has it proved possible to eliminate tuberculosis by this means. The effectiveness of the vaccine, in the sense of the relative infrequency of tuberculosis cases among the vaccinated, varies according to different sets of data within fairly wide limits. In some instances it has been shown that the incidence of the disease among the unvaccinated is between three and five times higher than among the vaccinated. In other cases this figure is as high as ten or twelve times. Obviously all these data can be considered as reliable since the effectiveness of vaccination against tuberculosis depends not only on the quality of the product itself but also on the condition of the human organism, the living conditions of the population and the intensity of the epidemic process, i.e. the frequency with which the population is infected with

tuberculosis. Tuberculosis has long been considered, and rightly so, to be a social disease, affecting mainly the poor and needy. The complex problem of eliminating tuberculosis at the present time is being tackled in many ways. The most important factor is the increase in the standard of living of the population, primarily improvements in housing and food, and also the higher level of health education. The use of modern methods of antibiotic therapy of tuberculosis, combined with lengthy hospitalization followed by treatment in clinics and sanatoria, makes cures possible and enables patients to be made non-infective for those around them, thus preventing the spread of the disease among the population. There is no doubt that these two measures are basic in the prophylaxis of tuberculosis. The experience in the economically developed countries where the incidence of tuberculosis is continuously falling and where the problem of the elimination of the disease has already been practically solved, shows that these are the methods of control which will lead to eradication. At the same time, active immunization against tuberculosis remains an important if subsidiary measure, the significance of which will decrease as the level of infection among a population decreases. It was on the basis of these principles, set forth in October last year by a scientific conference on immunization held in Morocco under the auspices of the European Office of the World Health Organization, that the conference worked out various measures of tuberculosis control applicable in different conditions and recommended the mass immunization of the population in childhood and youth for those countries where the incidence of the disease is still high.

As in the case of tuberculosis, immunization retains its importance as an auxiliary means of prophylaxis in many other infectious diseases. Its importance depends not only on the specific features of a particular infection but also on its incidence in the locality concerned and the possibility of adopting other more radical measures, which in turn depends in part on the economic resources of the local health authorities, veterinary services and other bodies responsible for prophylaxis against the disease. An example of this is typhoid fever. The best vaccine against this infectious disease is quite effective. The best samples of it may reduce the incidence of typhoid among those immunized as much as ten- and twelve-fold; at the same time, however, it is quite obvious that it is not

immunization but measures for improving sanitary conditions in the centre of population concerned which form the keystone of typhoid prophylaxis. Experience in economically developed countries, in whose cities and villages the population is provided with piped water of good quality and where the treatment of refuse and other waste matter to make it harmless to health is well organized through the construction of sewage systems and the regular operation of rubbish collection and disposal, shows that this is the way in which to eliminate typhoid in practice. If, in addition, the food trade is organized on the basis of our present-day knowledge of hygiene and the population also has a high standard of hygienic behaviour, there is naturally no need in such a country to immunize the people against typhoid. At the same time, immunization will retain its sometimes enormous importance in countries where a relatively high level of typhoid morbidity is maintained by the low standard of sanitation in population centres. While not solving the problem of eradicating typhoid, immunization in such cases, if correctly organized, can considerably reduce the incidence of the disease.

In the Soviet Union considerable success has been achieved by the use of a live vaccine for human prophylaxis against brucellosis. Brucellosis is found in several regions of the USSR, particularly where sheep farming is highly developed. A radical method of control is the carrying out of veterinary measures designed to eradicate brucellosis among the sheep. However, side by side with these measures, which require large financial outlay and considerable time for their execution, immunization with the live vaccine mentioned has been widely used in practice to control brucellosis among human beings in the USSR, since, while harmless in itself, the vaccine confers a high degree of immunity on the population. It is by this method that a considerable reduction and sometimes the almost complete eradication of human brucellosis has been achieved in many livestock rearing regions considerably earlier than the infected flocks of sheep themselves could be given a clean bill of health. Of course, as brucellosis is gradually eliminated among the stock, human immunization to prevent human infection with the disease becomes less important. In any case, as we can see, the rôle of immunization in brucellosis prophylaxis depends not only on the quality of the vaccine used but also on the specific features of the epidemiological situation, as in the case of tuberculosis and typhoid.

There is a large group of diseases occurring in natural foci with which man is infected from wild animals, in most cases through the intermediary of blood-sucking vectors. These diseases, such as tick-borne encephalitis, tularaemia, mosquito-borne encephalitis, etc., have probably existed in their natural foci for many million years and arose long before the appearance of man. Human infection with these diseases depends on features of the economic activity of man, as a result of which human beings come into more or less close contact with the natural foci. In the USSR, tick-borne encephalitis became a health problem mainly in the middle of the nineteen-thirties, when the intensive economic development of the uninhabited taiga and Far Eastern districts and the penetration of large numbers of people into the natural foci of tick-borne encephalitis began to lead to the appearance of the disease among human beings. A detailed study of the natural foci of these diseases showed that their eradication was possible only around centres of habitation, where the spraying of large areas of forest with insecticides successfully eradicates the tick and hence interrupts the circulation of the virus in nature. Effective protection against infection can also be obtained by regular use of individual means of protection against the tick - such as protective overalls and repellents. However, these measures do not guarantee that people will not be infected with tick-borne encephalitis and the eradication of the natural foci of this disease over the immense areas of the Siberian and Far-Eastern taiga is, to say the least, a fantastic dream at the present moment. For that reason, active immunization has a rôle of no small importance to play in protecting people against infection. Many years of experience of using the vaccine against tick-borne encephalitis by immunizing those groups exposed to the risk of infection by reason of their work in the natural foci of the disease (geologists, lumberjacks, workers on new construction sites, etc.) has shown the great effectiveness of this measure in the prophylaxis of tick-borne encephalitis.

Another example of such a use of immunization is the practice of using a live vaccine against tularaemia. This vaccine, which is completely safe, confers on the inoculated a high level of immunity, comparable with, or even perhaps surpassing, the immunity produced by smallpox vaccination. For that reason in practical tularaemia prophylaxis in the USSR, where the natural foci of the disease are spread over a huge territory, vaccination of the population against tularaemia has been extensively

practised. Of course, here also measures of individual protection against the bites of blood-sucking arthropods and agricultural improvements leading to the extermination of the rodents which carry the infection and hence to the elimination of the natural foci of tularaemia, occupy a predominant place. However, the possibility of using these measures and their effectiveness is considerably reduced in sparsely inhabited and uninhabited localities. At the same time the wide use of vaccination against tularaemia has achieved such an appreciable effect that the number of cases, which in the middle forties used to be as high as 100 000 per year, has now been reduced to a few hundred cases annually. Thus active immunization in certain conditions can play a primary rôle in the prevention of human infection with diseases with natural foci. The list of these infections increases every year and the problem of immuno-prophylaxis against them is therefore quite a topical one.

So far we have spoken of those infectious diseases in which, whether vaccination is the main method of prophylaxis or an auxiliary one, and whether or not its importance varies as a result of local conditions, the existing vaccines themselves are highly effective. There is yet another group of infections, however, in which, despite the limited effectiveness of the existing vaccines, the immunization of the population is so far the most promising prophylactic measure. In speaking of this group of infections I am thinking in the first place of influenza. Transmitted by droplet infection and possessing an extremely short incubation period combined with high infectivity, influenza is perhaps the only truly world-wide infection, knowing no state boundaries. I emphasize this description of it as a world-wide infection because a pandemic of influenza, unlike, for example, pandemics of malaria or smallpox, is not a rare and extraordinary event which may be prevented by quarantine measures, but represents the means by which the infection itself maintains its existence; since there are no endemic foci of influenza beyond which it could spread, influenza exists at the present moment as an infection of humanity as a whole. Experience of the last three pandemics and study of more moderate epidemics of influenza, which usually attack a considerable number of countries simultaneously or in turn, show that neither measures of general hygiene nor anti-epidemic and quarantine measures can do anything worth while to limit the spread of the infection among the population. The level of influenza morbidity and its

periodic variations are determined on the one hand by the level of immunity of the population to the various influenza viruses and on the other by the variations in the antigenic structure of the influenza viruses themselves, which take place gradually and simultaneously throughout the world. It is therefore natural to attempt to raise the level of immunity of the population by artificial methods, i.e. by means of mass vaccination. The virologists in various countries are following two lines of endeavour. Some of them are trying to obtain a sufficiently effective vaccine made from killed virus and others are trying to achieve their end by using vaccine made from attenuated live influenza viruses. Even if we disregard failures in large-scale vaccination experiments due to the use of a vaccine prepared from virus strains not equivalent to the immunological strains which cause epidemics and pandemics of influenza, the effectiveness of the vaccines used is still quite limited. In the mass, they cause a reduction in morbidity among those vaccinated of between two- and three-fold or, at best, between five- and six-fold, and this best is not often achieved. Probably these latter indices are the potential limit of effectiveness of an influenza vaccine, since even the natural influenza infection produces an immunity which is limited in intensity and duration. Although quite intense in the days and months following the illness, this immunity is considerably reduced after one to one-and-a-half years and the reduction is speeded up by the fact that the viruses themselves change their antigenic structure and consequently their immunological properties in the course of a few years. All these circumstances make it quite difficult to find a scientific and practical solution to the problem of effective immunization against influenza, since the very best vaccines are naturally unable to confer an immunity of greater intensity and duration than that resulting from contraction of the natural disease.

And yet active immunization against influenza, even today, seems to be the most promising measure of prophylaxis against the disease, until such time as other methods of control are discovered, such as antibiotics which might make the patient non-infective in a short time, or other preparations which may increase non-specific immunity to influenza. While these do not exist, the problem of influenza prophylaxis will probably be tackled by means of the further improvement of existing influenza vaccines and methods of administration, and the organization of

vaccine production on such a scale that sufficient amounts can be produced in a very short period, in order to be able to confer on large groups of the population a high level of immunity with which to face the attack of the influenza virus which is circulating. There is no need to point out that even this far from perfect method of influenza prophylaxis has still not been put into practice anywhere, and that to do so will require the surmounting of great scientific and organizational difficulties.

Similar difficulties also loom up when we consider the problem of immunoprophylaxis against other diseases similar to influenza (adenovirus infections, infections caused by para-influenzal viruses, etc.) and also the problem of prophylaxis against streptococcal infections.

I am, of course, in this opening speech, confining myself to giving a general outline of the problem of immunization, to considering the strategy and tactics of the campaign against human infectious diseases. There is no need to dwell on other theoretical and practical problems connected with this wide subject, which will be discussed later. I shall only touch upon two or three aspects of this problem which will doubtless attract the attention of participants in these Technical Discussions.

One of these acute problems is how to work out the best times for immunization against infectious diseases in childhood. Modern life is such that every new-born human being is faced with the dilemma either of suffering from numerous and almost inescapable infections at the most vulnerable age, that of childhood, or of submitting to numerous and often painful immunization procedures to provide protection against them. The number of vaccines which can be administered at the present day is large. While some of these are used only in restricted localities, others are used for protection against children's infections found almost throughout the world. Against what infections should children be vaccinated? At what ages is it best to vaccinate? How can the frequency of immunization be decreased? Is it possible (and if so, in what way) to combine various types of vaccination? What are the prospects of producing new combined preparations which will produce immunity against several infections? It seems to me that discussion of these questions will help us on the one hand to stimulate the essential theoretical research and on the other hand, by generalizing the knowledge we have now accumulated, to work out optimum schedules

of immunization in childhood which would solve the well-known mathematical task of how to achieve maximum effect with minimum means. I am sure that here, to use the same mathematical language, we shall find if not a precise at least an approximate solution for this complex task,

Another question which deserves most serious discussion is how to work out objective criteria for assessing the rôle and place of immunization in the prophylaxis of infectious diseases. Indeed, the whole of my speech so far has been an attempt, perhaps not an adequate one, to pose this question. I should like to see this question discussed more widely and from more points of view, and I think that in seeking the answer we must take into account not only the features of the infection but the features of the epidemiological and indeed the economic situation. For that reason the recommendations we work out here must not merely be general, but should also, as far as possible, be practically applicable in different countries and by different health services. Finally, I hope that here there will also be time for discussion of questions connected with medical legislation on immunization. There are different laws in different countries. In some cases inoculations are voluntary, in others obligatory and even forced. It is hardly possible here to work out general recommendations applicable to all countries, since in trying to solve this question we come up against variations in social structure, historical differences, different habits and customs, and special features of the health services, which have become so varied in the different countries. One thing seems to me indisputable, and that is the general tendency to attach greater importance to the rôle of the population itself in carrying out an immunization programme. The higher the level of the public's medical knowledge and health education, and the closer the contact between the health services and the public, the less necessary are all kinds of restrictive and compulsory measures. Experience in our country, particularly during the last few decades, has shown that if there is well organized medical propaganda among the population and close contact and mutual understanding between the health services and the masses of the people, any kind of compulsory measure simply becomes unnecessary. I also think that the lofty humane aims of the sphere of activity in which we work, I have in mind the health services and medical science, should be combined with humane methods of achieving those aims.

Thank you, Ladies and Gentlemen.