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## *Plasmodium falciparum* Response to Chloroquine in the Americas

*P. falciparum* resistance to chloroquine was first observed in 1960-1961 in patients coming from the Lake Maracaibo region in Venezuela, the Magdalena River Valley in Colombia, and the Amazon Basin in Brazil.

Between 1961 and 1964 a number of controlled field studies reinforced those observations, and some carried out in research centers confirmed resistance to the 4-aminoquinolines and to other malaria drugs.

In 1965 a WHO Scientific Group described a standardized procedure for the *in vivo* determination of the effect of the drug administered orally in a standard dose of 25 mg of cloroquine (base) per kg body weight for three days. To observe the immediate and curative effect of the drug, parasite counts are made daily during the first week following treatment and weekly during the following three weeks.

With this procedure different responses to chloroquine have been observed, depending on the proportion of susceptible plasmodia and the immunity level of the patient.

In Central America, Haiti, and Mexico, asexual parasitemia in patients studied in malarious areas is controlled in 48-72 hours and, in the last 20 years, no relapses have been recorded during the four weeks of observation, which indicates that the infections are *susceptible* (WHO, 1973).

In South America, about 40 per cent of the infections have been found susceptible to the standard dose in semi-immune persons living in areas in which transmission occurs in Bolivia, Brazil, Colombia, Ecuador, French Guiana, Guyana, Panama, Paraguay, Peru, Suriname, and Venezuela. Another 40 per cent of the infections in those countries relapse between the second and fourth week following treatment. In addition, recrudescence of infection has been observed in the first seven days or in infections in which the parasitemia is not controlled in the same period (15 per cent) and, finally, there are infections whose parasitemia remains at the same level or increases following treatment, with consequent worsening of the patient's condition (5 per cent). This last-mentioned group is found in particular in land-settlement areas in the basins of the major rivers of Brazil and Colombia.

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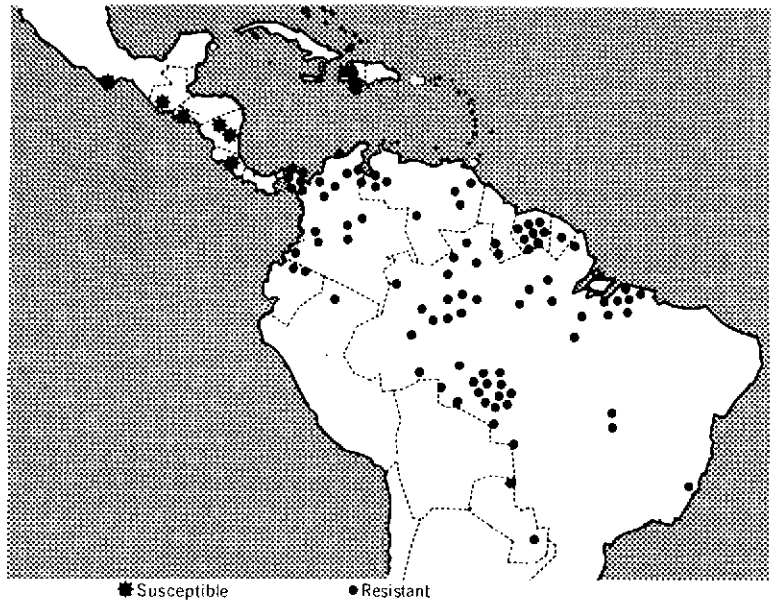
**Figure 1. Geographic distribution of the results of susceptibility tests of *P. falciparum* to cloroquine in the Americas, 1961-1980.**




To evaluate the inhibition of the maturation of the schizonts to different amounts of cloroquine (the same as or higher than the levels obtained with the recommended doses), a simple *in vitro* method has been used. The advantages of this method are as follows: on the one hand, the patient is not bothered with successive examinations over a period of several weeks; results are obtained within 24 hours and operating costs are reduced; on the other hand, such factors as the absorption and metabolism of the drug or the immunity status of the patient, which may alter the results of the *in vivo* tests, are ruled out.

In Central America, Haiti, and Mexico the inhibition of the schizonts 24 hours following incubation varies from $\leq 0.5$ nmol of chloroquine diphosphate per ml of blood in the more susceptible strains of Haiti to 0.75 nmol in Mexico, and 1.25 in Nicaragua. In South America, the inhibition of schizonts was found to be between 1.0 and $\geq 3.0$ nmol, but more resistant parasites have been found in Brazil and Colombia.

The malaria programs of the Region of the Americas, in cooperation with national institutions and PAHO, are endeavoring to expand studies of the resistance mechanisms, the genetic and antigenetic characterization of strains of various origins, the distribution factors in the human population, and different treatment schedules.

In addition, the Special Program for Research and Training in Tropical Diseases (WHO/World Bank/UNDP) has provided assistance in establishing a worldwide epidemiological surveillance system for the purpose of identifying susceptible and resistant strains as well as any changes that may occur.

Figure 1 shows the geographic distribution of *P. falciparum* reactions observed between 1961 and 1980 in the Americas.

(*Source*: Parasitic Diseases and Vector Control, Division of Disease Prevention and Control, PAHO.)