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IMMUNIZATION COVERAGE AND SURVEILLANCE: CHALLENGES FOR THE POLIOMYELITIS GLOBAL ERADICATION INITIATIVE

1. INTRODUCTION

In May 1988 the Forty-first World Health Assembly committed WHO to the global eradication of poliomyelitis by the year 2000 (Resolution WHA41.28). Global eradication, as has been achieved for smallpox, can be defined as the complete and permanent cessation of the natural transmission of an infectious-disease agent (32).

The broad objectives of the global poliomyelitis eradication initiative are to achieve, by the year 2000, no case of clinical poliomyelitis associated with wild poliovirus, and no wild poliovirus identified worldwide through sampling of communities and the environment (1).

Global poliomyelitis eradication will be highly beneficial. Apart

from the huge benefit associated with the control of the disease --more than 200,000 cases of paralytic poliomyelitis are estimated to occur each year--, the main cost savings for all countries, developed as well as developing, would be provided by abandoning poliomyelitis immunization. In the United States alone, the expected savings are estimated to be $114 million per year (14).

However, because of the epidemiological features of poliomyelitis, all control efforts directed at the disease can be dropped only when worldwide eradication has been achieved and certified.

Two of the main problems to solve before global eradication can be realized are how to implement and maintain a) high-coverage immunization programs and b) effective surveillance systems all over the world.

The purpose of this paper is to review the progress and the remaining problems in these two key areas.

2. BACKGROUND

For many years, poliomyelitis was considered to be primarily a problem of highly developed countries. In the past 20 years, however, a number of studies have shown that poliomyelitis is a worldwide problem. The prevalence of lameness due to poliomyelitis in children in developing countries is on the order

of 5 cases per 1000 population (5,37).

The initiative for the global eradication of poliomyelitis is being coordinated by the Expanded Program on Immunization (EPI), established by the World Health Assembly in 1974. One initial goal of the EPI was to provide immunization services by 1990 to all the children of the world during the first year of life against diphtheria, tetanus, pertussis, measles, tuberculosis and poliomyelitis (14). The WHO has coordinated the immunization programs, organized vaccine delivery and improved the cold chain system in its member countries on all continents (29).

In 1974, immunization coverage in developing countries was estimated to be less than 5 percent with vaccines distributed by the EPI. According to data reported to the EPI as of August 1991, 83 percent of children were receiving three doses of diphtheria-pertussis-tetanus (DTP) vaccine and 85 percent were receiving three doses of trivalent oral poliovirus vaccine (TOPV) in the first year of life. The EPI estimates that in 1990 immunization prevented a total of 442,000 cases of paralytic poliomyelitis (14).

The most promising evidence that poliomyelitis can be eradicated comes from the Americas. In May 1985, the Pan American Health Organization adopted the goal of eradicating the indigenous transmission of wild-type poliovirus in the Americas by 1990. In the first 38 weeks of 1991, only seven cases of poliomyelitis in Latin America were confirmed --six in Colombia and one in Peru (14). Current trends indicate that the entire Western Hemisphere

may soon be free of indigenously transmitted paralytic poliomyelitis (27).

Circulation of poliomyelitis worldwide has probably decreased also. In 1990, 113 countries reported zero cases of poliomyelitis compared with 74 countries in 1985. This was accompanied by a decrease in the number of countries reporting more than 10 cases per year (64 in 1985, 44 in 1989 and 26 in 1990) (43). Endemic poliomyelitis at the end of 1980s is restricted to developing countries in Asia and Africa, but, according to WHO, it is still responsible for more than 200,000 new paralytic cases annually (29).

3. IMMUNIZATION COVERAGE

3.1. Progress in increasing immunization coverage.

As a guide for planning, four stages in the progress of a country towards eradication have been devised. These stages reflect the status of the overall EPI and its ability to undertake special poliomyelitis activities (1):

Stage A. The country has a reliable reporting system, has reported no indigenous case of poliomyelitis for the last 3 years and has achieved polio immunization coverage of 80% or higher.

Stage B. The country has reported fewer than 10 cases per year for the last 3 years and has achieved polio immunization coverage of 50% or higher.

Stage C. The country has reported 10 or more cases of poliomyelitis per year and polio immunization coverage is 50% or higher.

Stage D. There are 10 or more cases of poliomyelitis per year or the number is unknown, and polio immunization coverage is less than 50%, or is unknown.

As of the end of 1990, most (68 percent) of the world's population lived in areas considered to be in stage C. Twenty-four percent were living in areas considered to be in stage A or B, and 8 percent were living in areas considered to be in stage D (14) (cf. annex 2).

Of the 18 countries/areas with OPV3 coverage of less than 50% and with a high risk of poliomyelitis, 14 (78%) are in the African Region (43). It is not surprising that regions with the highest incidence of poliomyelitis and the lowest coverage of anti-polio immunizations coincide with regions having poverty and deficient organization of the primary health care system (29).

3.2. Poliomyelitis eradication: required immunization coverage.

The immediate target of EPI is to achieve a minimum of 80 percent vaccine coverage among infants by their first birthday in each district in all countries (44). Based on the experience in developed countries, the administration of polio vaccine to a high proportion of children under one year of age will be the most crucial step in the initial phases of eradication (5). The

exact level of coverage needed is unknown but is certainly in excess of 80%. Countries in which poliomyelitis has been eliminated have typically achieved coverage on the order of 90% (5). Interrupting the transmission of wild poliovirus may require coverage levels in excess of 80 percent especially in areas of high population density (1) and where environmental sanitation is not good (32).

Most epidemic models suggest that when a high enough proportion of immunes is reached, herd immunity will protect the remaining susceptibles. Although the exact level of immunity required is not known, it is clear that the greater the level of susceptibility, the more likely that epidemic (or endemic) transmission might be established (23). Futhermore, the risk of transmission may increase by the coincidence of areas of lower coverage (e.g, in inner cities) with areas of higher exposure to wild poliovirus (23).

Poliomyelitis outbreaks have been reported from different areas in the world where immunization coverage levels were formerly regarded as sufficient. Several incidents in the "relatively polio-free regions" indicate the ease with which the apparently good vaccine-induced "herd immunity" can be disturbed (29). In 1978 more than 100 patients fell ill with poliomyelitis in the Netherlands. All patients belonged to a religious sect that had refused all vaccinations. However, the wild type 1 poliovirus responsible for this outbreak also spread to the vaccinated "normal" populatien. Furthermore, through overseas contacts

between members of the sect, the same genotype of type 1 poliovirus spread to the USA and Canada and gave rise to cases of paralytic poliomyelitis in these countries as well (29).
An outbreak comprising 9 paralytic cases and at least 100,000 infected persons in a vaccinated population took place in Finland in 1984-1985. The type 3 poliovirus circulated widely in the population and was apparently able to select persons who had remained unvaccinated (29).
In 1988 an outbreak of poliomyelitis involving 16 cases and caused by a type 1 virus occurred in Israel (29).
In these three situations, a high immunization coverage did not prevent wild poliovirus from spreading in the community. Several factors may have contributed to these outbreaks, these are: a) the exclusive use of inactivated poliovirus vaccine (IPV) which does not confer intestinal immunity (29), b) the relatively weak immunogenicity of the IPV preparation used (29), c) the antigenic difference of the epidemic strain from the type 3 strain in IPV (29), and d) the identification of specific subpopulations as reservoirs of infection.

Incidents occurred also with Oral Polio Vaccine (OPV)-immunized populations. In the West Bank and Gaza, during the 1970s, immunization using live TOPV covered more than 90% of the infant population. Nevertheless, the incidence of paralytic polio continued to be high (9). In Taiwan, an epidemic involving more than 1,000 paralytic patients occurred in 1982 (29). These episodes as well as the more recent one in Gambia indicate that an overall OPV coverage of 80% does not necessary protect the

population from outbreaks of poliomyelitis. Apparently, pockets of lower coverage of immunization can maintain the circulation of wild strains of poliovirus (29). Other factors may contribute to the persistance of wild polioviruses in community (c.f. 3.5.).

Although these incidents have important implications for the WHO's initiative to eradicate poliomyelitis globally, it is clear that a) maintaining OPV coverage to greater than 80% by 1 year of age is essential in countries that have substantially reduced or eliminated wild poliovirus infection (10,18), and b) raising and maintaining OPV coverage to this level or higher is the most important strategy to control poliomyelitis in the countries where the disease is still endemic.

3.3. Strategies of immunization coverage.

High immunization coverage can be achieved by different strategies. It may be accomplished through strong emphasis on routine administration of TOPV vaccine by the permanent health services and through the observance of national "immunization days" twice a year, one month apart. Mobile strategy (immunization in villages by mobile teams) is another effective complement (18); it is sometimes used in countries where the health care structure density is particularly low. In countries where effective surveillance identifies fewer than 50 cases of poliomyelitis per year, house-to-house immunization--so called mopping-up immunization--is an important part of prompt intervention in areas where cases are identified (14).

Routine immunization.

The dose at birth, also called "OPV zero" is particularly important in cities and in other areas with high population density (1). TOPV is the recommended vaccine because of its low cost, ease of administration, superiority in conferring intestinal immunity, and ability to infect household and community contacts, thus extending vaccine coverage.

Programmes employing routine immunization schedules have already brought about dramatic reductions in paralytic poliomyelitis in several developing countries (5). Furthermore, these programmes are an integral part of, and strengthen, basic health services. This support is particularly important in most of the poorer countries where major mortality from measles, malaria, gastroenteritis, pertussis and tetanus still exists. Because the vaccine is delivered as part of the MCH services, a greater continuity of follow-up is assured, and all the MCH activities benefit. At the same time, the integration of immunization into the primary health-care services increases their acceptability and use by the community and opens the way to progress in the other elements of care, including environmental sanitation (33).

However, improvements in health-care services are often slow and, in many developing countries, routine health services have been shown so far to be inadequate to achieve satisfactorily high level of vaccine coverage. Therefore, a special strategy, specifically, the use of National Vaccination Days has evolved. The most dramatic example of this approach has been in Brazil

(5).

National Vaccination Days.

In the late 1970s it became apparent that routine health services in Brazil would not be adequate to meet the goal of EPI. Consequently, it was decided to embark on an accelerated strategy through the use of national vaccination days: two per year at least 4 weeks apart, to vaccinate as many children younger than 5 years of age as possible, regardless of their vaccination status (16). These activities were proposed to supplement the routine immunization program through regular health services. After 4 years of highly successful efforts against polio, diphtheria-pertussis-tetanus toxoids and measles vaccine were added to the national vaccination day in most parts of the country in 1984 (16). Since 1984, all polio endemic countries in the western hemisphere have successfully adopted this strategy (16). A similar, but more regional approach called "pulse" immunization has also proved to be successful in India (5).

It is not known yet if the National Vaccination Days strategy is successfully exportable to African countries. Cultural particularities, logistic issues, and the existance of conflict zones should be taken into account when establishing suitable immunization coverage programs.

It is important that immunization campaigns be always carefully articulated to health-care services and be considered as a temporary immunization strategy. Dr. R. Henderson of the World Health Organization expressed concern that large, intensive, short-

lived campaigns could drain the resources and the attention of the authorities and the public from the less glamourous, but in the long run necessary, sustained health program (37).

According to Robinson (33), the campaign approach, as a long-term strategy ,may be politically unattractive, administratively difficult, and economically extravagant. Furthermore, the success of the campaign strategy could decrease after some years because the public attitude toward vaccines in those countries where they have been most successful is often one of apathy (33).

3.4. Immunization coverage costs and political will.

The Global Poliomyelitis Eradication Program is currently facing two major issues: an increase in the estimated costs of eradication and a stagnation in the partners' political will.

In 1988, the World Health Organization estimated the total cost of the global eradication effort from 1989 to 2000 to be $155 million more than the amount needed for routine activities of the EPI (14). In the light of the experience in the Americas, these estimates are being revised. Depending on the quantities of polio vaccine required in excess of the routinely scheduled doses, the total cost may be as much as 10-fold higher (14). It is important to add the qualification that the estimates do not include the cost of sustaining high levels of immunization coverage in developing countries. These latter costs total some $ 1 billion per year and are borne in large part by the developing countries themselves, particularly the costs of personnel (14).

Furthermore, since experience showed that poliovirus could successfully infect unvaccinated individuals in the face of OPV immunization levels in the general community of approximately 80% (Taiwan, 1982), higher immunization levels could be needed in order to interrupt wild poliovirus transmission. The cost of this increase in coverage will probably be high because one percent of coverage gained above 80% is much more expensive than one percent gained around 50%. This is because special strategies are necessary to reach the last fraction of the population once high levels of coverage are achieved.

Economic and social research is also needed to provide information on costs, and to provide the means to understand how best to design and implement control programmes and identify and overcome obstacles to their effectiveness (28).

According to Creese (34), there are just three potential sources of increased economic support for immunization: domestic economic growth, a shift in priorities for domestic expenditure and foreign aid.

Economic growth will occur in some developing countries, and some of it will allow an expansion of primary health care, but the poorest countries are likely to experience little if any real growth of per capita income in the next decade (34). Per capita income of the 40 poorest countries has declined over the past five years and the percentage of national budgets spent on health has been unchanged or has diminished for eight years (28).

The second source of funds, domestic expenditure priority shift,

is unlikely because polio immunization alone is not apriori the top priority for increased resource allocation in most developing countries. There has been a scaling exercise in which poliomyelitis was assessed together with a long list of other disease problems. In 1981, the Ghana Health Assessment Project Team ranked 48 disease problems in that country in terms of economic burden (34). Their calculations took account of estimated incidence, case fatality rate, age at death, and level and permanence of disability for each disease. Overall, poliomyelitis in Ghana ranked 33rd of the 48 diseases considered (34). Malaria and measles were at the top; and tuberculosis, neonatal and adult tetanus, typhoid, and pertussis were all in the top 25.

It should be added that since the time of this study, several new public health problems have tended to drain the resources and the attention of the authorities. Among them are the resurgence of cholera, the increasing incidence of sexually transmitted disease and the appearance of the AIDS pandemic.

Foreign aid clearly favors immunization, doubtless partly because of the visibility of its results (34). However, in international organizations, there is a great amount of competition among the existing health programs for the limited public health resources available (32). These resources are limited for a variety of reasons, including the fact that aid contributions of the goverments of industrialized countries to global development are well below the amounts previously promised (0.7% of the National Product).

Recently, however, other sources of financial aid have helped off-set the shortfall in aid from governmental sources. By 1988, Rotary International, had raised over US$ 219,000,000 in support of poliomyelitis eradication. Rotary has provided over 82 nations with financial aid for vaccine programs, in addition to participating directly in local immunization campaigns (27).

3.5. Does coverage mean protection?

As immunization coverage levels improve, it will be increasingly important to evaluate the efficacy of TOPV and the immunization schedules currently in use. Although the protection conferred by immunization is very high under optimal conditions, it seems to be influenced by different factors such as: choice of vaccine, use in developing countries, vaccine thermolability and quality of the cold chain, dosage of vaccine, optimal intervals between doses, and fidelity to the recommended immunization schedule.

Both IPV (inactivated poliovirus vaccine) and OPV (oral poliovirus vaccine) have been successful in controlling poliomyelitis in the USA and other developed countries. A primary series of either IPV or OPV generally induces seroconversion against all three virus types in more than 90% of recipients. Available evidence indicates that the resultant clinical protection is long-lasting, and probably lifelong (5). However OPV offers two important advantages over IPV: a) it can spread to close contacts of the vaccinee--virtually all OPV recipients excrete vaccine virus--, thereby extending protection, and b) it

often induces local intestinal immunity, which impedes the ability of the recipient to spread wild poliovirus on subsequent exposure (5). The mucosal immunity obtained by parenteral immunization with killed virus is far below that following poliovirus infection, whether natural or OPV-derived (29). Some investigators have suggested that IPV might also be able to induce a good mucosal immunity, because polio-specific secretory IgA is detected in saliva and breast milk. However, IgA is probably only a part of the system responsible for the elimination of poliomyelitis from the body (29). Thus, OPV is more effective than IPV in limiting wild virus transmission; it can compete with wild poliovirus for circulation whereas IPV can not compete in this way (23).

Using decision analysis, Hinman (23) calculated that more susceptibles would be present in USA if IPV was used. Because of lack of "extended protection", more cases of paralytic poliomyelitis would result (74.1 vs 10.0 cases per year) (23). With the OPV alternative, most cases would be associated with vaccine, whereas under the IPV model virtually all cases would be due to wild virus (23).

On the other hand, a combined schedule of OPV and IPV is also being used or considered in some countries, particularly in view of the success of the strategy in the Gaza strip (5,9). The combined use of IPV and OPV is probably a perfect combination, since OPV confers a good mucosal immunity and IPV results in seroconversion to all three serotypes. However, the relatively

high price of this program will certainly delay its wide acceptance (29). The cost of IPV remains relatively high (approximately 30 times that of OPV), and its administration requires more highly trained personnel than does OPV (5).

While OPV has been highly effective in industrialized countries, its performance in some developing countries has been considerably lower than expected (5,14,19,27,28). Several instances of failure to seroconvert after receipt of three doses have been reported. The rates of seroconversion are suboptimal. Thirty-two studies in 15 developing countries evaluated the response of 20 or more children to TOPV as formulated by World Health Organization. There was wide variation in the percentage of seroconversion, with mean rates of only 73 % (range, 36%-99%) for poliovirus type 1, 90 % (range, 71%-99%) for type 2 and 70 % (range, 40%-99%) for type 3 (14,27). Outbreaks related in part to such circumstances occurred in north-east Brazil and the Gambia in 1986. They occurred also in Taiwan (1982) and Oman (1987) in spite of successful immunization programs (5,18).

Different factors may contribute to the low immunogenicity of OPV in tropical developing countries, and these are discussed below.

a) Vaccine potency.

There is a discrepancy between the potency of the vaccines used in the United States and those used in other countries (19). The requirements set forth by the Expert Committee on Biologic Standardization, WHO, are that each dose of TOPV contain, at minimum, 10exp6 50% tissue culture infectious doses (TCID50) of

type 1, 10exp5 of type 2, and 10exp5.5 of type 3, with a titer 95% confidence limit within +/- 0.5 log unit. Lots prepared for the use of EPI in many countries meet but do not greatly exceed the minimum WHO standard. The manufacturer for the United States routinely exceeds the minimum requirement by at least 0.6 logs. A recent potency test showed a increased potency of 300%, 250%, and 700%, for types 1, 2, and 3, respectively, compared with the TOPV used in the EPI (19). This discrepancy in potency may sometimes contribute to the lower rate of seroconversion in developing countries. However, somewhat contradictory evidence was reported by investigators in India, where there was no improvement in immunogenicity with a twofold increase in dose (19).

b) Vaccine formulation.

It was recognized very early in the development of live attenuated vaccines that the three independently derived Sabin types had different growth characteristics. Specifically, type 2, when administered in conjunction with types 1 and 3, tended to exclude infection by the other types (19). "Balanced" formulations were later developed as a means of compensation for these differences and were shown to effectively increase rates of seroconversion to types 1 and 3 (19). The "balanced" 10:1:3 formulation has been successful in industrialized countries but may be not optimal for developing countries. Changes in the ratios of the three components may prove to be an effective way of enhancing the immunogenicity of TOPV, particularly of type 3 (19).

c) Vaccine stability.

TOPV is the most thermally labile of all vaccines used in the EPI and is chemically stabilized with magnesium chloride or sucrose to minimize losses in potency when exposed to high ambient temperatures. Studies simulating actual field conditions indicate that the overall potency of TOPV is reduced by as much as 0.5 logs after storage at 41°C for 1 day (19). Breaks in the cold chain and suboptimal practices of vaccine handling have been the most common reasons cited for failure in tropical areas (13,19). However, improved training and supervision of EPI staff, coupled with rapid technologic advances in ensuring proper storage temperatures for TOPV have led to fewer documented failures of the cold chain over the past decade (19). Furthermore, relatively low rates of seroconversion have been reported in spite of optimal conditions for vaccine handling (19).

d) Interval between doses.

Studies of excretion patterns of vaccine virus following administration of monovalent and trivalent OPV indicate that excretion can occur for up to three months, with a median of 21 days. Because of interference among the three components of TOPV, it is likely that continued excretion of virus could interfere with the response to subsequent doses (19). Data from developing countries suggest that the 4-week interval between doses recommended by EPI may play some role in suboptimal seroconversion rates (19). Studies are being undertaken by the EPI to determine the optimal interval between doses (14).

e) Adherence to the recommended immunization schedule.
In countries with endemic poliomyelitis, EPI recommends that TOPV should be administered at birth and at 6, 10, and 14 weeks of age (14).

Reported immunization coverage data are sometimes based on the number of delivered doses without taking into account the date or schedule of vaccine administration. All children having received three doses of OPV are considered covered. However, the recommended immunization schedule, and particularly the intervals between doses, may not be fully respected. This situation combined with the suspicion that the recommended 4-week interval may be too short and hence sub-optimal may partly explain low responses in some developing countries.

This author and his colleagues conducted an immunization coverage survey in a rural African district in October-November 1990, using the standard procedure recommended by WHO (unpublished data). A sample of thirty clusters of 7 infants from 12 to 23 months of age had been randomly selected from throughout the district and visited. Coverage data, including the date of each vaccine administration were collected only from health charts. The results indicated that 70.5 percent of the children had received the 8 doses recommended against the 6 EPI diseases (cf annex 3,4). However, if the EPI vaccine schedule is taken into consideration, only 51 percent of the children were correctly immunized, and only 40 percent were correctly immunized before 1 year of age. Twenty-eight of the 161 children "completely"

immunized against polio (17%) were vaccinated incorrectly with respect to date. The number of incorrect immunizations was higher for polio vaccine (28) than for the others (DTP:24; Measles:23) (cf annex 5).

Similar discrepancies between the percentages of children "completely" versus "correctly" immunized were found in an other province. Such failure to adhere to immunization schedule may contribute to suboptimal OPV immunogenicity in developing countries. Intense training and supervision of the health workers could increase dramatically the performance of the program. Furthermore, it would be highly cost-beneficial since vaccines, cold chain and public confidence and motivation are already acquired (cf annex 6).

This survey also indicates that 10 percent of the children on at least one occasion received a DTP dose without polio dose. The most reported reason was shortage of polio vaccine. Data analyses showed that when a polio dose is missed but a DTP dose is administered, there is a 60% chance that the polio dose will never be (correctly) given. These findings suggest that improved management of polio vaccines could easily contribute to increased immunization coverage.

Another finding of this survey was that an appreciable proportion of the children could be immunized earlier in the first year of life (cf annex 7). Only twenty five percent of the children are completely immunized against polio before the age of 20 weeks, 50 percent before the age of 30 weeks and 75 percent before the age

of 1 year.

4. SURVEILLANCE

In addition to achieving and maintaining high immunization levels, the development of effective surveillance systems for wild type viruses in the population and community will be critical. Such systems are essential to define the extent of the problem and to guide control efforts (5). Standard techniques will be needed to survey for the wild poliovirus in the environment, and once the disease is under control, to establish the absence of virus circulation.

4.1. Disease surveillance.

To obtain critical information on poliomyelitis, the surveillance system should involve all institutions and medical-care providers who are likely to see suspected cases of poliomyelitis, and involve regular (including negative) reporting from each site (5).

As a result of EPI's increased emphasis on the timely and complete collection of data, reporting of poliomyelitis cases has improved at the global level, as well as in many individual countries (43). In October 1991, 100% of countries reported 1990 data in 3 WHO Regions (the Region of the Americas, the European Region and the South-East Asia Region). Reporting completeness improved in the remaining 3 Regions: 62% of countries in the African Region, 83% of countries in the Eastern Mediterranean

Region and 97% of countries in the Western Pacific Region (43).

Although countries pursuing a goal of eradication are building active surveillance systems for poliomyelitis cases, most countries still rely on passive surveillance systems. Passive systems are likely to detect only a small fraction (sometimes less than 10%) of the cases that occur (43).

In the Americas, however, the development of effective surveillance systems has permitted strategies for control to evolve in response to changes in needs. At present, 80 percent of the nearly 20,000 health facilities in the regional system of poliomyelitis surveillance are reporting weekly on the presence or absence of flaccid paralysis (14). Uniform case definitions have been adopted by all countries of the region.

Case definition:
A clear case definition of poliomyelitis is essential for surveillance. For reporting purposes, EPI suggested the following:
A case of poliomyelitis is defined as any patient with acute flaccid paralysis (including any child less than 15 years of age diagnosed with Guillain-Barre syndrome) for which no other cause can be identified.

However, other conditions can cause paralysis and can be confused with poliomyelitis. Some infections due to other enteroviruses have the capability to mimic poliomyelitis. An epidemic of seven hundred and five cases due to enterovirus 71 occurred in Bulgaria

in 1975. Symptoms observed included gastroenteritis, aseptic meningitis, encephalitis,and myelitis with 149 cases of paralysis and 44 deaths (37). Enterovirus 70 and coxsackie viruses A7, B1, and B5 have also been implicated in acute flaccid paralysis.

Because acute flaccid paralysis has multiple causes, laboratory-based surveillance systems must also be developed, at least on a regional basis, in addition to the clinically and epidemiologically based system (5,22).

Laboratory isolation.

Laboratory isolation of wild poliovirus from the stools of children with AFP is necessary for confirmation of wild poliovirus transmission (22). Established techniques for the diagnosis and surveillance of poliovirus infections rest entirely on cell culture isolation of virus (27). It should be possible to develop modern solid-phase immunoassays for diagnosis of past and recent poliovirus infections. Solid-phase immunoassays have the potential to be both inexpensive and suitable for use by minimally trained individuals in the field (27). Presently, the recommended approach is to send specimens by cold chain to the closest reference laboratory. The method for sampling and shipping is explained in the Manual for the Virological Investigation of Poliomyelitis published by the World Health Organization.

In the Americas, about 80 percent of the patients with reported cases are being seen by trained epidemiologists who collect two stool specimens from each patient and one specimen from each of

five contacts. In 12 months in 1991, stool sample from 1860 patients with flaccid paralysis were submitted to a network of eight laboratories for poliovirus isolation (14). During 1991, only nine AFP cases out of over 2000 reported cases of AFP were confirmed by culture as poliomyelitis caused by wild-type poliovirus (22).

According to Sabin, The extensive use by PAHO of highly sophisticated regional virus laboratories has led to the recognition that, in areas from which poliomyelitis caused by polioviruses has been largely eliminated, there are thousands of cases of acute flaccid paralysis, previously clinically diagnosed as "probable poliomyelitis", that have no viral etiology (40).

The maintenance of such a laboratory network requires trained staff, a reliable transport system, and laboratories with reliable diagnostic capabilities (14).

4.2. Molecular epidemiological surveillance.

Because a high proportion (>99%) of poliovirus infections are subclinical, the standard epidemiologic techniques of case-contact investigations are often unable to reveal the origins of wild viruses. Molecular methods, based primarily on comparison of poliovirus genomic sequences, and the recognition that genetic relatedness implies epidemiologic linkage, offer a powerful, independent approach for epidemiologic surveillance (6,10). Poliovirus genomes experience rapid variation upon replication in humans. The average rate of fixation of mutations over the entire

genome is about one to two nucleotide substitutions per week , and most of these mutations are fixed cumulatively (6,10). The extent of sequence divergence between related wild poliovirus isolates provides an approximate measure of the number of intervening infections separating the cases (10). Furthermore, epidemicity could be distinguished from endemicity by measuring the extent of sequence heterogeneity among contemporary isolates within a country or region (10,41).

Three methods are used for characterizing poliovirus isolates and they are summarized below.

1. Genomic Sequencing.

Comparisons of selected genomic regions, representing as little as 2% of the total RNA, provide detailed information on the genetic relationships among polioviruses. The VP1/2A (90 nucleotides from VP1, 60 from 2A) region has been selected for poliovirus partial genomic sequencing (10).

2. Oligonucleotide Fingerprinting.

Fingerprints are usually produced by digestion of the viral RNA with ribonuclease T1, and electrophoretic separation of the resulting fragments. This resolves into patterns of spots highly characteristic for each RNA sequence (10).

3. DNA Probe Hybridization.

This is a rapid and simpler method for determining sequence homologies within defined genomic intervals, but one should know in advance the genotypes that may be present (10,29). It is

likely that probe hybridization in combination with polymerase chain reaction (PCR) will find wide application in virus diagnostics (10). PCR may achieve highly sensitive detection of specific viral genomic sequences.

Recently, genomic analysis indicated that the poliovirus responsible for a large outbreak in a developing country with high immunization coverage was an imported and not an indigenous poliovirus strain (Oman 1989) (18). This incident highlights the need for maintenance of high immunization levels and surveillance for poliomyelitis, even in countries that have substantially reduced or eliminated wild poliovirus infection (18).

4.3. Environmental surveillance.

4.3.1. Polioviruses in the environment.

Numerous studies have readily demonstrated the presence of polioviruses in sewage. Polioviruses multiply primarily in the alimentary tract and are excreted in substantial amounts (as many as 10exp10 per gram of feces) for varying periods of time, with a mean shedding period of up to 50 days (39). At present in countries in which live poliovirus is widely used, the excreted polioviruses are usually vaccine-derived (39).

Polioviruses, like other enteroviruses, survive relatively well outside the human body. There is circumstantial evidence suggesting survival for several months or even years in sewage, at least in temperate climates (4,29). Recent studies also

demonstrated that enteroviruses may migrate through soils and possibly contaminate groundwater supplies (12). Recently, enteroviruses were recovered from wells located as much as 67 m down gradient from a domestic subsurface wastwater treatment systems, indicating extensive migration of enteric viruses in soil (12).

Different factors may influence virus survival in the environment. The effects of these factors are as follows.

a) Temperature.

Temperature has a considerable influence on virus inactivation rates in the environment. The survival times of viruses are shorter at high temperature. Thus, viruses are likely to persist longer in the environment during the colder months of the year (12). For example, the period of time for 99% inactivation of poliovirus type 1 from septic tank affluent in a sand type soil has been reported to be approximately 416 days at 1-8°C versus 27 days at 20-25°C (12).

b) Soil moisture.

Soil moisture also influences virus survival in soils. Authors have reported more rapid virus inactivation in dried than in wet soils. Poliovirus type 1 inactivation was considerably more rapid in drying soil as the moisture content decreased from 13 to 0.6% than in the same soil type maintained at 15 or 25% moisture content. Inactivation of 99% of the initial viruses occurred within 1 week in drying soil but took 7 to 8 and 10 to 11 weeks in soils with 25 and 15% moisture content, respectively (12).

c) Soil microbial activity and related chemical activity.

Soil microbial activity and perhaps related chemical activity due to microbial enzymes and other chemicals appear to decrease virus survival in the environment (12). In studies by Sobsey et al.(11) on rates of poliovirus inactivation in eight different soil suspensions in settled sewage at 20°C, the time required for 99% inactivation was almost always shorter in nonsterile than in sterile suspensions. A temperature effect on microbially mediated antiviral activity also was reported (12).

d) Effects of ionic salts and pH.

Direct effects of different pH and salt levels on virus survival in aqueous solutions have been reported, and similar phenomena may occur in the soil environment (12). Poliovirus type 1 was inactivated more rapidly at the pH extremes of 3 and 9 than at the intermediate pH levels of 5 and 7. Virus inactivation rates also increased with increasing concentration of NaCl, and the effect was most pronounced at pH 3 (12).

e) Soil type, virus association with soils, and virus aggregation.

The association of viruses with soil particles enhance or reduce their survival, depending on the chemical properties of the soil material. A number of investigators have observed that virus absorption to soil particles prolongs their survival (12). Recently, poliovirus 1 has been found to survive up to 19 days in seawater with sediments or suspended solids added, while no virus was detected after 9 days in seawater without particulate matter

(12).

Virus aggregation tends to enhance the survival of viruses exposed to various antiviral agents, and this phenomenon has been extensively studied in chemically defined solutions containing purified virions and known quantities of specific disinfectants. The results of studies in water showed that virus aggregates survive better than dispersed viruses (12).

4.3.2. Role of polioviruses surveillance.

The detection of poliovirus in sewage has been successfully used to monitor virus excretion during outbreaks and vaccination campaigns (29). During an outbreak of paralytic poliomyelitis in Finland in 1984 and 1985 the widespread circulation of the causative wild-type serotype 3 poliovirus in the population was documented by demonstrating the virus in water specimens (4).

Sewage water analysis also turned out to be a useful tool in evaluating the efficacy of a nationwide vaccination campaign with oral poliovirus vaccine (4). The efficacy of the vaccination campaign in regard to elimination of the epidemic type 3 strain was evaluated by a follow up study on viruses in sewage waters which continued for 12 months through the subsequent expected season of poliomyelitis. Several types of enteroviruses, including five vaccine-related poliovirus strains, were identified in the 72 virus-positive specimens out of 93 studied. No wild-type polioviruses were found, indicating the success of the campaign (4).

Prior to the widespread use of OPV, routine screening of sewage for poliovirus during nonepidemic periods has also been considered a useful tool to detect an emerging outbreak (29). However, in spite of the fact that polioviruses are detected in high numbers in sewage and sewage-polluted waters, poliomyelitis outbreaks attributed to polluted water have been very rare. A total of eight outbreaks in Europe and North America had been reported, but only one of them was adequately documented. This occurred in Huskerville, Nebraska in 1952 at which time at least 45 became ill after contamination of the local water system (39).

At advanced stages of poliomyelitis control, when vaccine coverages are high, very few wild poliovirus infections may result in paralytic cases. Under these conditions, standard case surveillance and characterization of clinical isolates may not be sufficiently sensitive to detect continued circulation of wild poliovirus (10). It may be possible, through environmental sampling, to detect widespread subclinical wild virus infections, signaling the need to mobilize further control measures.

At the final stage, a critical line of evidence for certification of eradication of indigenous wild polioviruses will be the consistent inability to detect their presence in either clinical or environmental specimens (10).

4.3.3. Research needs.

In spite of important progress in environmental sampling and analysis, several technical problems are yet to be solved and

further research is needed.

a) An important research need is how to demonstrate the presence of a small proportion of polioviruses among other enteroviruses, and especially how to detect a minority of wild-type viruses among OPV strains. The existence of small amounts of wild polioviruses in specimens containing relatively high concentrations of vaccine viruses cannot be excluded so far (4). PCR may be a successful approach to this problem. However, a disadvantage of this method is that it must be known in advance what poliovirus genotypes are being sought (27).

b) Several sampling methods for polioviruses in sewage are currently in use. Sampling site, sampling method (grab or continuous), sample size, and sampling frequency should be standardized. Duration of environmental surveillance needed after global disappearance of clinical cases should also be considered (2).

c) The environmental surveillance methods should be adaptable to different local situations. For example, many cities in the developing countries do not have sewage system. Sampling latrines may be an alternative, although it is more complicated. Furthermore, it may prove unreliable, since infants often don't use them.

5. CONCLUSION.

Many problems remain before poliomyelitis global eradication can be accomplished and it is unlikely that the aim will be reached before the year 2000 or even 2010.

The main remaining impediment is probably the difficulty for some developing countries in ridding poliomyelitis endemicity by reaching a high level of OPV immunization coverage. Obstacles are numerous, involving insufficient health budget, lack of political will, draining of resources by recent major public health problems (cholera epidemic, sexually transmitted diseases, AIDS pandemic), undeveloped health-care systems, untrained personnel, and persistence of conflict zones (wars) in some parts of the world.

Primary health-care systems are improving quite slowly in several developing countries. However, this basic health system is the best type of health service to take over and maintain the high immunization coverage levels achieved, for example in the Americas, by the campaign immunization strategies. Time and resources will be needed to reinforce these primary health-care systems in developing countries.

Two other important impediments are associated with the surveillance of poliomyelitis.

a) The disease is still underreported from several countries/areas and laboratory-based diagnosis of poliomyelitis is not yet available troughouth the world. The causes mentioned

for insufficient immunization coverage levels contribute to this insufficient surveillance system.

b) The second objective of the global poliomyelitis eradication initiative is to achieve no wild poliovirus identified worldwide through sampling of communities and the environment (1). Despite the important progress accomplished in environmental poliovirus sampling and identification, further research is needed to standardize and to increase the sensitivity of these methods. A very high of sensivity in identifying wild-type poliovirus circulation has to be reached, since it will not be possible to prove the absence of wild-type poliovirus in the environment but only to estimate the probability of the absence of the wild-type poliovirus.

Considering the importance of these remaining problems, it is likely that a long-term program involving activities of research, surveillance and implementation of immunization, planned on a period of 30 to 40 years, will be necessary before poliomyelitis global eradication can be accomplished.

Finally, it is important to emphasize that the eradication initiative must remain integrated with primary health care in order to maintain its role of leader in the improvement of basic health services.

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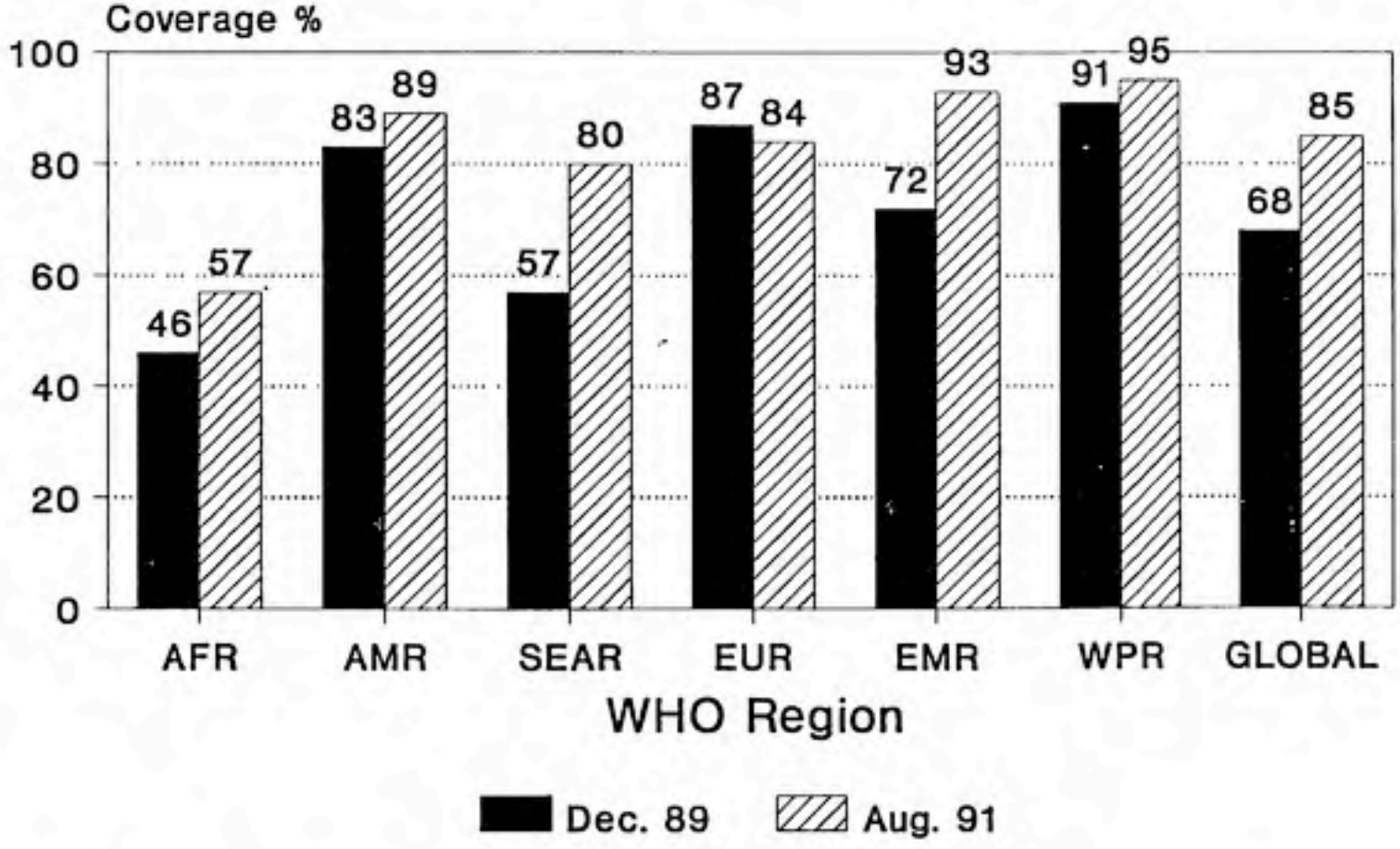
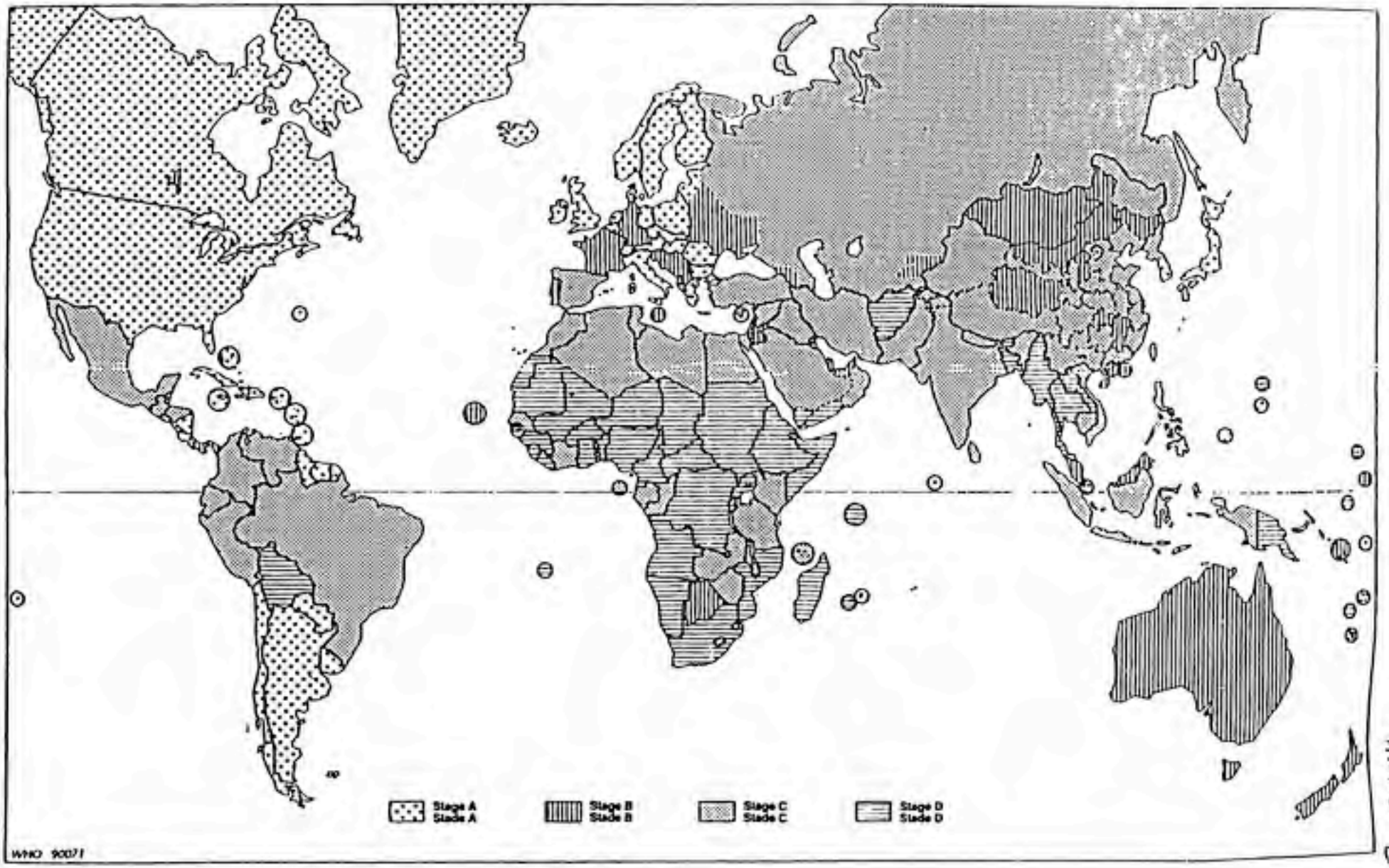
7. ANNEXES

immunization coverage with polio vaccine in children <1 year, by WHo region



data reported to WHo

MAP. 1. COUNTRIES/AREAS BY STAGE OF POLIOMYELITIS ERADICATION, DECEMBER 1989
CARTE 1. PAYS/ZONES PAR STADE D'ÉRADICATION DE LA POLIOMYÉLITE, DÉCEMBRE 1989

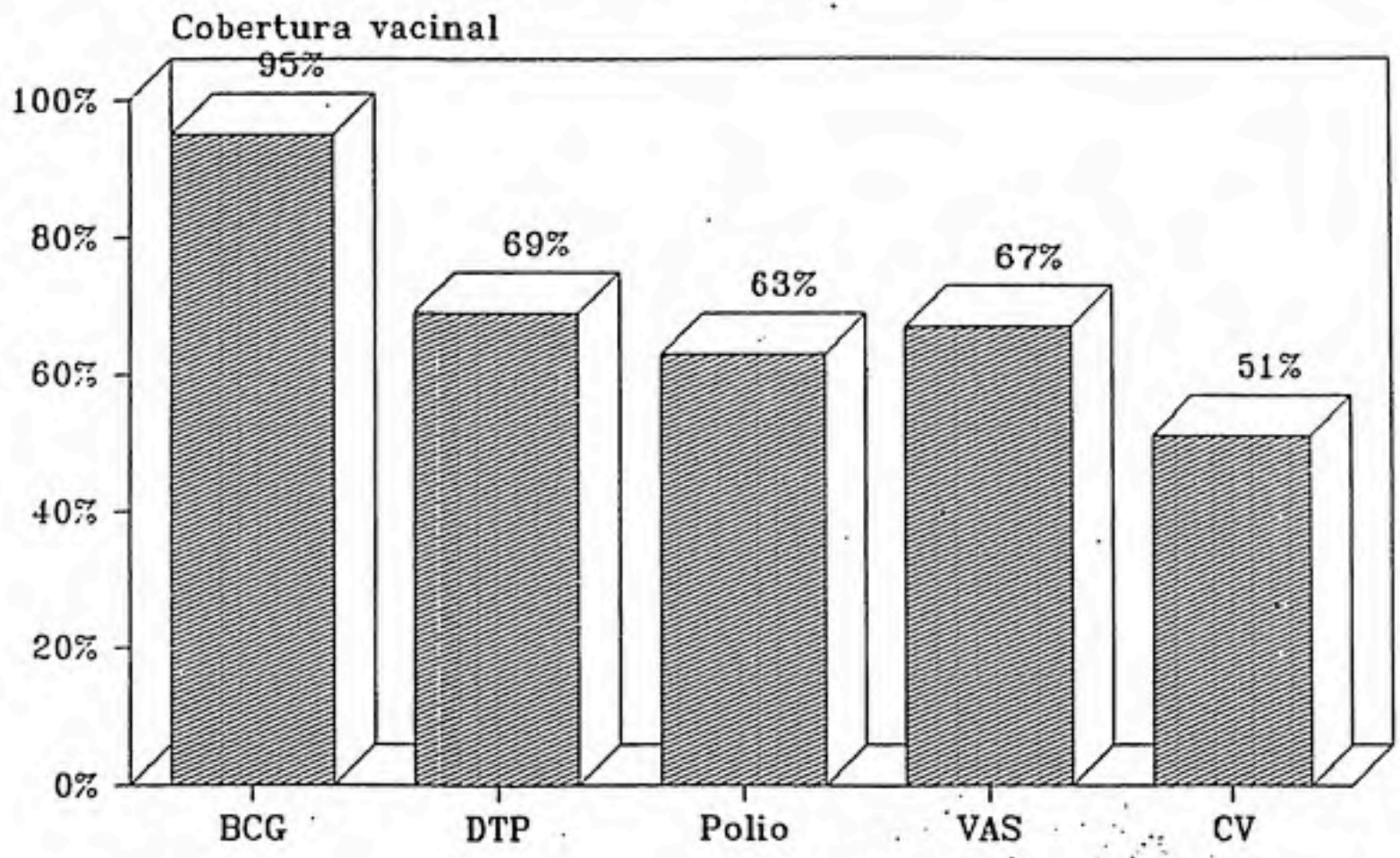


ANNEX 2

Relev. épidémiol. hebd. (WHO) 43 (1990)

42

Cobertura vacinal
Distrito de Inhassoro, 1990



(Grafico 2)

Resumo da Cobertura Vacinal
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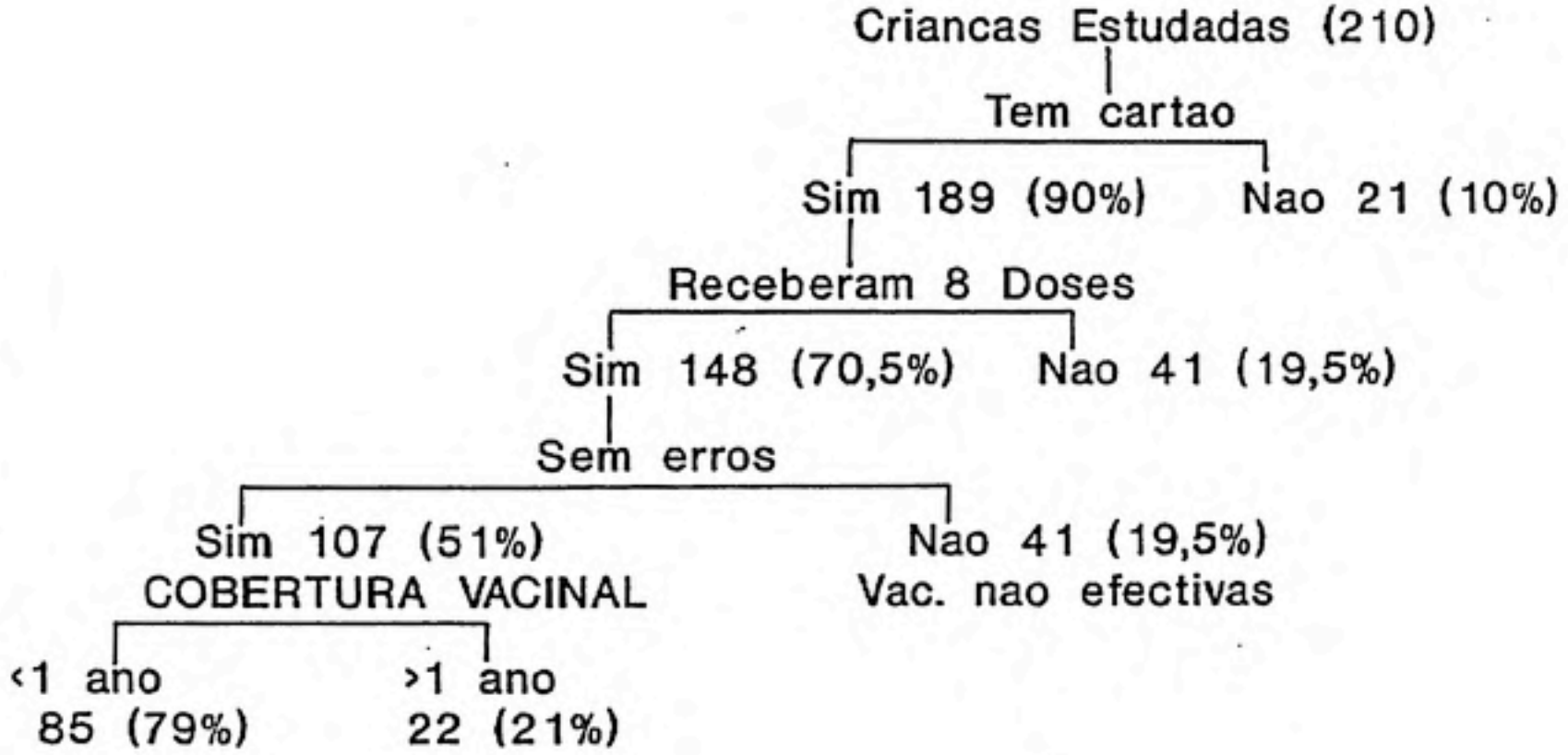

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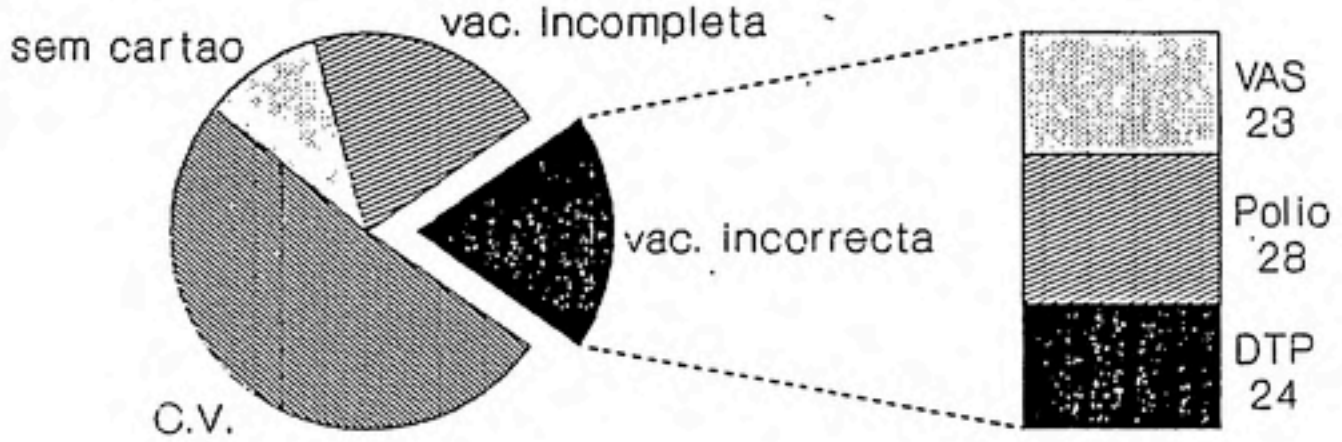
Annex 3

Cobertura Vacinal
Distrito de Inhassoro, 1990.



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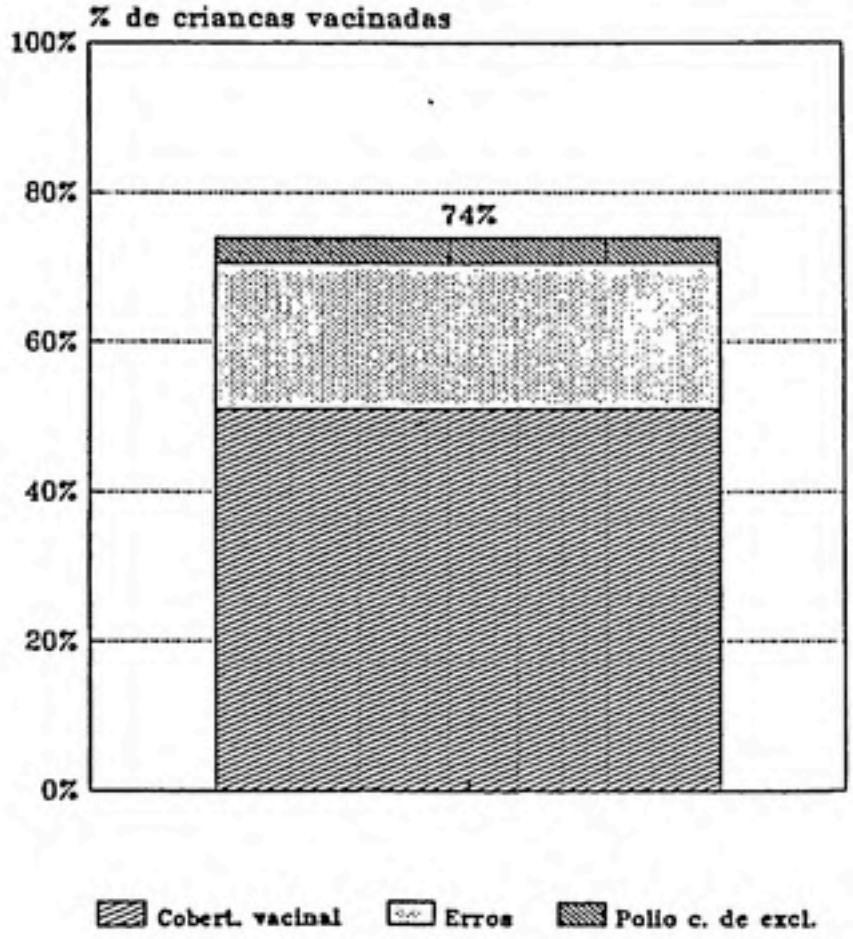
45

ANNEX 5

Cobertura vacinal potencial
Distrito de Inhassoro, 1990.

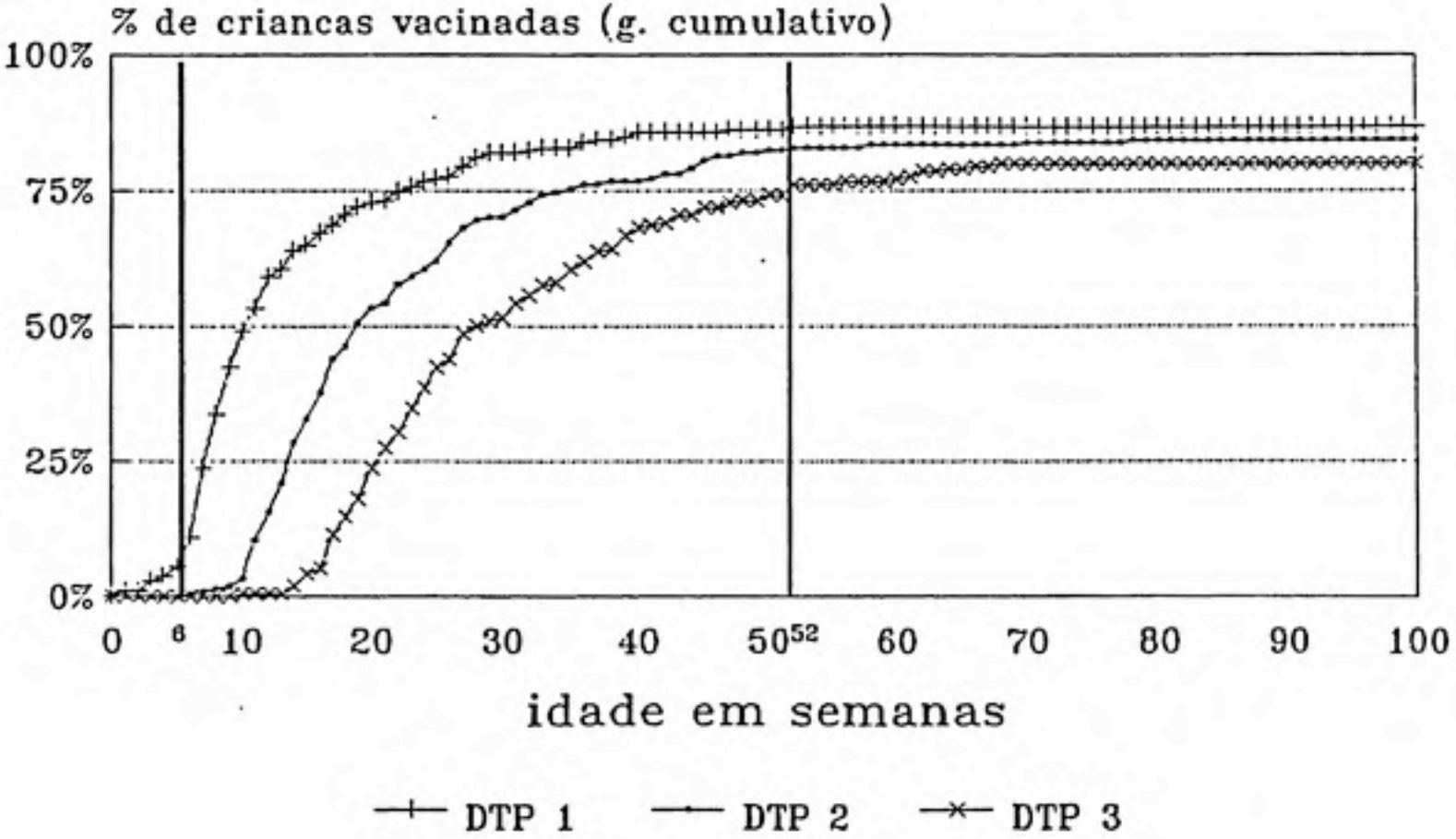


(Grafico 4)

ANNEX 6

DTP

Idade de aplicacao



(Grafico 5)