Endemic and epidemic diseases in Amazonia

Malaria and other emerging diseases in riverine areas of the Madeira river. A school case.

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Introduction

A few years ago, the media prominently reported an outbreak of malaria in Parati, an elegant tourist resort in the state of Rio de Janeiro, where six autochthonous cases had occurred (Folha Online, 2002; O Estado, 2008). For some, this news seemed to be "a sign of the deficiency and degradation of our health services." At that time, most Brazilians were concerned with the inability of the very same health services to control a dengue fever epidemic that was razing the country, and this sign reinforced the pessimism of public opinion regarding health care around the nation.

Paradoxically, however, the exact opposite could also be inferred, namely, that this sign was a good sign, not only in regard to malaria, but also because it was indirectly educational with respect to the future control of dengue fever and other emerging and reemerging diseases, which are always on the stakeout in Brazil and around the planet. Indeed, the incidence of malaria in Parati implies an epidemic, because, as the epidemiologists say, in each locality, every occurrence of a disease that exceeds the average of incidence in previous periods characterizes an epidemic. Parati's, however, was a microepidemic, and this makes all the difference. In Africa, we regularly find macroepidemics of malaria in areas where the disease is endemic or from where it has been absent for long periods.

These epidemic peaks are generally associated with the social turmoil, wars, revolutions or economic crises that disorganize the (already deficient) sanitation structures of African countries. Brazil has also suffered this type of epidemics. For instance, during the construction of the Madeira-Mamoré Railway (EFMM) in Rondônia in the early 20th century. It happened a second time, in the northeast, in the 1930s, after the arrival, by maritime traffic, of the African mosquito Anopheles gambiae. The An. gambiae entered through the city of Natal (Rio Grande do Norte state) and spread throughout the northeastern hinterland, causing thousands of deaths, before being eliminated in a memorable campaign led by entomologist Fred Soper from the Rockefeller Foundation (Deane, 1986; 1988). More recently, the country suffered a third macroepidemic, in the early stages of the colonization of the Amazon region in the 1970s. But all this has nothing to do with what happened in Parati.

Microepidemics similar to the one in Parati can be found in various regions around the planet. They originate from infected mosquitoes transported by airplane or otherwise or by the arrival of infected humans, who contaminate local vector mosquitoes, making for the transmission of the disease in previously unscathed areas. Thus, microepidemics have been confirmed in relatively recent years in the Zurich and Charles de Gaulle (Paris) airports (Giacomini et al., 1995; Guillet et al., 1998; Frey-Wettstein et al., 2001; Christen et al., 2006). Microepidemics were also observed a few years ago in the cities of Guarujá and Foz do Iguaçu, equally elegant tourist resorts in the states of São Paulo and Paraná, respectively (Camargo, 1993; Bértoli & Moitinho, 2001). Precisely for the fact that they were both controllable and controlled, remaining as "micro", these malaria epidemics attest that the health services are working well and are capable of swiftly identifying, characterizing and controlling the threats, whether in Parati or in Zurich, thus preventing their dissemination.

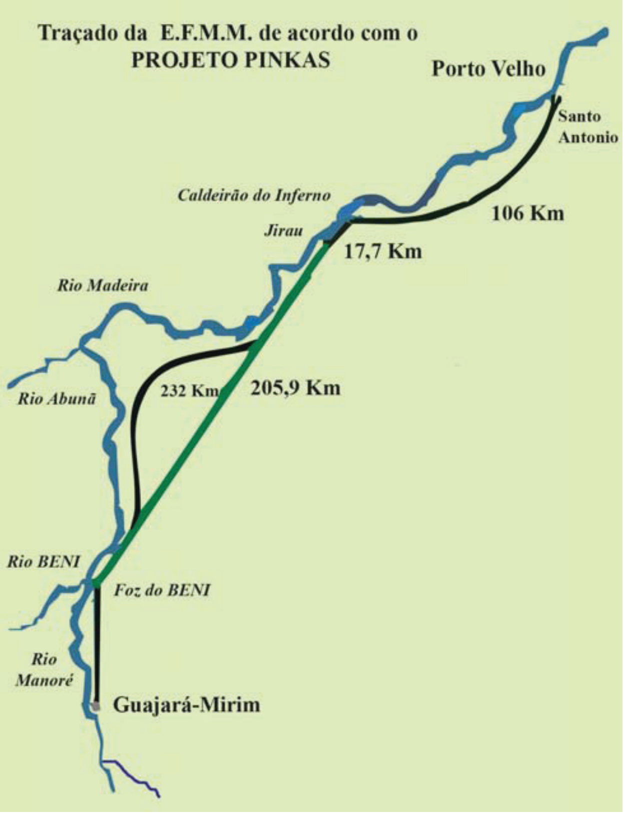
Malaria vector mosquitoes exist everywhere in Brazil, but today the disease is only actually endemic in the Amazon basin. Malaria has been kept under control around the basins of the Paraná, Prata, São Francisco, Doce, Tietê and Paraíba rivers, to name only a few, as well as in the coastal regions (such as the coastline of São Paulo and state, and the coast and lowlands of Rio de Janeiro state, among others), which were previously highly prone to the disease. It is estimated that there were 5 million annual cases of malaria in the Brazilian southeast before 1950, when the country's population was around 40 million (Pessôa & Martins, 1982). At present, the 400,000 to 500,000 annual cases of malaria reported in Brazil are restricted to the Amazon region, also known as "Legal Amazonia". Most of the Brazilian territory is now deemed to be non-endemic in terms of malaria, but is susceptible to emergence of microepidemics and, therefore, health services must remain constantly watchful and on the alert.

In the endemic area of the Amazon basin, sporadic outbreaks (mesoepidemics) also occur as a result of local incidents. These include the invasion or squatting of forested areas, as well as the disorderly implementation of settlements with no health infrastructure, and lead to episodes of "frontier malaria" (Sawyer et al., 1988). What motivated us to write this paper is precisely the possible occurrence of macroepidemics during the construction of hydroelectric power plants in the cities of Santo Antônio and Jirau, on the Madeira river. Our concern is not only malaria, but also arthropod-borne viral diseases and infections transmitted by or associated with water – such as typhoid fever, gastroenteritis and leptospirosis. These pose a great challenge for Brazil's health services, which must show that the country has evolved from the conditions that allowed the epidemics of 1907, 1930 and 1970. We will here focus specifically on the problem of malaria because of the greater availability of data and information on the endemic situation of the disease in the region.

A brief history of malaria in the state of Rondônia

There are still ruins of an 18th century Portuguese military edification in Rondônia (the Príncipe da Beira fort), but the first significant migratory movements into the region would only begin 100 years later, when rubber prices rose because of growing demand caused by the Industrial Revolution in Europe and the United States in the 19th century. The rubber tree Haevea brasiliensis, particularly abundant in what are today the states of Rondônia and Acre, attracted multitudes from other regions of Brazil and from neighboring countries. Being a frontier region between Brazil and Bolivia, it was the stage of violent conflicts between the two countries. In the late 19th century, the Petropólis Treaty was signed, transferring to Brazil the region that today constitutes state of Acre. In return, besides offering financial compensation, Brazil pledged to build a railway connecting Guajará Mirim (in the Brazil-Bolivia border, on the margins of the Mamoré river) and Porto Velho, on the Madeira river. The railway would be a means to avoid rapids of the Madeira river between the two cities (see Figures 1 and 2), which hampered navigation, and was expected to contribute to the exportation of the region's rubber, both Brazilian and Bolivian.

The Brazilian imperial government had previously invited several domestic and European contractors to take on the work, but the undertaking was never successful, mainly because of malaria, yellow fever and other unknown infections of the forest, which caused dramatic rates of morbidity and mortality among the workers. After the proclamation of the Republic in 1889, the new government took upon itself, as a matter of honor, the fulfill the commitments agreed upon in Petrópolis [in 1903] and accepted the proposal of a great American capitalist of the time, Percival Farquhar. This entrepreneur obtained important loans from American banks to carry out the endeavor. A contract was signed in 1905 and work began in 1907. Thousands of workers were recruited from the Antilles, Europe and India, in addition to numerous Brazilian migrants, who came mainly from the northeast region. The construction took six years, from 1907 to 1912, and, according to historians, caused more than 10,000 deaths ("a corpse for each crosstie"), essentially from malaria (Figure 3). At the time, the only available prophylactic and therapeutic measure was the use of quinine, with its various and quite pernicious side effects (Ferreira, 1981; Hardman, 2004).

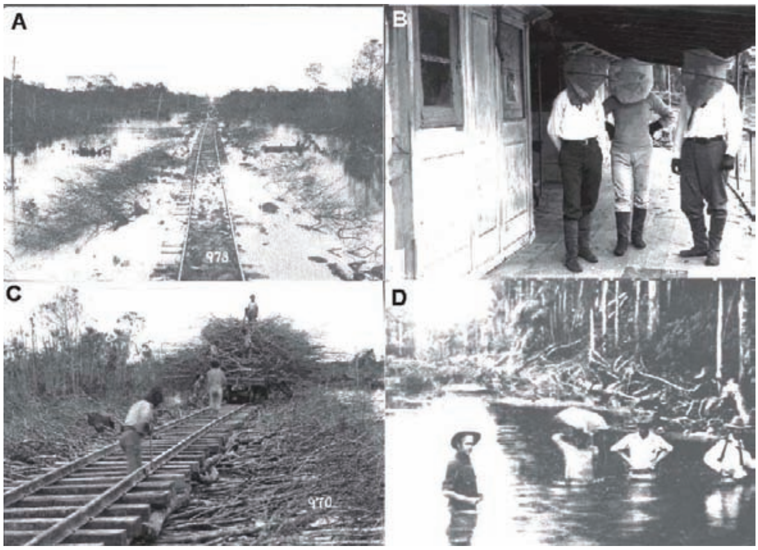


Source: BNDES-Centro-Oeste (1993)

Figure 1 – Route map of the Madeira-Mamoré Railway (1907-1912) between Porto Velho and Guajará Mirim

Source: Katsuragawa (2008)

Figure 2 – Fisherman in Madeira river waiting for the moment to catch a "leather fish", a scaleless catfish, during the rainy season in Cachoeira do Teotônia, near the city of Porto Velho, Rondônia.



Source: BNDES-Centro-Oeste (1993).

Figure 3 – Images of the construction of the Madeira-Mamoré Railway (1907-1912). A: flooding of the tracks opened in the forest. B: antimosquito protection used by the engineers. C: workers reinforcing crosstie & rail support. D: workers in flooded area along the rails.

Ironically, the conclusion of the Madeira-Mamoré railway in 1912 coincided with the beginning of the decline of the "rubber cycle", a result of the introduction of Haevea plantations in Malaysia by the English in the late 19th century. This led to the sudden and long-lasting fall of rubber's commercial value; local extractive production became unfeasible and the inevitable collapse of the railway began.

In the second half of the 20th century, Rondônia received another migratory wave, this time caused the military government's project of "national integration", which opened new roads in the region and created new settlement projects. In addition, huge alluvia of gold were discovered in the riverbeds. These new immigrants came especially from the southern region, which was suffering the consequences of agricultural modernization and mechanization, and from the northeast, where unemployment was a chronic malaise.

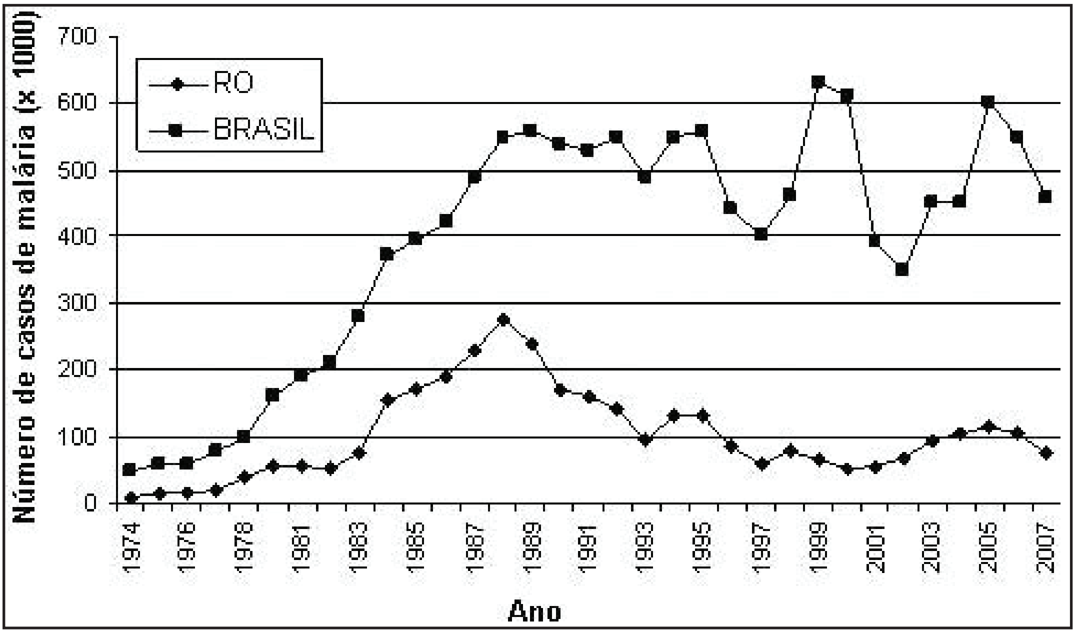
Once again, the ramshackle houses, the disorganized human concentrations, the lack of sanitation and the predatory invasions of the forest caused major outbreaks of malaria, with high morbidity and mortality rates. The number of cases of malaria in Rondônia flared from several thousand to more than 300,000 a year in the late 1980s, in a population that had exploded from 100,000 to 1,3 million (Table 1). Rondônia received the title of "world capital of malaria" at the time.

Table 1 – Demographic evolution in Rondônia: 1950-2007

Year	Urban	%	Rural	%	Total
1950	13,816	37.4	23,119	62.6	36,935
1960	30,186	43.2	39,606	56.8	69,792
1970	59,564	53.6	51,500	46.4	111,064
1980	227,856	46.4	263,213	53.6	491,069
1991	658,172	58.2	472,702	41.8	1,130,874
1996	762,755	62.0	466,551	38.0	1,229,306
2000	884,523	64.1	495,264	35.9	1,379,787
2007	1001,082	69.6	452,674	30.4	1,453,756

Source: IBGE (2008).

In the late 1980s, the "annual parasite index" (or API, the number of malaria cases per 1,000 inhabitants per year) in Rondônia was 128 (Barata, 1995). Almost half of the cases of malaria in Brazil were concentrated in the state. This crisis led the federal government to reinforce a disease-control campaign and create hundreds of units to diagnose, treat and fight the vectors in the endemic areas. The results were quite positive. Graph 1 shows the progressive reduction of the incidence of malaria, which fell to 50,000 cases in 1996. The anti-malaria campaign in Rondônia followed the precepts laid down by the World Health Organization (WHO), which had been defined at the 1993 Ministerial Conference on Malaria in Amsterdam, as we shall see.



Source: Sivep-Malária (2008).

Graph 1 – Evolution of malaria cases in Brazil and in Rondônia, 1974-2007.

However, the quality and effectiveness of these control actions fell abruptly when the management of the campaign was transferred from the federal to the local level, which reflected in an increase of the incidence rate in the first years of the 21st century: 100,000 new cases were reported in 2004, showing the importance of continuity in disease control measures (Graph 1).

In addition to its autochthonous cases, studies show that the state of Rondônia "exports" malaria to other regions of Brazil, specially through truck drivers, who have a massive presence in the state (Melo et al., 2005; Scandar et al., 2005). Only in the last two years has there been any improvement in this situation (Sivep Malária, 2008)

A parenthesis to present some data on the biological cycle of the malaria parasite

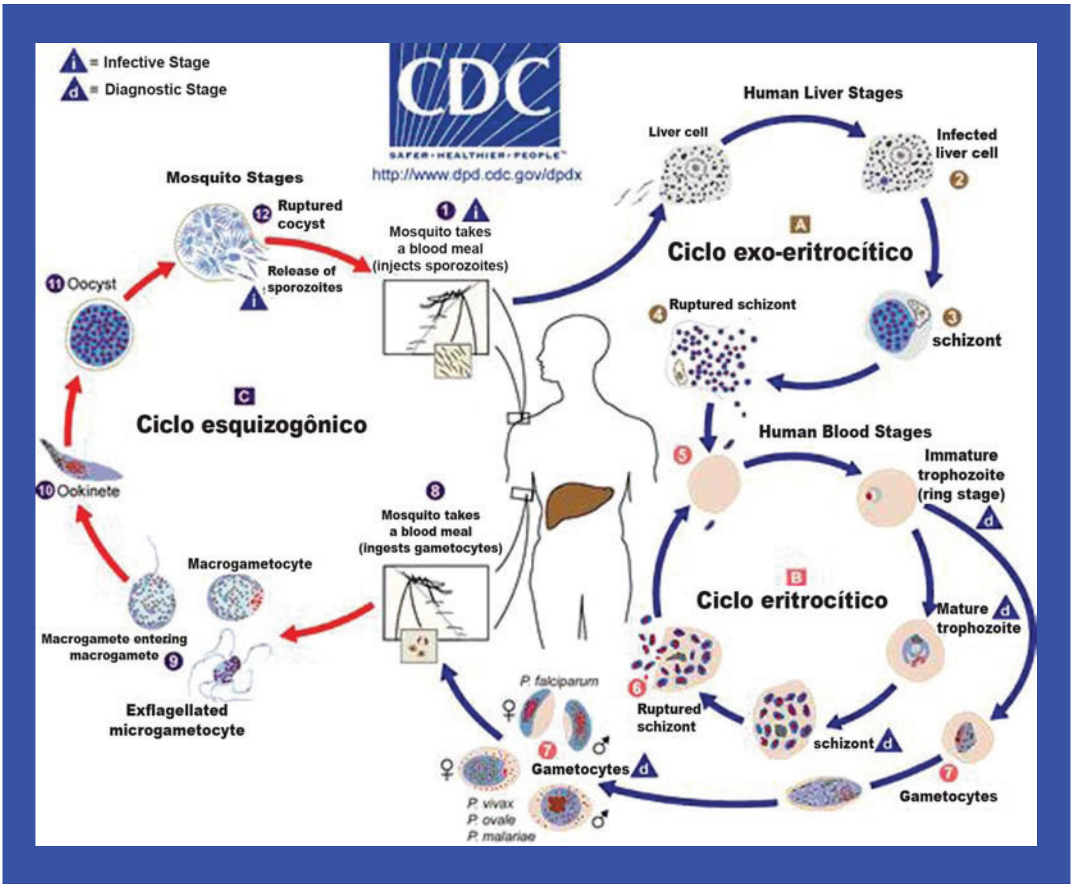
This article is aimed at readers who do not necessarily have a background in parasitology and tropical medicine; therefore, to help their understanding of the matter, it might be useful to make a quick reference to the biological cycle of human plasmodia – which are, after all, the villains of this story.

Figure 4 is a public domain drawing of the evolutionary cycle of human plasmodia, prepared by the United States Centers of Diseases Control and Prevention – CDC. The caption of the figure allows the reader to follow the parasite's cycle in the mosquito and in a human host. We would only like to draw attention to an important difference in the cycles of the *Plasmodium vivax* and of the *Plasmodium falciparum*.

In both species, the forms of the parasite inoculated by the mosquito (sporozoites) invade the liver cells, multiply and give rise to 7,000 to 10,000 descendents. These are called merozoites and they invade the red blood cells (erythrocytes), beginning the erythrocytic cycle that causes the symptoms of malaria.

The erythrocytic cycles are repeated indefinitely if they are not interrupted by treatment or by the development of natural immunity. In the case of *P. falciparum*, no form of the parasite remains in the liver after the erythrocytes are invaded, whereas in the case of *P. vivax* (and P. ovale, non-existent in Brazil) some forms remain dormant in the liver, receiving the name hypnozoites [or dormozoites]. Months later, they can be activated and begin to multiply, giving rise to a new cycle of erythrocytic infection.

This process explains why, in vivax malaria, a patient that was cured from the first infection with chloroquine can suffer a second infection months later, caused by hypnozoites, regardless of having acquired a second infection or not. These relapses constitute a major problem in malaria control and will be dealt with later on.



Source: Centers of Diseases Control and Prevention (modified).

Figure 4 – The malaria parasite life cycle involves two hosts. During a blood meal, (1) the mosquito inoculates sporozoites into the human host, infecting the liver cells and (2) initiating the pre-erythrocytic cycle; (3) the parasites multiply, forming the so-called schizonts; (4) the liver cells containing schizonts are ruptured and release merozoites; (5) the merozoites infect red blood cells, initiating the erythrocytic cycle (which gives rise to the schizonts); (6) after the rupture of the red blood cells that contain them, merozoites are released and invade other red blood cells; (7) some parasites differentiate into male (microgametocytes) and female (macrogametocytes) sexual forms; (8) the mosquitoes, by feeding off infected patients, ingest the gametocytes; (9) the gametocytes evolve into gametes, and the microgametes penetrate the macrogametes, generating zygotes, which in turn evolve into motile ookinetes; (10) these invade the midgut wall of the mosquito, where they develop into oocysts; (11) where sporogony takes place, releasing sporozoites; (12) which make their way to the mosquito's salivary glands.
Note: in *Plasmodium vivax* and *Plasmodium ovale* (the latter not found in Brazil), a dormant stage (hypnozoite) may persist in the liver and develop later, giving rise to new blood infections that constitute the malaria relapses. This does not occur with *Plasmodium falciparum*.

Another parenthesis on the vectors of malaria in Amazonia

The identification of the anopheline mosquitoes as the vectors that caused human malaria dates back to the late 19th century and was the work of an Italian, Giovanni Battista Grassi. The identification was followed by numerous studies by European and American entomologists, who ascertained the various species of *anopheles* responsible for transmitting malaria in the different regions of the world. Approximately 400 species of *Anopheles* have been described, 60 of which are implicated in transmitting malaria somewhere in the globe (Rey, 2001). With regard to Brazil, among dozens of species described, three of them, belonging to the genus *Anopheles*, were identified as the main vectors in different regions. The first is *Anopheles aquasalis*, so called because its larvae are resistant to high saline concentrations and, therefore, well adapted to proliferate in the brackish waters of the coast. A. aquasalis was identified as the main vector along the Brazilian coastline, from São Paulo to Pará.

The second important species is *Anopheles cruzi* (and its near relative, *Anopheles belattor*), the females of which have the particularity of depositing the eggs (that will hatch into larvae) in the water that accumulates among the leaves of bromeliads. This species was identified as the main vector of malaria in the Atlantic forest in southern Brazil, which is rich in bromeliads.

Finally, the third species, *Anopheles darlingi,* was identified as the main vector in most of the Brazilian territory. It can be found in practically every river basin of the country: the Amazon, to be sure, but also the basins of the Paraná and Prata rivers in the south and southeast, and of the São Francisco, Paraíba do Sul and Doce rivers. Detailed studies carried out by entomologists, by the Ministry of Health and, in particular, by René Rachou, Leônidas de Mello Deane and their disciples, established that the breeding ground for the Anopheles darlingi are large expanses of partially sunny, semi-stagnated water rich in organic material. The work of Lourenço-de-Oliveira and Luz (1996) showed that An. darlingi is rarely found in the forest environment of Amazonia and, therefore, its proliferation and progressive ascension as the dominant species in areas of endemic malaria are the result of human action during the process of colonization, which created "veritable pools" conducing for their proliferation (Deane et al., 1948, 1988). Breeding grounds appear in the enormous tanks of fish farms, derive from the natural erosion of river beds, or arise in the large expanses of water that accumulate in man-made depressions during deforestation or the construction of roads and dams.

Still another parenthesis on the campaign to eradicate malaria in the 1950s and on the 1993 Ministerial Conference on Malaria in Amsterdam

The proposal to eradicate malaria arose after World War II, under the auspices of the World Health Organization, when the powerful insecticidal action of DDT (dichloro-diphenyl-trichloroethane) was confirmed. Synthesized in Germany in 1874 by the young chemist Othomar Zeidler, its properties as an insecticide were discovered in 1939 by the Swiss Paul Herman Müller and confirmed in the treatment of lice during the war. With regard to the treatment of malaria, the 4-amino-quinoline drugs (including chloroquine) were synthesized by German chemists in 1934, although their powerful anti-malarial effects were only confirmed in the 1940s. The first positive experiments in the control of malaria with these new instruments took place in Italy in 1946, when DDT was applied to households in the valley of the Po river; combined with chloroquine treatments, it led to the eradication of malaria from the region. The United States immediately launched a campaign in 1947 spraying DDT in 4.5 million households in the Mississippi valley. There had been 15,000 cases of malaria in the US in 1949, only 2,000 in 1950 and the disease was considered eradicated from American soil in 1951.

A worldwide campaign to eradicate malaria, sponsored by the WHO, was launched in 1955, based essentially on the combined use of DDT and chloroquine. Its success had wide repercussion and led to the effective eradication of malaria from most European countries, the north of the Mediterranean and North America.

In the mid-1960s, however, negative news began emerge around the world. The appearance of chloroquine-resistant lineages of *P. falciparum* was confirmed in Colombia and Brazil. Stocks resistant to sulphonamides and antifolics (pirimetamine) appear in African and Asian countries. Social crises and revolutions associated with the processes of decolonization in Africa and Asia interrupted many campaigns against malaria, which were neglected or abandoned altogether. Lineages of mosquitoes resistant to DDT also appeared and, even more serious, there were numerous cases of grave, even deadly, intoxication caused by the intensive use of DDT, specially when used to fight crop pests. These factors led to its prohibition in the United States in 1970 and, later, to resolutions by the WHO severely restricting its use.

In Brazil, the campaign was also highly successful at first. In the late 1950s and early 1960s, malaria was controlled and, later, practically eradicated along the country's coastline, in the basins of the rivers Paraná, Prata and São Francisco, and in smaller basins in the southeast and south. In the 1960s, malaria was restricted to the Amazon basin and a few areas in the northeast and mid-west, with less than 50,000 annual cases.

In the Amazon region, because of the primitive nature of the houses and the dispersion of the rural population, application of insecticides failed as a control measure. Some alternative methods were tried, including the widespread distribution of chloroquine-salt mixtures for day-to-day use. These measures heralded positive results only in limited areas, such as the Icomi Project in Amapá. They were, however, abandoned and even condemned by the WHO because they could contribute to the development of chloroquine-resistant plasmodium stocks.

In the 1970s, the military government brought together all endemic disease control programs into a single structure, the Public Health Campaigns Authority (Sucam). At the same time, the National Integration Program was launched to "occupy" the borders in Amazonia, at the time literally uninhabited. Major roads – such as the BR-364 federal highway and the Transamazonic highway – were opened, providing easy access to the north of Brazil and the Bolivian border. The construction of these roads was followed by numerous rural settlement programs throughout Amazonia, by the building of hydroelectric plants and by the development of projects for the exploitation of natural resources. These endeavors attracted massive waves of migrants to the region, who came from all over the country and from where malaria had been eradicated for more than ten years. The new houses (which were built in such a way as to hamper the application of insecticide), the predatory exploitation of the rain forest and the concentration of thousands of unrestrained gold prospectors, together with the increase of favorable conditions for the proliferation of Anopheles darlingi, led to major new epidemic outbreaks in the region. Thus, the number of cases of malaria grew ten-fold, from 50,000 in the mid-1960s to 500,00 in 1987, and the incidence of the disease in Brazil began to hinge around 400,000 and 500,000 cases per year – more than 95% of which in the Amazon region.

With the end of the military regime in the early 1980s and the country's redemocratization, Brazil began to gradually recover from that dramatic situation and the incidence of malaria seems to be in a downward trend, albeit with periodic oscillations, thanks to a major effort by the Ministry of Health and the reorganization of its technical and administrative programs – not to mention the decentralization of health initiatives with the Unified Health Services (SUS) program, established by the 1988 Constitution. Thus, it was with great satisfaction that Brazil's health authorities participated in the 1993 Ministerial Conference on Malaria in Amsterdam, sponsored by the WHO, which brought together one hundred heads of State and health ministers from Europe, Asia, Africa, and the Americas. The goal of the meeting was essentially to prioritize anti-malaria campaigns around the world at a time when several new problems were amassing, namely: (1) the ban on the use of DDT, leaving sanitation workers with much less effective insecticides and larvicides – e.g., pyrethroid derivatives, certain organochlorides and organophosphorus compounds – with limited use because of their toxic side-effects; (2) the appearance of anopheline lineages resistant to existing insecticides and larvicides; and (3) the widespread dissemination of stocks of P. falciparum resistant to chloroquine and other aminoquinolines, to sulphonamides and to pirimetamine, among others, as well as the appearance of malaria patients with resistance to new drugs such as mefloquine.

From the numerous discussions and debates certain practical conclusions emerged. First of all, the reinstatement of a more humble outlook; the expression "malaria eradication" was eliminated from the technical vocabulary and replaced with “malaria control”. Next, a certain number of practical measures: (1) systematic studies on the actual prevalence of resistance to anti-malarial drugs; (2) avoidance of therapies using only one anti-malarial agent and promotion of multiple-drug treatments; (3) reorganization of patient care units to foster early diagnosis and treatment, that is, before the parasites in the patient’s blood have time to evolve and produce infectious forms for the mosquitoes (the so-called gametocytes). In the case of P. falciparum, for instance, it is known that the gametocytes only appear in the patient’s blood one or two weeks after the manifestation of symptoms; this means that if patients are treated early enough, they will not transmit the disease; (4) campaigns to control the vectors of malaria, associated with measures for early diagnosis and treatment.

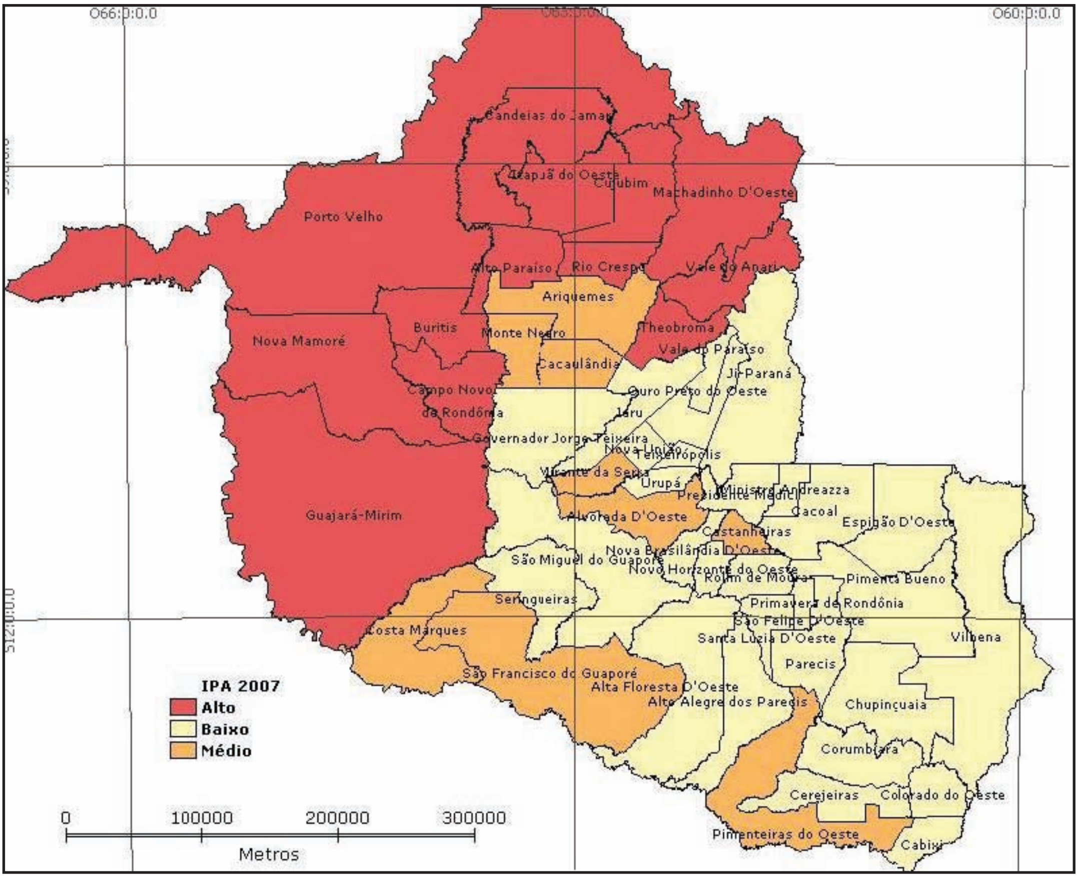
In Rondônia, these measures were adopted in the early 1990s, with positive results, as attested by the reduction of the incidence of the disease, which fell progressively to 50,000 cases in 1996 (Graph 1). Unfortunately, the lack of continuity of these actions and the havoc caused by the ill-planned and ill-executed decentralization of the malaria control operations led to a further increase in the rate of incidence in the early 21st century, with more than 100,000 cases/year again.

Current incidence and geographic distribution of malaria in the Amazon region and particularly in Rondônia

Textbooks that describe the status of malaria in the world and in Brazil often contain maps where a large portion of Brazil is drawn in black, like sub-Saharan Africa, the Indian subcontinent and the islands of the Indonesian archipelago (Pessôa and Martins, 1982; Rey, 2001). This representation ignores important quantitative and qualitative differences, for instance, that the incidence of malaria is three logarithmic orders of magnitude greater in the African continent than in Brazil. Even more serious, however, is that this graphic representation conveys the idea that the incidence of malaria is continuous throughout Brazil’s northern region – which is simply false. If the map of Amazonia is sufficiently detailed to show the local level, it will show that the distribution of malaria is quite heterogeneous in the state of Rondônia (Figure 5).

We learn that the 80,000 to 100,000 annual cases of malaria in the state over the last few years correspond to an average annual parasite index (API) of 70 – an incidence rate considered high. However, of the state’s 52 municipalities, 17 have incidence rates below 1 – the average API is 0.56 –, which practically defines the region as non-endemic. It should be stressed that this area, containing 30% of the state’s population, includes important cities such as Cacoal, Ouro Preto d’Oeste, Rolim de Moura, Ji-Paraná and Vilhena.

At the other extreme, 15 municipalities, containing 50% of the state’s population, have APIs between 20 and 400 – a high average incidence rate. This



Source: Sivep-Malária (2008).

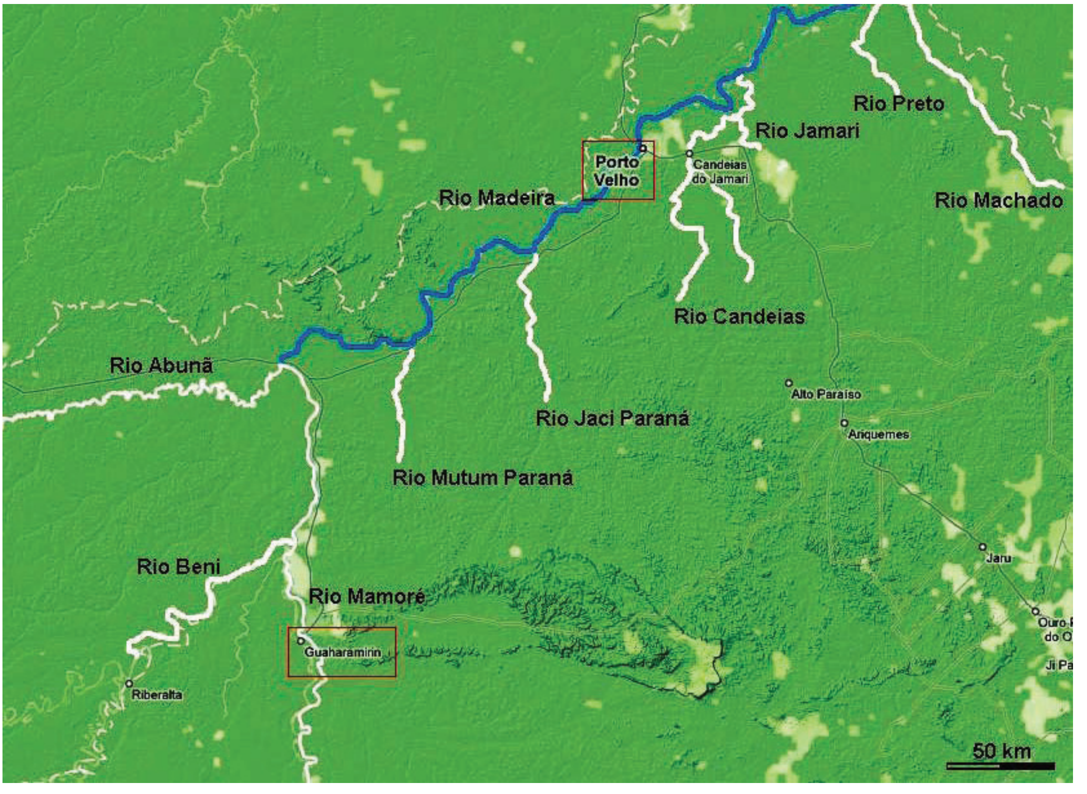
Figure 5 – Annual Parasite Index (API) in Rondônia, 2007.

group includes Porto Velho, the state's capital, and Ariquemes, the second most important city.

In the remaining municipal districts, with 20% of the population, the average annual parasite index is 6.2, which characterizes a low incidence rate. It is instructive to note that among the 15 high-incidence municipalities, 12 are traversed by the Madeira river or its major tributaries – Candeias, Jurupá and Machado. As we will see, the riverine areas are particularly prone to the transmission of malaria, which explains the high incidence rate in the cities crossed by the Madeira river and its tributaries.

Incidence and geographical distribution of malaria in the city of Porto Velho

The Porto Velho municipality, capital of the state of Rondônia, covers 34,082 km2 [13,159 sq. mi.]. It is, therefore, larger than Belgium (32,545 km2/12,565 sq. mi.). To the south, it borders Bolivia, and to the north, the state of Amazonas. The Madeira river, formed by the confluence of the Mamoré and Beni rivers, traverses the district from the southwest to northeast for



Source: Google Maps (modified).

Figure 6 – Illustrative map of the region between Porto Velho and Guajará Mirim. The Madeira river is formed by the junction of the Beni and Mamoré rivers. The image shows the major tributaries of the Madeira river (Mutum Paraná, Jaci Paraná, Candeias, Jamari, Preto and Machado).

approximately 300 kilometers and crosses over into the state of Amazonas. Until the 1960s, most of Porto Velho was still covered by rain forest, which include the vicinal woods along the Madeira river and its major tributaries – Mutum Paraná, Jaci Paraná, Candeias, Jamari, Preto and Machado, that flow into the Madeira river within the Porto Velho district limits (Figure 6).

The colonization of Porto Velho from the 19th century to the 1960s was carried out by river. The migrant populations came in successive waves, attracted initially by the rubber and later by prospecting, and established themselves along the margins of the Madeira river and its tributaries. They were first "ribeirinhos" [riverside inhabitants] of the region and miscegenated widely with the natives. When the BR-364 federal highway was built and several rural settlements were established, the city received additional significant waves of immigrants by land, undergoing particularly extensive and intensive deforestation and environmental degradation. The 2007 population was estimated to be 369,345 (IBGE, 2007), concentrated mainly in the city of Porto Velho, on the right-side margin of the Madeira river, with 330,000 inhabitants. It is the municipality of Rondônia with


Photo: Folha Imagem/Antônio Gaudéria – 11.19.2003

Indians from the cinta-larga ethnic group work in illegal diamond prospecting in Indian land. Aripuanã Park in Pimenta Bueno (435 miles from Porto Velho), in the state of Rondônia.

the largest number of malaria cases and was the epicenter of the great epidemics of the 1970s and 1980s, when nearly 40,000 prospectors were working in barges along the Madeira river. The mortality rate from malaria, added to the number of deaths due to violence among the prospectors themselves, reached more than 1,000 per year at the time. When the prospectors were at last partially regulated, the incidence of malaria stabilized around 40,000 cases per year – with a tendency to fall. The ribeirinhos and their descendents are, therefore, the most ancient residents of the place, which explains their immunity to malaria, having been exposed for year to the anopheline vectors that are abundant in riverine areas.

The ribeirinhos were probably responsible for the malaria outbreaks that afflicted the workers of the Madeira-Mamoré railway in the 19th and 20th centuries and, more recently, also the prospectors. As with the state as a whole, the distribution of malaria in the municipality is quite heterogeneous (Table 2 and Figure 7). The urban region (Region 1) is practically malaria-free; the disease is found only in the outskirts, where there is no sanitation and no drainage of surface waters. Riverside malaria is today the main form of malaria in the district, both in the suburban and rural areas (Regions 2, 3, 5 and 6). Some pockets of malaria still remain in the frontier, in the settlements and invaded areas, where there is no health care infrastructure and where the annual parasite index is extremely high (Regions 7, 8 and 9).

Table 2 – Evolution of the number of cases of malaria in Porto Velho, by operational region of malaria control by the Municipal Health Department of Porto Velho (Semusa), 2006 and 2007

			2006		2007	
Operational region	Population	Covered area	Cases of malaria	API	Cases of malaria	API
1	335,000	City of Porto Velho	5,472	16.3	6,347	18.9
2	12,100	Outskirts of Porto Velho	6,195	512.0	5,659	467.7
3	7,200	Santo Antônio to Jaci Paraná	3,136	435.6	3,482	483.6
4	9,100	Extrema, Nova Califórnia	3,270	359.3	2,015	221.4
5	7,900	Calama and riverside area	5,081	643.2	4,183	529.5
6	5,300	Jaci Paraná, MutumParaná and Abunã	3,899	735.7	3,362	634.3
7	3,300	Invasions and settlements	3,047	923.3	3,144	952.7
8	1,990	Invasions and settlements	2,696	1354.8	2,366	1188.9
9	2,900	Invasions and settlements	3,228	1113.1	2,306	795.2
TOTAL	384,790		36,024	93.6	32,864	85.4

Source: Semusa-Porto V0elho.

The specific situation of areas environmentally impacted by the construction of the Santo Antônio and Jirau hydroelectric plants

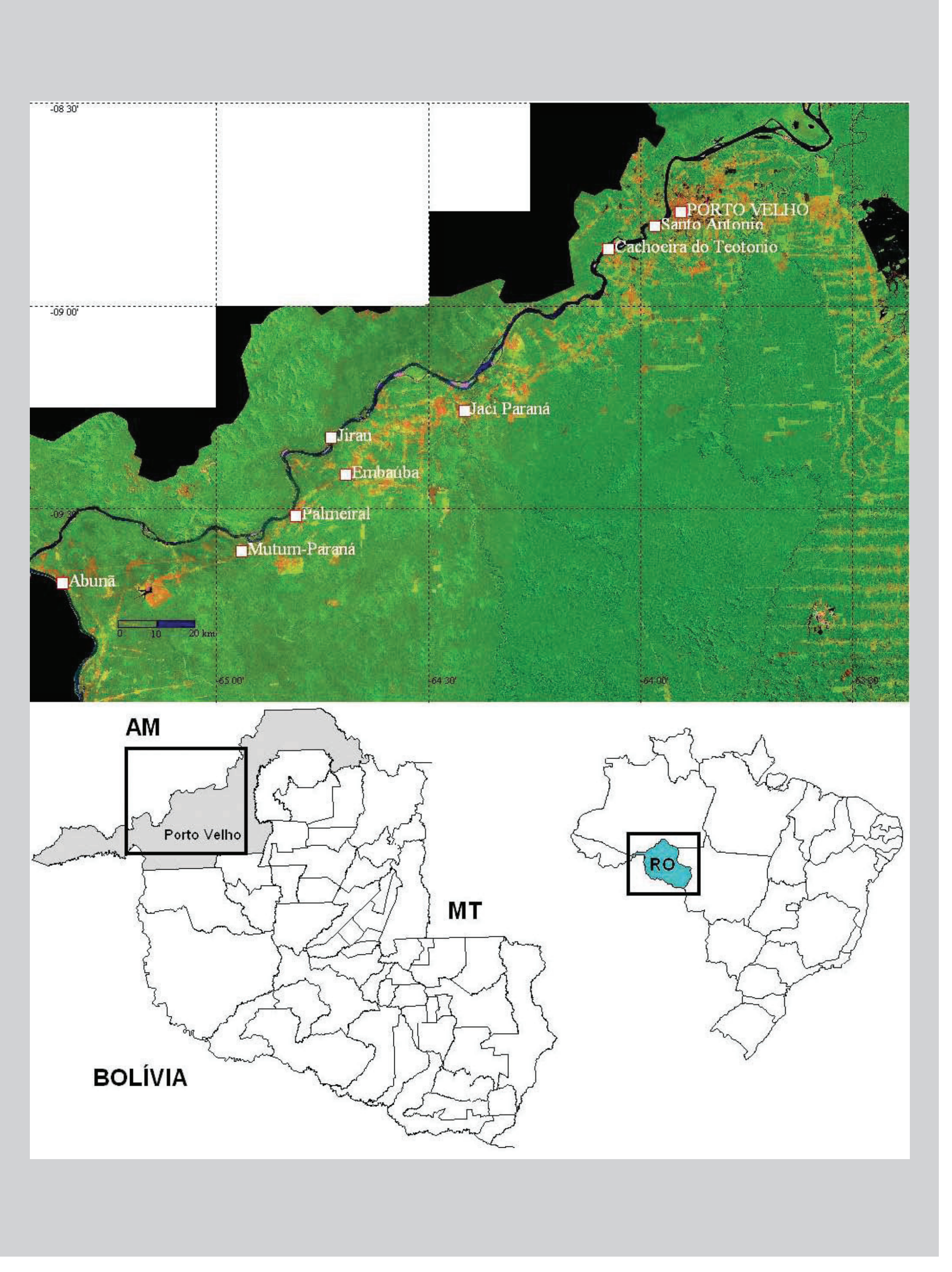
The impact zones of the Madeira river hydroelectric plants (the required dams are planned for the cities of Santo Antônio and Jirau – Figure 8) correspond to Regions 3, 4 and 6 of the municipal district, where the incidence of malaria is extremely high. The impact studies were carried out in two stages by teams from the Tropical Pathologies Research Institute (Ipepatro).

Source: Semusa-Porto Velho.

Figure 7 – Map of Porto Velho showing the distribution of the operational regions for malaria control of the Municipal Health Department of Porto Velho (Semusa)

In the first stage (2005-2006), six localities in the area directly impacted by the Santo Antônio plant were selected: one urban (Vila Candelária), two suburban (Bate Estaca and Santo Antônio) and three rural (Engenho Velho and Cachoeira do Teotônio on the right and on left bank of the river) (Figure 9). In these sites, which have been studied by the teams for several years now, the annual parasite indexes are high: between 250 and more than 1,000 (Table 3). The teams attempted to interview the entire population of residents with a new and detailed demographic questionnaire (residential). Householders were asked to participate in a longitudinal survey that included a brief clinical and epidemiological examination, an individual medical record and the collection of a blood sample for clinical/laboratorial evaluation (with exams by microscopy, serology and molecular methodology). Of the 1,068 residents surveyed, 827 (77%) agreed to participate in the study.

Analyzing the results, the prevalence of asymptomatic malaria (individuals with plasmodium in the blood but with no clinical symptoms of the disease) became evident. The incidence was higher among the ribeirinhos than among those living on nearby roads (Tables 4 and 5). Equally evident was the prevalence of carriers of hepatitis types B and C, infections by Treponema pallidum (syphilis) and low- and/or moderate-frequency HIV (data not presented).

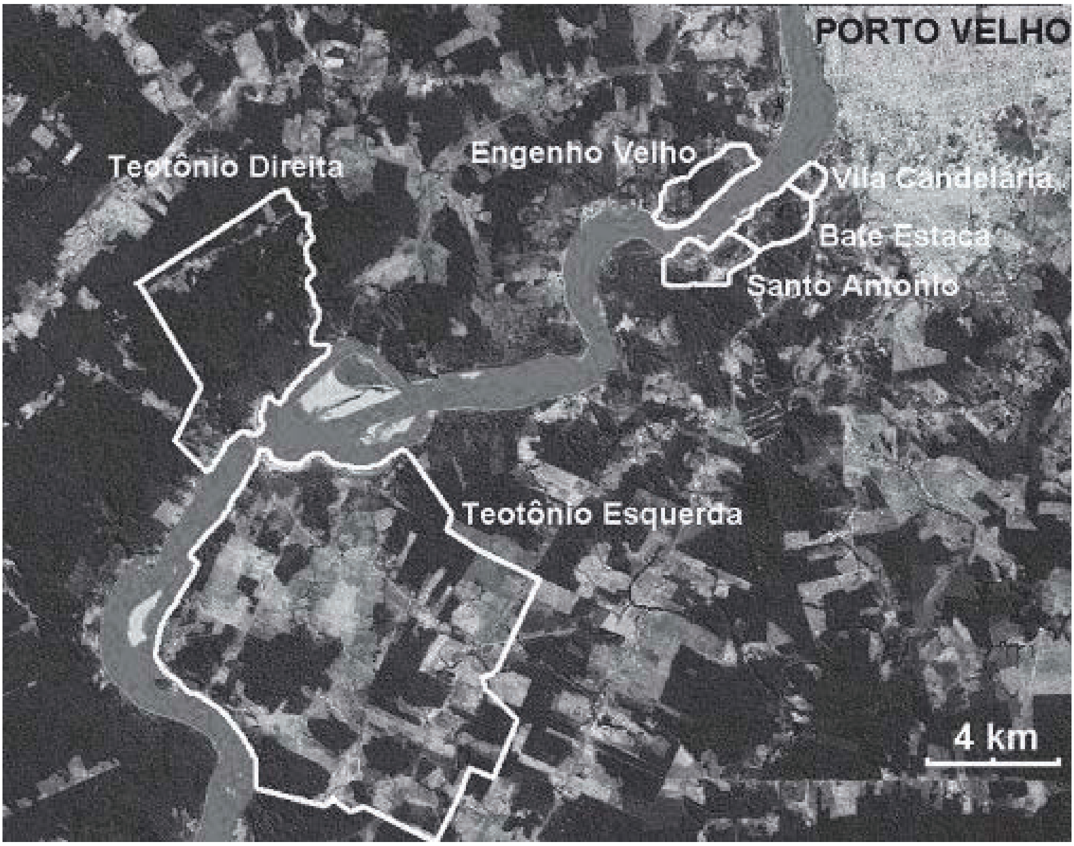


Source: adapted from Miranda & Coutinho (2004).

Figure 8 – Map of Porto Velho and towns along the Madeira river, and the localization of Santo Antônio and Jirau, where the hydroelectric plants will be built.

Table 3 – Incidence of malaria in the riverine communities of the Madeira river that will be directly impacted by the construction of the Santo Antônio hydroelectric plant, from 2003 to 2007.

Site		Engenho Velho	Santo Antônio	Bate Estaca	Vila Candelária	Cachoeira Teotônio (right bank)	Cachoeira Teotônio (left bank)	Total
No. Households		42	67	35	100	63	37	344
No. of residents		141	224	117	335	158	93	1,068
No. of participants		121	197	102	205	120	77	822
% of participants		86.0%	87.8%	87.0%	61.2%	76.2%	82.2%	77.0%
2003	Cases of vivax							
	Cases of falci-	66	…	…	108	111	31	
	parum	23	…	…	42	47	20	
	Malaria (total)	89	…	…	150	158	51	448
	API	632.6	…	…	447.0	996.8	562.2	616.2
2004	Cases of vivax							
	Cases of falci-	49	14	48	109	121	72	
	parum	6	1	4	11	37	19	
	Malaria (total)	55	15	52	120	158	91	491
	API	390.9	66.8	435.0	358.2	1003.2	983.8	459.7
2005	Cases of vivax							
	Cases of falci-	40	46	122	113	239	138	
	parum	14	19	38	27	57	45	
	Malaria (total)	54	65	160	140	296	185	900
	API	383.8	289.6	1364.3	417.9	1879.4	2033.0	842.7
2006	Cases of vivax							
	Cases of falci-	66	63	21	102	168	131	
	parum	16	23	8	18	41	23	
	Malaria (total)	82	86	29	120	209	154	
	API	581.6	383.9	247.9	358.2	1322.8	1655.9	685.4
2007	Cases of vivax							
	Cases of falci-	26	99	13	69	190	87	
	parum	7	31	5	20	52	23	
	Malaria (total)	33	130	18	89	242	110	622
	API	264.0	625.0	145.2	282.5	1273.7	932.2	582.4



Source: Google Maps (modified).

Figure 9 – Map of the overall study area, with the localization of six riverine communities: Vila Candelária, Bate Estaca, Santo Antônio, Engenho Velho, Teotônio Direita (right bank) and Teotônia Esquerda (left bank).

The extremely high anopheline density (Graph 2) means that, in certain months, each person receives 100 or more insect stings per night and, therefore, that the conditions in the region are very favorable for the transmission of malaria. The danger of an epidemics among the non-immune migrants who might reside in the area is indisputable. Field studies in the six communities have shown the existence of large expanses of surface water derived from human activity – e.g., fish farm tanks (active or abandoned), dammed streams or tributaries, discharge water from reservoirs, areas of seasonal crops in dry months etc. (Figures 10 and 11) –, all of which are excellent breeding ground for Anopheles darlingi.

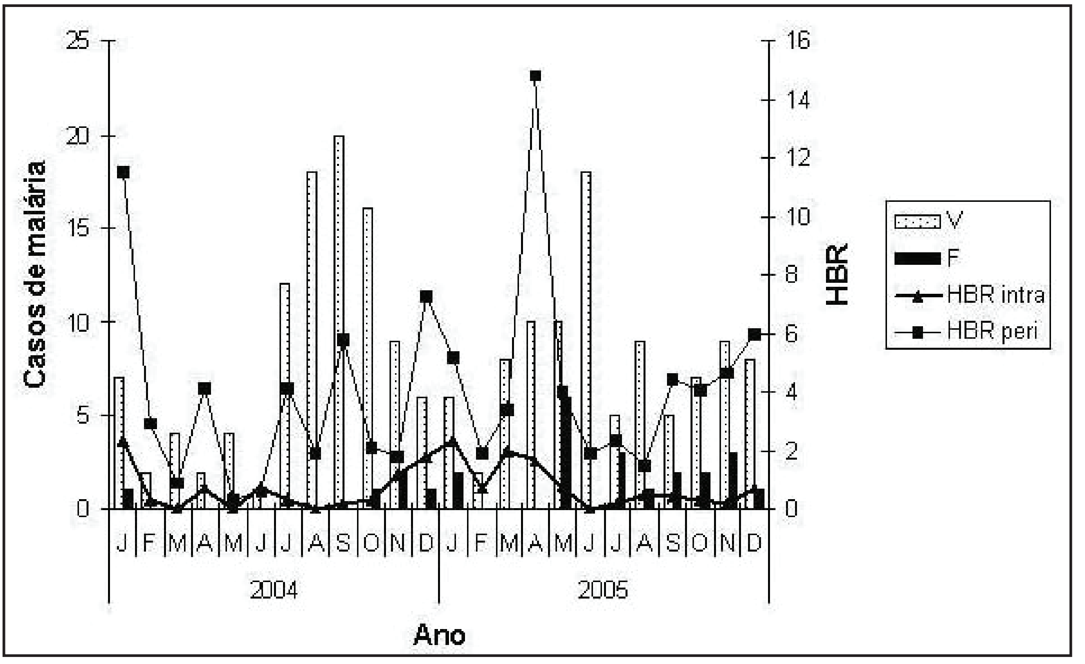
In brief, these observations lead to the conclusion that: (1) the high anopheline density implies that each riverine inhabitant may suffer more than 4,000 insect bites per year inside the home; if he or she remains exposed outdoors, the number of bites can be multiplied by ten; (2) the incidence of malaria in the communities is very high, with an annual parasite index above 500 or even 1,000; and (3) there are asymptomatic carriers of the malaria parasites.

Table 4 – Prevalence of asymmetric forms of malaria in riverine communities and in communities along BR-364 highway

Site		Popu-lation	Positive for malaria		Positive for *P. falciparum*		Positive for *P. vivax*	
	Name	n	n	%	n	%	n	%
Riverine communities	Santo Antônio (waterfall)	72	33	45.8	6	8.3	26	36.1
	Teotônio	108	28	25.9	6	5.5	20	18.5
	Jirau	20	2	10.0	…	…	2	10.0
	Santo Antônio (village)	103	55	53.4	11	10.7	30	29.1
	Subtotal	30	118	38.9	23	7.6	78	25.7
Communities along BR-364 highway	Jaci Paraná	94	17	18.1	5	5.3	10	10.6
	Embaúba	4	1	25.0	…	…	1	25.0
	Palmeral	5	…	…	…	…	…	…
	Mutum Paraná	40	6	15.0	1	2.4	5	12.5
	Abunã	52	6	11.5	…	…	6	11.5
	Subtotal	195	30	15.4	6	3.1	22	11.3
	Total	498	148	29.7	29	5.8	100	20.1

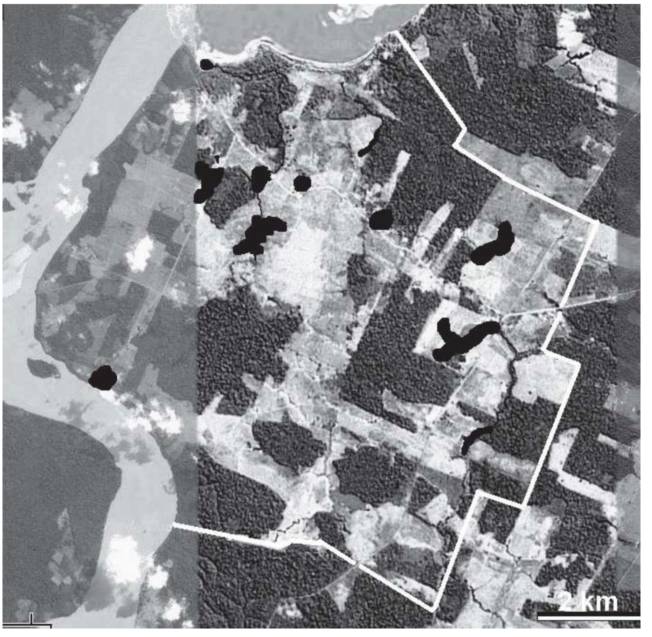
Table 5 – Prevalence of asymptomatic infections in the six localities directly impacted by the Santo Antônio hydroelectric plant

Locality	Date	Popu-lation	THICK SMEAR				PCR			
			n	V	F	F+V	n	V	F	F+V
Engenho velho	Jul 06	141	121	1	0	0	121	35	7	5
Santo Antônio	Aug 06	224	194	2	1	0	194	34	5	1
Bate Estaca	Aug 06	117	98	0	0	0	98	9	7	1
Vila Candelária	Sep 06	335	205	0	1	0	205	22	3	1
Teotônio (right bank)	Nov 06	158	119	4	0	0	119	18	0	0
Teotônio (left bank)	Nov 06	93	77	0	1	0	77	11	2	0
TOTAL		1,068	814	7	3	0	814	129	24	8



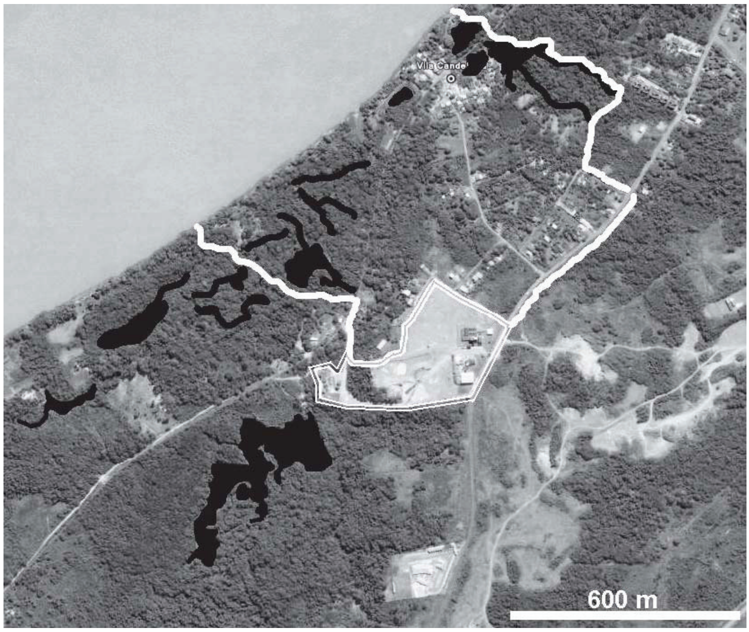
Source: data collected by Ipepatro teams.

Graph 2 – Seasonal variation of anopheline density in Vila Candelária, related to the incidence of clinical malaria. (HBR = *hourly biting rate* = number of insect bites per person per hour.)



Source: Google Maps (modified).

Figure 10 – Map of Cachoeira do Teotônio (right bank) showing deforested areas and surface water deposits (dark spots).



Source: Google Maps (modified).

Figure 11 – Map of Vila Candelária showing accumulated surface water deposits (dark spots). The area highlighted by a double white line indicates the state government's water treatment station.

These elements highlight the importance of outdoor transmission and demand innovative control methods, with emphasis on sanitary measures, to significantly lower the anopheline densities in the areas of transmission.

Why the dams being built for the Madeira river hydroelectric plants can create favorable situations for outbreaks of malaria epidemics

1. The incidence of malaria is soaring among the *ribeirinhos* (those who live on the margins of the Madeira river and its main tributaries and on nearby areas) because these populations are exposed to the intense seasonal variations of the region's hydrologic cycle that contribute to the cyclical development of high densities of anophelines when the waters are high.

2. The elevated transmission rates among the ribeirinhos and their stable behavior abet the development of immunity to malaria. The same happens in the hyper-endemic areas of Africa. This creates an ample human reservoir of parasites to infect the mosquitoes. Immune people harbor, for long periods, low-level parasitemias that nevertheless infect the vectors. Because they do not suffer from the acute feverish syndrome of malaria, they don't seek diagnosis and treatment to eliminate the infection.

3. The migrations that occurred after the opening of highway BR-364 brought in a large population of new migrants who settled along the road (in open lines according to the colonization process established by the National Institute for Colonization and Agrarian Reform – Incra) or in areas of uncontrolled squatting. These non-immune people constituted a population mass in which lineages of vivax and falciparum plasmodia, previously found only among the ribeirinhos, began to circulate. The incidence of malaria in the studied communities reached 300/1,000 among the ribeirinhos and 600/1,000 among the residents of vicinal roads.

4. A major migratory process is expected with the construction of the hydroelectric plants. Up to 20,000 new workers will be recruited to build the two reservoirs – Santo Antônio and Jirau –, increasing the number of migrants to 50,000 if their families are taken into account. The construction companies have pledged to hire workers who already live in the area, but it will be impossible to restrict recruitment only to local workers.

5. The presence of this new human community of employees, boasting high incomes for the region, will attract additional migrant populations, who will take jobs in commerce, leisure, education, and formal and informal services.

6. Brazilian labor legislation requires contractors to provide adequate housing and health care for the workers they hire and their families. Other migrants, however, cannot count on the same benefits, and the new arrivals, whose number may reach tens of thousands in the next few years, will spread out through the region, tending to concentrate in areas near the rivers or along the highways near the building sites and other urban areas. This combination creates favorable conditions for serious epidemic outbreaks of malaria, as has been the case in the past.

7. State and local governments do not have the financial, physical and human resources needed to meet the additional needs for sanitation and health care imposed by the new migratory wave. Local resources are insufficient even to cover the needs of the populations that have already established themselves.

8. The recent social and political events in Bolivia, which has borders with the municipal districts of Porto Velho and Guajará Mirim, can evolve further and cause migratory movements of Bolivians into Brazil. Considering that malaria is highly endemic in areas of the Bolivia/Rondônia frontier, these would-be migrations can become another source of reservoirs for the malaria parasite.

Other forest-related tropical diseases that may establish epidemics in the impact areas of the hydroelectric plants

Leishmaniasis is another important source of concern. Tegumental leishmaniasis stems directly from the contact between humans and the forest, the habitat of wild rodents (reservoirs) and sand flies [*Phlebotominae*] (vectors). The Amazon region currently harbors approximately half of the 20,000 annual cases of tegumental leishmaniasis in Brazil and the number of cases has increased with the increase of settlements and the exploitation of forest resources. Most cases of the disease take on cutaneous forms. Mucocutaneous forms have been registered in the state of Pará, but, in spite of the important work carried out by the teams of Lawson and Shaw at the Evandro Chagas Institute, the taxonomic identification of the various species of *Leishmania* found in Amazonia remains deficient because such identification depends essentially on molecular methodology, which the region's laboratories still do not master. With regard to visceral leishmaniasis [kala-azar], the disease has been described in older settlement areas in Pará, but not yet in other areas of the Amazon region. However, *Phlebotomus longipalpis*, the vector of *Leishmania infantum* in the Brazilian northeast, was found in the forests of Rondônia and it is possible that, as deforestation advances favorable conditions arise for the proliferation of the vector that disseminates the disease.

Infections transmitted by ticks – in particular, rickettsiosis and human borreliosis, as well as babesiosis and theileriosis in domestic animals – have not been much studied in Amazonia, but have now merited the attention of a project developed by the Institute of Biomedical Sciences of the University of São Paulo in the city of Monte Negro, Rondônia.

Viral infections are a greater worry for sanitation workers in the Amazon region, because they involve an entire family of agents, most of them practically unknown, whose emergence or reemergence remains a constant threat. Arboviruses of the Flaviviridae family, dengue fever and yellow fever have been the object of numerous studies and interventions, and are undoubtedly important emerging diseases in Amazonia. Other arboviruses have likewise been studied, especially by teams from Evandro Chagas Institute, which has distinguished itself for the important works published on reservoirs and vectors of arboviruses, culminating in the masterly An overview of arbovirology in Brazil and neighboring countries (IEC edit., 1998), which contains detailed descriptions of individual arboviruses, their vectors and reservoirs by experts from the IEC, from Fiocruz' Orstom and from the University of São Paulo. In this treaty, among other valuable information, one reads that "the Amazon region of Brazil is probably the world's largest reservoir of arboviruses." The 183 different types of arboviruses detected in the region correspond to one third of 533 found and described all over the world. Of these, 136 are endemic in Amazonia and 36 infect human beings.

IEC studies show that Amazonian arboviruses are associated with a broad variety of vertebrate hosts and bloodsucking arthropods, including nocturnal or diurnal mosquitoes, sand flies and ticks. Among the vertebrates, they can be found in primates, rodents, marsupials and birds. In other words, many species of viruses exist in a wide range of reservoirs. Thirty-six arboviruses and forest viruses have been associated with human diseases, five of which are considered the most important: dengue, mayaro, oropouche, rocio and yellow fever viruses. Dengue and oropouche viruses have been found in urban epidemics, while the incidence of the other three is essentially rural. Diseases associated with these viruses, with the exception of dengue and yellow fever, have not been studied in depth. Oropouche causes a fever process, generally benign, but may be accompanied by aseptic meningitis. Mayaro and dengue are associated with more serious fever processes, with exanthemas, although the hemorrhagic forms of dengue have been more frequent in the last epidemic cycles. The rocio virus is responsible for encephalitis. The other 31 viruses have been found in sporadic cases of transitory fever processes, but their study remains undeveloped as yet.

In conclusion

The control of transmissible diseases and, in particular, the ability to control epidemic cycles depends on five essential factors: (1) detailed scientific knowledge of the infectious agents and, when pertinent, of the vector(s) and reservoir(s), as well as detailed knowledge of the cycle of evolution of pathogenic agents, their eventual animal reservoirs in nature, and the direct and indirect methods and mechanisms of transmission; (2) identification of weak and/or accessible points to intervene in the natural cycle of pathogenic agents; (3) availability of technical and material resources to fight against these agents and/or against their vector(s), developed from scientific knowledge; (4) human, cultural and technical empowerment of the sanitary units in charge of disease control, including not only the technicians and professionals directly involved, but also the general population of the affected areas, who must have access to information; (5) political and administrative gumption to define priorities and allocate resources.As we write this paper, it seems to us that the elements pertaining to the first four items have been achieved with regard to malaria and can be complemented for other foreseeable diseases. With regard to the Jirau dam, although we lack the necessary information, there is still time to obtain it. It also seems to us that, regarding the fifth item, federal and local governments seem to be moving in the right direction, allowing us to expect the immediate prioritization of the requisite actions. It is hoped that, with all these elements in place, our health services will this time be capable of avoiding an outbreak of epidemics in the Madeira river valley, which has already given the country two dramatic episodes in the past.

Acknowledgments

The authors wish to thank the Ministry of Science and Technology and the Ministry of Health for providing funds to study malaria in the

Madeira river valley. We would also like to acknowledge the CNPq-Decit and CNPq-Universal contracts, as well as the contract with Odebrecht Engenharia e Construção, which allowed us to carry out studies on malaria in the Madeira river valley and that are here presented in part.

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ABSTRACT - The authors present a short review on the evolution of malaria incidence in the Brazilian Amazon, with particular reference to the state of Rondônia and the municipality of Porto Velho, where dramatic epidemics of malaria and other tropical diseases have been registered in the past. Next, they analyze the present endemic malaria situation in the Madeira river valley, where two important hydroelectric power plants will be constructed in the localities of Santo Antônio and Jirau. Longitudinal surveys performed in the last four years in this area allow them to demonstrate the high prevalence of symptomatic and asymptomatic malaria carriers in the area, associated with the presence of high densities of the malaria vector Anopheles darlingi all over the year. These elements are correlated to the expected arrival of a large number of human migrants from non-endemic areas of Rondônia and other Brazilian states, attracted by the possibility of jobs in the hydroelectric plants and by secondary opportunities in commerce, leisure, education and domestic activities. These associations create favorable conditions for malaria outbreaks and other tropical diseases that must be avoided by the establishment of additional control measures, in particular in the sanitation domain.

Keywords: Epidemics. Malaria. Asymptomatic carrier. Hydroelectric plants. Amazonia.

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Received on 9.25.2008 and accepted on 9.29.2008.

Translated by Carlos Malferrari. The original in Portuguese is available at http://www.scielo.br/scielo.php?script=sci_issuetoc&pid=0103-401420080003&lng=pt&nrm=iso.