

## **Panamerican Symposium on Immunizations organized by the Secretaría de Salubridad y Asistencia**

### **CONCLUSIONS**

**T**HE Panamerican Symposium on Immunizations organized by the Secretaría de Salubridad y Asistencia in Mexico City on April 26 and 27, 1979, was a significant event in the framework of activities of the International Year of the Child. As a result of the activities there were some important conclusions, concerning specially to the availability of products for immunization of satisfactory quality from the immunological medical and epidemiological points of view, for the prevention of diseases included in the World Health Organization Expanded Program on Immunization; on this grounds it can be concluded that the problem for obtaining an optimum prevention of these diseases is mainly administrative.

During the symposium, a review was undertaken of the biologics of major importance in relation to schemes for application and their relevant characteristics, including new products that may be of interest in the future. The present day information of

diseases preventable by immunization and the methods applicable to the satisfactory implementation of programs, were reviewed.

The role of the community, fundamental to achieve maximum coverages in immunization programs through educational activities taking in consideration sociocultural patterns, received special attention.

In this chapter we will present a panoramic view of the more relevant concepts of the event which was organized as follows:

The first part was devoted to a general review, basic and doctrinary, on immunizations: in a second stage the immunization agents presently available were reviewed from the points of view of their composition, biological properties, protective efficacy, etc.; and finally, an analysis was made of administrative-operational factors, required to improve immunization coverage.

Dr. GRINSTEIN from Argentina in his presentation **What is immunity and how it is conferred**, underlined the importance of biological environment for explaining several variants in frequency and distribution of

diseases, taking as an example the difference existing among Brazil and Argentina in relation to the problem of meningococcal meningitis A, presenting higher incidence in the first country, and apparently explained by wide circulation, in the second one, of *Bacillus pumilus*, a bacterium crossing serologically with *N. meningitidis*. He put emphasis in higher purification of future vaccines, fractions of microorganisms and preparations of genetic engineering, illustrating the experiments with the introduction of virus DNA to *E. coli* genome, and virus DNA of foot-and-mouth disease codifying for certain protective antigens.

Dr. W. CHAS COCKBURN from World Health Organization developed the subject of **Importance of immunization in preventive medicine services**. Concerning this point he noted that in countries with comprehensive preventive and curative health services, the past 20-30 years have witnessed dramatic reductions in morbidity and mortality from the infectious diseases.

Immunization has been the major contributor to these achievements.

Death rates from poliomyelitis, diphtheria, whooping cough and tetanus have fallen by 87% up to 99%.

In four countries chosen as representative of Central and South America the decrease in the same diseases over the same period have also been considerable, ranging from 48% for poliomyelitis to 89% for measles and diphtheria. However, the current death rates for diseases which can be prevented by immunization are from 50 to 450 times greater than in the more favoured countries. Central and South America could, and will reach the same pinnacle of success with immunization in the next 5-10 years as, for example, North America and most of Europe have done in the past 20 years. However, the killers of 75% of children under five years of age in much of Central and South America are the diarrhoeal diseases and the acute respiratory infections and the effectiveness of immunization may well be obscured unless much greater effort than at present is made to improve nutrition

and environment and to limit family size.

Dr. ALBERT B. SABIN presented an interesting paper, summarized as follows:

The magnitude of paralytic poliomyelitis as a public health problem, deserving special measures in economically underdeveloped countries, is not adequately reflected by the number of officially reported cases. Clinical for poliomyelitis lameness in school-aged children, recently reported from Ghana, Burma, Egypt and the Philippines, have shown how very high the average annual incidence can be in both rural and urban areas in the absence of epidemics. There is a great need for similar clinical surveys in many other countries. Paralytic rates higher than those during the peak, prevaccine era in the USA have been found in countries with high infant mortality rates and continuing poverty with its undernutrition, malnutrition, and absence of basic sanitary facilities. Analysis of reports of a lower frequency of antibody response to one or two doses of oral poliovirus vaccine (OPV) in infants in economically under developed, subtropical and tropical countries, revealed the importance of insensitive neutralization tests as well as of a phenomenon similar to that involved in the lower seroconversion rates encountered in the early 1960's among older children and adults in the USA. The phenomenon is based on the fact that immunity following infection with polioviruses can in some persons consist of intestinal resistance to reinfection with very low or undetectable levels of antibody. Neutralization tests for antibody that begin with 1:8 or 1:10 dilutions of serum not only miss a certain proportion of persons that are already immune before receiving OPV but also fail to detect those with a lower antibody response.

There is no question that a high prevalence of concurrent nonpoliovirus enteric infections can modify, delay, and lower the frequency of antibody response to one or two doses of OPV, even though some field studies have reported no such effect. It has, nevertheless, been established that this impediment to optimum effectiveness of OPV in

some infants in the tropics is overcome by multiple doses. Prolonged breast-feeding, which is often mentioned as another impediment to the effectiveness of OPV, has been found to be without inhibitory effect in the routine use of OPV in infants in the USA and in the tropics.

The problem of eliminating poliomyelitis as a public health problem in economically underdeveloped countries is administrative and not immunological or epidemiological. It is also obvious that both a different and specially concentrated effort is needed in countries in which most of the cases occur during the first two years of life and paralytic polioviruses are propagating year-round in the intestinal tracts of a large proportion of the infant population. The problem is predominantly administrative because the highly desirable expanded routine infant immunization programmes, which include OPV but reach at best only 20-40% of the total infant population with one or more doses of the vaccines that require multiple doses for maximum effectiveness, cannot be expected to protect the unvaccinated and inadequately vaccinated children in the community. Use of multiple doses of quadruple vaccine (DPT + inactivated polio vaccine) would not only greatly increase the cost of routine immunizations but would not achieve more or as much as the feeding of OPV at the time of the DPT injections.

In countries with small numbers of professional health personnel and many other year-round problems, the best results can be expected from annual mass vaccination campaigns on only 2 days of the year 2 months apart, during which OPV is given to all children under 2, 3 or 4 years of age (depending on the epidemiologic situation in the regions) without reference to the number of doses they may have before. A plan for such mass campaigns based on central national planning and decentralized regional and local implementation using large numbers of unpaid, unskilled, well-rehearsed volunteers will be described. A WHO anti-epidemic program is suggested for helping needy countries that for one reason or another

will continue to have epidemics. Some of the causes of occasional paralytic illness, simulating poliomyelitis but not caused by polioviruses, in well vaccinated children are described.

Dr. J. DE MUCHA, Director of the National Institute of Virology informed that measles vaccine is now made in Mexico at the National Institute of Virology, utilizing the Edmonston-Zagreb strain. This is entirely similar to Schwartz strain, in relation to immunologic strength and other characteristics. As an essential part of the program for the development of this vaccine, a field trial was undertaken in collaboration with the National Program for Integral Development of the Family (DIF); the results were completely satisfactory and will be published in the future.

In his excellent paper on rabies vaccine, Dr. ATANASIU referred to the vaccines available and their characteristics:

1. The vaccine of the future is a purified glycoprotein obtained from the culture supernatant of vaccine virus grown in diploid cells.

2. The evaluation of a vaccine should not be based only in the determination of circulating antibodies but in the induction of interferon and stimulation of the immune system, measured by blastoid transformation and other appropriate techniques.

3. Dr. ATANASIU gave general information on recommended procedures for the application of the vaccine, schemes for vaccination, etc.

4. He recommended immunization schemes reduced to seven doses with 4 additional booster injections; the use of this scheme has been useful in France for reducing to zero the incidence of immunization side effects.

In relation to viral combined vaccine we had the valuable presentation by Dr. GRINSTEIN who dealt with the usefulness of vaccines for mumps and cerebrospinal meningitis in closed populations such as recruits of the Argentinian Army submitted

to programs for the control of these diseases, with excellent results.

Dr. GEOFFREY EDSALL was unable to attend because of personal health reasons, but he sent an interesting paper on the basic knowledge relative to diphtheria and tetanus toxoids, which are the better known products for immunization.

Among the relevant aspects we would mention:

1. Schemes for immunization.

It is advisable to apply 3 doses of DTP vaccine with an interval of 6 weeks from the third month of life, and one additional dose after one year. There are other schemes more reduced because of logistic problems of application.

2. He dealt extensively with the prospective search for simplified schemes that could be useful to prevent:

- a) desertion of the population.
- b) undesirable side reactions.

3. He reported on the research undertaken to modify the present day antigens and to increase the potency of the vaccines, consideration given to a better knowledge of the mode of action of these substances.

In relation to *pertussis* vaccine, Dr. CAMERON discussed several problems still waiting for solution in the metabolism of *Bordetella pertussis* and in the production and safety control of this vaccine.

He made a brief review of the development of culture media for growth, from the complex medium of Bordet-Gengou to the media now used which are chemically defined.

Agar inhibits growth of *B. pertussis* and this toxicity can be neutralized by such agents as charcoal, erythrocytes, anion exchange resins and serum. The source of agar has an influence and there is a difference even among different lots of the same agar.

Colonial variation was discussed. This phenomenon allows to make a selection of clones capable of producing more mouse

protective antigen and less histamin-sensitizing-factor. Clonal selection offers a means to obtain more protective and less reactive strains of *B. pertussis*, until the protective antigen is isolated, characterized and shown free of undesirable reactivity-assuming this to be the case; this is a field still unexplored.

In the formulation and control of *pertussis* vaccines, other problems were reviewed: the mouse protection test, the significance of agglutinin response, the effect of adjuvant, the benefits in the use of adsorbed vaccines particularly DTP (diphtheria, tetanus, *pertussis*), the differences among vaccines and the necessity of reference preparations for the measurement of entities thought to be related to safety and efficacy, e.g.: histamin sensitizing factor and lymphocytosis promoting factor. In the meantime, while the mentioned stages of research are accomplished, there will remain the necessity for such reference preparations because of the growing interest in the reactivity of *pertussis* vaccine.

In relation to enteric vaccines, Dr. FERNANDEZ DE CASTRO reminded that typhoid vaccine was effective in Mexico during the 1972-1973 epidemic, and presented the possibility of application of new vaccines based in different principles, such as live attenuated vaccines made of microorganisms with metabolic deficiencies. In addition, he made a brief mention of new agents now under development for active immunization against amoebiasis and other infectious agents.

Dr. VILLAREJOS from Costa Rica presented an overview on the development of new viral and bacterial products for immunization, with special reference to hepatitis B vaccine, now in the phase of development, and to multiple polyvalent vaccines for pneumonia.

The review on the diseases preventable by vaccination in Mexico was made by Dr. MARIO CALLES LOPEZ NEGRETE, main authority in this field of the country, who pointed out the importance of preventive medicine as the medicine of the future. He

stated that diseases preventable by vaccination still have a high incidence in Mexico, and he agreed with Dr. SABIN that the main problems are administrative, to reach success in the achievement of the proposed goals.

He explained the variants in strategy followed by the present administration, the change from mass campaigns to routine programs and the adoption of a combined system in the fight for the control of poliomyelitis.

He pointed to differences in coverage by the various health institutions, which are with better proportion in the SSA, and particularly low in the ISSSTE. He presented tables with data from three Mexican cities, showing that the vaccine is not reaching the group more susceptible to the diseases under consideration and in this way we are wasting resources in the vaccination of children above the ages more adequate to confer protection.

Dr. VILLAREJOS made an interesting review on the present state of diseases preventable by vaccination in Central America, of special interest in relation to polio and measles. A reduction has been obtained but no complete eradication in all countries except Panama, where poliomyelitis was eliminated.

#### **State of diseases preventable by vaccination in South American and the Caribbean**

Under this heading, Dr. FINKELMAN from OPS made a wider review including all the American continent and using as a framework the available tables of *per capita* income and the figures of budgetary investment in health activities, to underline the relationship existing among the components of the socioeconomic complex.

For the purpose of analysis he divided the region in North, Meso, and South America and compared the morbidity and mortality rates. He emphasized the steep reduction of rates in North-America, with a smaller

slope in South America and stationary in Meso-America.

He also noted the differences in favour of countries with an integrated health system.

In relation to mortality in preschool age children an accelerated descent can be observed in North America and a stationary level in general in the countries south of Rio Bravo.

Brazil, Colombia and Mexico are the main contributors to polio morbidity in Latin America, and for that reason these countries should make a special effort to control the disease.

Dr. MARIO CALLES LOPEZ NEGRETE presented the National Card for Vaccination, as an instrument to reach higher levels of coverage; the purposes of this instrument are to obtain:

- a) Reliable figures of susceptibles for vaccination.
- b) To plan ahead the demand of biologics.
- c) To assist in epidemiological studies.
- d) To obtain information on the number of children failing to the scheme of vaccination.
- e) To avoid the waste of biologics.

All this is supported by a system of information and assessment: the card for vaccination. Its establishment was made on the basis of a statistical study enabling the Mexican authorities to obtain such informations as:

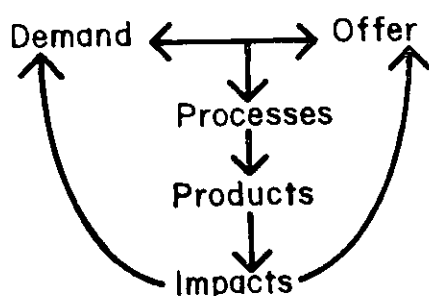
- a) the knowledge, or better to say, the lack of acquaintance of the public with vaccines.
- b) a lack of personal documents to attest vaccination, that could be given by health services of any type in the country, including institutions of social service.

An enquiry was made at the same time with legal experts and it could be established that the National Card for Vaccination should not represent an impairment for freedom of the citizenship but it was rather an

instrument of social welfare that even could represent an increase of that freedom.

On January 1st, 1979 in a ceremony the Card for Vaccination was presented by the President of Mexico and Mrs. LOPEZ PORTILLO; at the moment of his presentation at the symposium about 2 million cards had been distributed through the established channels.

Lecturing on "Planning of immunization programs", Dr. FINKELMAN recommended, as a fundamental point, no to plan without previous assesment of the situation, and proposed a map of evaluation, as follows:



He made a study of the factors involved in the demand: population structure and density; health conditions; awariness of disease susceptibility; location of health services, and people's geographical-socioeconomical circumstances.

In regard to the offer he spoke on the organization and functions of the services, as well as the legal support existent in each country. Besides on the subject of resources he pointed out the importance of the "cold chain" and the quality and availability of vaccines. A relevant point he stressed was that qualification and number of personnel at all levels.

About the processes, he presented the strategy and scheme of health services delivery and gave, as an example of the factors conditioning the response, that one of the design of a good vaccination schedule to reduce the contacts personnel-public.

In relation with the products, he raised two points:

1. **Coverage:** It's important not to take the volume of vaccine distributed as equivalent of coverage.

2. **Costs:** he informed, as a reference for planning, that the cost of vaccinating a child is about two dollars (although in some countries it can be as high as nine dollars).

Analyzing the impacts, he revised objetives to reach, being the main the modification of risks on:

- a) Disease.
- b) Incapacity.
- c) Death.

Dr. FINKELMAN'S presentation touched the programs of epidemiological surveillance which have to be in close agreement with the activities for the control of the diseases wichever they were, mentioning also the pronostics as and important chapter for the long-term planning and for the desingning of the evaluation indicators.

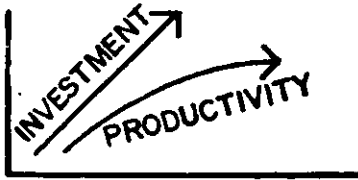
Among other problems he put special emphasis on the following:

a) Correct disease diagnosis and case reporting for getting permanently a picture of the present epidemiological picture. It's also relevant to study problems of specificity and sensitivity of the diagnostic methods.

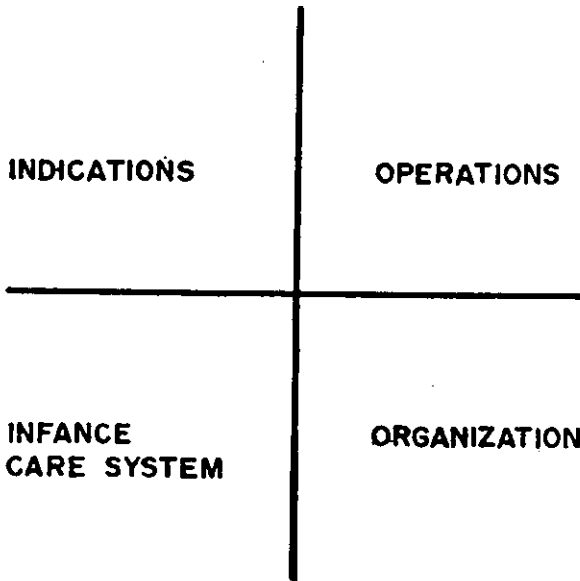
b) Criteria of applicability, inolving the main factors such as the number of susceptibles, and protective efficacy of the vaccines according to previous field trials.

Mixing of cohorts. It should be taken into account that a given population is always an heterogeneous one, so it's necessary to asses the reached previous coverages in each separate cohort, for calculating the existent protection levels.

c) Cost/productivity relation. It's very well known that boths factors go together in close association; but, in certain point, they dissociate one from each other, and the productivity is not expected to increase more by increasing the investment.



Finally, Dr. FINKELMAN recommended to introduce system analysis, crossing four fundamental factors to study:



**Programs of information, promotion and education in immunizations**

1. Motivation to a person must consider various aspects in relation to accesibility, not only in relation to availability of services but to understanding by people of the diseases as a risk, was one of the relevant features of paper by Dr. NILO VALLEJO, from PAHO. He referred mainly to sociocultural accesibility.

2. Dr. Vallejo discussed the necessity of taking into consideration population heterogeneity in the handling of educational promotions adressed to different groups.

Otherwise the increased flow of messages won't be able to bring about a concomitant increase in their reception by people.

3. Analysis of behaviour of individuals and groups, enabling us to foresee what can be expected from our programs.

4. Establishment of educational objectives, giving consideration to previous knowledge of the community.

5. People participation in planning.

6. Supervision of educational personnel.

7. Utilization of natural leaders.

In his paper, Dr. PATRICIO HEVIA RIVAS from DIF emphasized the following points:

1. This work was initiated with the description of historical background of Pediatrics, from the early times, going through the important fact's of XVIIIth and XIXth centuries, to end with actual point of view on XXth century.

2. The theory and practice of modern Pediatrics is analyzed, including the concepts and doctrinary basis, the basic functions, nowadays practice and the new trends.

3. A schematic presentation of the conceptual and methodological basis of a pediatric system, according to the following aspects:

The persons-actors (human individual, family, community, human resource in children's health).

The fundamental objeive.

The methodological instruments (inter-institutional coordination, levels of care, regionalization, sectorization, formation of human resources, projection to the community and integration of the institutional and communitary systems of health).

- The pediatric responsibility (at the institutional and individual level).

4. Several general considerations are done about the pediatric contribution to vaccination programs with special reference to underlying background, to plans in the international context and to advances made in Mexico.

5. A discusión was presented and followed by conclusions at the levels of official institution and private practice.