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 latest 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*, raise great concern regarding the possibility of urbanization of jungle YF.

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 conducted in Brazil in 1937. Following these studies 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 wide 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 population and isolated communities (as observed in the Amazon region) pose additional problems in reaching high-risk groups.

In countries where routine vaccination programs are carried out, the vaccine is delivered through stationary health facilities. 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. The vaccinees are issued a certificate, but because the document is often lost, many revaccinations are probably performed unnecessarily.

In addition to these activities, vaccination is recommended for persons who travel from urban centers to rural endemic areas. In accordance with International Sanitary Regulations, individuals who travel abroad are also vaccinated. A total of 78 mobile and 66 stationary teams are maintained by Brazilian health authori-
ties. Most of the stationary teams are assigned to large cities. In Venezuela, a radio communication system links a central station with the 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. In certain colonized areas such as the Trans Amazonian highway, YF vaccination was required for the settlers before they were permitted to work.

Vaccination Campaigns

During YF outbreaks, most countries institute massive vaccination programs. In such circumstances vaccination teams are transported to the problem areas. Information on their arrival and activities is widely disseminated to the public by radio broadcasts and other means.

In certain outbreaks, new colonizers and temporary workers arriving from nonendemic areas are the main target for the disease; every effort should be made to immunize these population subgroups. In such cases, vaccination teams are deployed along the route taken by these 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.

Since the campaigns are hastily implemented, many persons are often unnecessarily revaccinated; this problem is difficult to overcome. In any event, the campaigns are undoubtedly very useful, not only in controlling epidemics but also in preventing the recurrence of more extensive and lengthy outbreaks in areas where adequate vaccination coverage is achieved.

In French Guiana, campaigns have been conducted at 10-year intervals since 1967. Over 90 per cent of the population was immunized in both the 1967 and 1977-1978 campaigns. The YF vaccination is compulsory in French Guiana, and is routinely administered, even during the campaign year.

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 per cent 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 the containment vaccination tactic when sporadic cases are documented in the absence of evidence of an epidemic. The containment consists in vaccinating residents of the surrounding area where the reported case was living or working.

Vaccine Administration Methods

The ped-o-jet injector method of vaccine administration permits large numbers of persons 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 the 1978 outbreaks which occurred in the northern part of the country. Cases were reported in the vicinity of certain Colombian towns highly infested with *Aedes aegypti*, and several patients required hospitalization in various towns, indicating that the risk of YF urbanization was imminent. The availability of the ped-o-jet facilitated prompt action and in the city of Valledupar, for instance, 92 per cent of its 117,000 inhabitants were vaccinated in four days. In Bolivia and Paraguay, also, ped-o-jets are used 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. In French Guiana, however, this method is employed during campaigns as well, 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. Certain countries, however, administer the vaccine mainly to children above the age of one year.

Table 1 shows the number of persons vaccinated or the number of vaccine doses administered in seven countries and French Guiana, during the past five years (1978-1982). In general, countries consider the popula-
Table 1. Estimated population at risk and yellow fever vaccination coverage in some countries of the Americas and French Guiana, 1978-1982.

<table>
<thead>
<tr>
<th>Country or territory</th>
<th>Estimated population at risk</th>
<th>No. of persons vaccinated or vaccine doses administered</th>
<th>Estimated vaccination coverage in endemic areas (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bolivia</td>
<td>1,766,015</td>
<td>1,350,497</td>
<td>76</td>
</tr>
<tr>
<td>Brazil</td>
<td>6,000,000</td>
<td>710,071</td>
<td>80-100</td>
</tr>
<tr>
<td>Ecuador</td>
<td>309,818</td>
<td>137,720</td>
<td>44</td>
</tr>
<tr>
<td>French Guiana</td>
<td>...</td>
<td>26,133 prob. &gt; 80</td>
<td></td>
</tr>
<tr>
<td>Panama</td>
<td>96,212</td>
<td>39,617</td>
<td>41</td>
</tr>
<tr>
<td>Paraguay</td>
<td>1,744,973</td>
<td>682,349</td>
<td>39</td>
</tr>
<tr>
<td>Peru</td>
<td>3,638,602</td>
<td>979,582</td>
<td>27</td>
</tr>
<tr>
<td>Venezuela</td>
<td>1,076,633</td>
<td>826,073</td>
<td>77</td>
</tr>
</tbody>
</table>


*bIncludes revaccinations among the indigenous population and vaccinations of fluctuating populations.

*cData from Panama refers to 1977-1981.

...Data not available.

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, and 88 per cent had 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 per cent of virus challenge at a 1:10 dilution (starting dilution) were considered positive. In Brazil at least 95 per cent of about 80 serum samples collected from persons bled 30 days, after vaccination under field conditions, had PRNT antibodies to the FN strain. In French Guiana 51 of 55 persons (92 per cent) had 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.

Vaccination Applications

It is estimated that tens of millions of persons have been immunized with the 17D vaccine which induces a seroconversion rate greater than 95 per cent. Less than 20 cases with neurological complications associated with its use have been reported, only one of which was fatal. These observations demonstrate that the vaccine is highly immunogenic and safe.

Vaccination Production in South American Laboratories

Most 17D vaccine used in the Americas is prepared in Brazil and Colombia. The two laboratories annually produce approximately 10 million and 2 million doses, respectively. Recently, potency tests with some lots of the vaccines made in these countries have been performed regularly under PAHO's coordination at the Bureau of Biologics, U.S. Food and Drug Administration. 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.

Needs in Vaccine Production

Several improvements are required in the production and testing of the vaccines prepared in the South American laboratories. Lack of adequate thermal stability is a major constraint, and because of this, the vaccine...
requires a cold chain which is often difficult to maintain continuously, particularly in remote areas. Other major problems identified in vaccine production include:

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

Such constraints have been identified by a group of experts during a PAHO/WHO meeting of the Working Group on Modernization of Yellow Fever Vaccine Production held in Washington, D.C. in January 1981. As a result of identifying and analyzing these shortcomings, the group made two recommendations: 1) modernize current production techniques of the presently available egg vaccine; and 2) conduct research on the development of a vaccine produced in cell cultures; this would greatly improve the speed and possibly the economy of vaccine production and allow rapid expansion in the event of emergency situations.

In response to the first objective, Brazil and Colombia have improved the physical structure of their vaccine production laboratories using national funds. Besides, both laboratories are modernizing their vaccine production methods, with funds made available by the International Development Research Centre, Canada, and the Canadian International Development Agency. A portion of these funds was also provided to conduct research on thermostabilizing media for yellow fever vaccine.

Aiming to implement the second objective, PAHO is planning to convene a meeting in Washington, D.C. for 21-23 February 1984, to develop guidelines and protocols for the adaptation of yellow fever vaccine production to cell cultures.

(Source: Epidemiology Unit, Health Programs Development, PAHO.)

Editorial Comment

A previous report (Epidemiological Bulletin Vol.4 No.1, 1983) presented information on the yellow fever (YF) situation in the Americas in 1981-1982. Since vaccination is the only effective method for preventing jungle YF, it seems opportune to review the vaccination programs carried out by affected countries to protect susceptible populations.