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YELLOW FEVER VACCINATION IN THE AMERICAS

Yellow fever (YF) continues to be a major threat in endemic areas of South America and in adjacent areas where the virus may reappear even after long intervals of quiescence. In the Americas, this disease primarily affects workers engaged in forest activities. The last cases of urban YF documented in the Region were recorded in Brazil in 1942, although there is evidence that urban transmission took place during the 1954-1955 outbreak in Trinidad. Outbreaks in recent years in the vicinity of certain South American towns infested with *Aedes aegypti* have raised great concern regarding the possible urbanization of jungle yellow fever.

Vaccination Programs

Vaccination is the only effective method of protecting man against jungle YF, and the 17D strain of YF virus is now used almost exclusively for vaccination against the disease. The first 17D vaccine field trials were con-

ducted in Brazil in 1937. Following these trials, which showed that a practicable, safe method of large-scale immunization against YF was available, several South American countries initiated vaccination programs. As a result, in subsequent years these countries observed a significant reduction in the number of YF cases.

Routine Vaccination

Some countries maintain routine vaccination programs in areas where jungle YF is endemic. The criteria for selecting these areas is based on the occurrence of cases of the disease; forested areas with monkeys and vectors are also taken into account by certain countries. The latter criterion seems justified, since YF has reappeared in some places after a dormant period of two or more decades.

Good vaccine coverage is hampered by the size of the endemic area, which covers practically half of South America. Operational

limitations, such as transportation and communication difficulties and the lack of an adequate infrastructure to ensure a reliable cold chain, are some of the drawbacks programs in many places commonly face. Moreover, dispersed populations and isolated communities (such as those in the Amazon region) pose additional problems for those seeking to reach high-risk groups.

In most countries where routine vaccination programs are carried out, the vaccine is administered at fixed health installations. In Brazil and Venezuela, however, this activity is also carried out by mobile teams. In Brazil, rural communities located in endemic areas are visited by teams at five-year intervals. Since small-town residents within the same area may be in constant contact with forests, they are also vaccinated. Each vaccinee is issued a certificate, but because the document is often lost, many revaccinations are probably performed unnecessarily. In addition, Brazil recommends vaccination for persons who travel from urban centers to rural endemic areas; and in certain areas of colonization, such as those opened by the Trans-Amazon Highway, YF vaccination has been required of settlers in order for them to work in the area.

In Venezuela, a radio communication system links a central station with vaccination posts, allowing daily monitoring of vaccination activities.

Other countries which regularly vaccinate against YF maintain stationary posts strategically located in endemic areas. Educational methods (including posters) are used to remind the population at risk to obtain YF vaccination. In some countries, vaccination stations are placed along the routes of migratory populations moving to endemic areas.

Vaccination Campaigns

During YF outbreaks, most countries institute massive vaccination programs. Vaccination teams are transported to the problem

areas, and information about their arrival and activities is widely disseminated.

In certain outbreaks, new colonizers and temporary workers arriving from nonendemic areas are the main targets of the disease, and every effort should be made to immunize these population subgroups. In such undertakings, vaccination teams are generally deployed along the route taken by migratory workers. In some instances roadblocks are built to detain vehicles transporting the migrants so that the vaccination teams may complete their work.

Although such campaigns usually are effective at halting the progression of the outbreaks, by the time they begin a great number of cases have often occurred. Moreover, epidemics in South America often involve extensive areas, and consequently the campaigns may not effect an immediate reduction in the number of cases.

In French Guiana, campaigns have been conducted at ten-year intervals since 1967. Over 90% of the population was immunized in both the 1967 and 1977-1978 campaigns. YF vaccination is compulsory in French Guiana, and is administered routinely, whether or not a campaign is in progress.

In Trinidad and Tobago a mass vaccination campaign was undertaken in response to an outbreak of jungle YF that struck the island in 1978-1979; 96.4% of the population over one year of age was immunized. A prior campaign aimed at vaccinating persons from forested areas was conducted in 1972 (in the absence of YF cases).

Certain countries adopt a containment approach when sporadic cases are documented in the absence of evidence of an epidemic. Such containment is attempted by vaccinating residents of the area surrounding the places where the people with the reported sporadic cases were living or working.

Vaccine Administration Methods

The ped-o-jet injector method of vaccine administration permits large numbers of per-

sons to be vaccinated in a short period of time and should be used in emergency situations. During the 1973 YF outbreak in the State of Goiás, Brazil, 1,240,249 vaccinations were administered in approximately three months.

The same method proved very useful in Colombia during outbreaks which occurred in the northern part of the country in 1978. Cases were reported in the vicinity of certain Colombian towns highly infested with *Aedes aegypti*, and the fact that several patients required hospitalization in a number of towns suggested that the risk of YF urbanization was imminent. The availability of the ped-o-jet facilitated prompt action; in the city of Valledupar, for instance, 92% of its 117,000 inhabitants were vaccinated in four days. Bolivia and Paraguay also use ped-o-jets to vaccinate large population groups.

Vaccination by needle is the method elected for routine programs when a small number of persons is to be immunized. French Guiana also employs this method during campaigns, possibly because the country's population is small and dispersed.

Minimum Vaccination Age and Vaccination Coverage

In compliance with WHO recommendations, the minimum age adopted for vaccination is six months. However, certain countries administer the vaccine mainly to children above one year of age.

Table 1 shows the number of persons vaccinated or the number of vaccine doses administered in seven countries and French Guiana during the period 1978-1982. In general, countries consider the population at risk to be that living in rural endemic areas. Caution must be used in interpreting coverage data in terms of vaccination coverage in the endemic areas, however, partly because a fraction (albeit small, except perhaps in Brazil) of the vaccinees probably lives in large urban centers, and (more importantly) because many persons are probably being revaccinated. Consequently, the true vaccination coverage may actually be lower than that indicated.

On the other hand, it should be noted that

Table 1. Estimated population at risk and yellow fever vaccination coverage in seven countries of the Americas and French Guiana, 1978-1982.

Country or territory	Estimated population at risk	No. of persons vaccinated or vaccine doses administered	Estimated % of vaccination coverage in endemic areas
Bolivia	1,766,015	1,350,497	76
Brazil ^a	6,000,000	7,410,874 ^b	80-100
Ecuador	309,818	137,720	44
French Guiana ^a	... ^d	26,133	probably <80
Panama ^{a, c}	96,212	39,617	41
Paraguay	1,744,973	682,349	39
Peru	3,638,602	979,582	27
Venezuela	1,076,633	826,073	77

^aVaccination campaigns were undertaken in selected areas of Brazil during 1973 and 1980-1982, in Panama during 1974, and in French Guiana during 1977.

^bIncludes revaccinations among the indigenous population and vaccination of fluctuating populations.

^cData from Panama refer to 1977-1981.

^d... Data not available.

several countries undertook extensive vaccination campaigns in the 1973-1977 period. Therefore, if persons immunized at that time and those immunized by routine vaccination programs were included in the vaccination coverage estimate, the figures would obviously be higher.

In any event, it is important to develop a monitoring system to more accurately determine the vaccination coverage of the populations at risk, particularly in those areas where outbreaks are known to occur. Such systems should estimate the coverage by locality.

Evaluation of Immunity

A few studies have been carried out recently to assess immunity among vaccinees. In Bolivia, 142 persons from Santa Cruz presumably vaccinated against YF were examined in 1982; 88% were found to have neutralizing antibodies to the French neurotropic strain (FN) of YF virus; antibodies were measured by a plaque reduction neutralization test (PRNT), and serum samples which neutralized 90% of a virus challenge at a 1:10 starting dilution were considered positive. In Brazil, at least 95% of about 80 serum samples collected from persons bled 30 days after vaccination under field conditions were found to have PRNT antibodies to the FN strain. In French Guiana, 51 of 55 persons (92%) were found to have hemagglutination-inhibiting antibodies to YF antigen.

Although these studies indicate a good vaccine response, their limitations are obvious. It would be desirable, therefore, to assess the immunity to YF in representative samples randomly selected from certain population groups in endemic areas.

Vaccine Production and Complications

It is estimated that tens of millions of persons have been immunized with the 17D vaccine, which produces seroconversion in 95% of the recipients. Less than 20 cases of neurologic complications associated with its use have been reported, only one of which was

fatal. These observations have demonstrated that the vaccine is safe and highly immunogenic.

Most 17D vaccine used in the Americas is prepared in Brazil and Colombia. The two laboratories involved annually produce approximately 10 million and two million doses, respectively. In recent times potency tests with some lots of the vaccines made in these countries have been performed regularly through PAHO coordination at the U.S. Food and Drug Administration's Bureau of Biologics. Although the vaccines have met the WHO criteria for potency when kept frozen, some lots showed a decrease in virus titer (sometimes to levels below acceptable standards) after storage at +4°C for a few months.

Overall, it appears that several improvements are needed in the production and testing of the vaccines prepared by these South American laboratories. Lack of adequate thermal stability is a major constraint; and, because of this, the vaccine requires a cold chain that is often difficult to maintain continuously, particularly in remote areas. Other major production problems include:

- disparity among seed lot substrains and the presence of avian leukosis viral contaminants;
- a high content of egg protein in the final product;
- a certain degree of instability in some seed lots, even when maintained at -70°C, after desiccation;
- the low quality of some egg batches used;
- deficiencies in the freeze-drying process that lead to undesirable moisture content levels;
- inconsistency and cumbersomeness of vaccine titration in mice;
- a shortage of rhesus monkeys for testing the secondary lot substrains;
- difficulties in large-scale production.

These problems were identified by a group of experts during a PAHO/WHO meeting of the Working Group on Modernization of Yellow Fever Vaccine Production that was held in Washington, D.C., in January 1981. To deal with this situation, the group made two basic recommendations: (1) modernize current production techniques of the presently available egg vaccine; and (2) conduct re-

search on development of a vaccine that could be produced in cell cultures; this latter would greatly improve the speed and possibly the economy of vaccine production and allow for rapid expansion of production in the event of emergency situations.

In response to these recommendations, Brazil and Colombia have improved the physical facilities of their vaccine production laboratories using national funds. In addition, both laboratories are modernizing their vac-

cine production methods with funds made available by Canada's International Development Research Center and the Canadian International Development Agency. A portion of these latter funds has also been provided to conduct research on thermostabilizing media for yellow fever vaccine.

Source: Pan American Health Organization (Epidemiology Unit, Health Programs Development), *PAHO Epidemiological Bulletin* 4(6):7-10, 1983.

VACCINES USED IN THE EXPANDED PROGRAM ON IMMUNIZATION (EPI): INDICATIONS AND CONTRAINDICATIONS

Introduction

Immunization is one of the most powerful and cost-effective weapons of modern medicine. Immunization services, however, remain tragically underutilized in the world today. In developing countries, it can be expected that some 0.5% of all newborns will become crippled from poliomyelitis, 1% will die from neonatal tetanus, 2% will die of pertussis, and 3% will die from measles. In all, some five million children die from these diseases each year, 10 children with each passing minute.

These diseases are preventable with currently available vaccines if children can be immunized early enough in childhood. Therefore, the decision to withhold the benefits of immunization from an eligible child, whatever the reason, should not be taken lightly. Unfortunately, health workers in many countries are faced with long lists of contraindications which, when followed scrupulously, result in many children remaining unimmunized. The problem resulting from deferring immunization is greatest where access to health services is limited and where the morbidity and mortality from vaccine-preventable diseases are

high. Immunization is frequently postponed if children are ill, malnourished, or about to be hospitalized; yet these are the very children for whom immunization services are most needed, for they are the ones most likely to die should they acquire a vaccine-preventable disease.

The purpose of this work is to review the benefits and risks of routine immunization of children with BCG, DPT, measles, and poliomyelitis vaccines, and (particularly for ill and malnourished children) to suggest circumstances in which immunization may be in the child's best interest.

Adverse Reactions to Immunization

Despite the high degree of safety of the vaccines used in the EPI, complications do occur. Their rates are difficult to estimate precisely, but it is known that they are far less frequent than the complications caused by the diseases themselves (see Tables 1-3). Some conditions, particularly fever and neurologic syndromes, also occur spontaneously among unimmunized children; and against this background it is sometimes difficult to determine if a recent immunization is causally or merely coincident.