



Malaria¹

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In 1990, Florida experienced its first human malaria case in 42 years in a female resident of Bay County in the Panhandle (Centers for Disease Control, 1991b). Although now rare except for imported or 198 induced cases, malaria was one of the major endemic diseases in the United States for more than four centuries (Russell, 1968). As recently as 1935, malaria caused 4,000 deaths in the United States. However, ten years later, the annual death toll had been reduced to 400, and by 1952 it was down to 25, with little or no local transmission. In the United States and elsewhere, malaria was eradicated by draining larval habitats (especially for agricultural use), treating patients with antimalarial drugs, applying mosquito larvicides and adulticides, and screening doors and windows.

While malaria was eradicated through the above methods in industrialized countries, it still remains the most important vector-borne disease in the developing world and is found in 102 countries (Oaks et al. 1991). Annual case estimates range from 100 million to 489 million, of which 1 million to 2.3 million are fatal (Strchler, 1989). Residual indoor spraying, chemotherapy, chemoprophylaxis and, more recently, insecticide-impregnated bed nets are used to control

malaria, but the spread of drug and insecticide resistance has seriously hampered antimalarial efforts. In addition, lack of trained manpower, rising costs, and reduced support and interest have contributed to its increase in many areas of the world. Although considerable funds have been spent on vaccine development, an effective vaccine for use in the field is still years away.

Therefore, it is not surprising that there are on average over 1,000 reported imported malaria cases a year for the last nine years in travelers returning to the United States and foreign visitors, including migrant workers (Centers for Disease Control, 1989). In Florida there were 67 and 55 imported cases in 1989 and 1990, respectively (Centers for Disease Control, 1990a, 1991a).

Besides these imported cases of malaria, outbreaks of malaria (transmitted by U.S. mosquitoes) occurred in California in 1952, 1986, 1988, 1989, 1990, the one in Florida in 1990 (Centers for Disease Control, 1990b, 1991b), and more recently, three in New Jersey (W. Crans, 1991).

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What is Malaria?

Alphonse Laveran, in Algeria, first discovered the microscopic pigmented protozoan parasites in the erythrocytes in human blood in 1880. In 1897 Sir Ronald Ross, in India, found a developing form of the malaria parasite in *Anopheles stephensi* that had previously fed on a malarious patient. Although human malaria is sometimes considered as a single disease, it actually is four different diseases with a variety of symptoms caused by four different species of protozoan parasites, all of the genus *Plasmodium*: *P. vivax*, *P. malariae*, *P. falciparum* and *P. ovale*.

All four species are transmitted from person to person via the bite of mosquitoes only from the genus *Anopheles*. Thus, part of the complex malaria life cycle occurs in humans and part in the mosquito.

Briefly, the cycle begins when an infected *Anopheles* female attempts to take a blood meal and inoculates sporozoites into the blood stream. Within minutes the sporozoites travel to the liver, where they develop into a schizont that produces a large number of merozoites, which are liberated into the blood stream. Each merozoite (sometimes two) invades a single red blood cell. In *P. vivax* and *P. ovale*, a latent liver stage (called hypnozoite) can delay up to five years before developing into liver schizonts, which produce merozoites, which then invade the red blood cells at a later time. This is called a relapse. In *P. falciparum* many merozoites emerge from the liver simultaneously, causing an overwhelming and often fatal blood infection. There are no delayed hypnozoites in the liver infected by *P. falciparum*, and thus no relapses. The asexual parasites first appear as rings in the red blood cell (the early trophozoite). After one or two days the trophozoite develops into a schizont that matures to produce more merozoites, which invade other red blood cells. Fever and other symptoms appear when the red blood cells rupture in a characteristic periodicity (48 hours for *P. falciparum*, *P. vivax*, and *P. ovale*, and 72 hours for *P. malariae*). This erythrocytic cycle may be repeated many times in chronic infections.

Some merozoites in red blood cells develop into male or female gametocytes, which are ingested by another *Anopheles* female. The gametocytes mature

into male and female gametes, which fuse to form a zygote. The zygotes penetrate the mosquito's gut wall as ookinetes and form oocysts, which enlarge and mature. Ten to 14 days after taking a blood meal, depending on temperature and malaria species, the mature oocysts rupture, releasing sporozoites into the body cavity. Some sporozoites travel to the salivary glands, where they remain until the female mosquito takes another blood meal and the cycle is repeated.

The malaria responsible for the most cases in the world, *P. vivax*, occurs throughout most of the temperate zone, large areas of the tropics, and less commonly in tropical Africa. The primary attack ranges from mild to severe but is usually not fatal. *Plasmodium falciparum* is generally confined to tropical or subtropical regions and is particularly severe and often fatal (within 18 hours of first symptoms) in infants, young children and adults with no previous exposure or immunity. *Plasmodium malariae* is frequently named quartan malaria because the fever reoccurs on the fourth day after a two-day interval, whereas fevers associated with the other three malaria species reoccur on the third day after a one-day interval. In both tropical and subtropical areas, however, the disease is less severe but may persist for 30 to 50 years. *Plasmodium ovale* is similar to *P. vivax*, but with a prolonged latency and generally older clinical symptoms. It is most common in West Africa.

Symptoms will vary depending on the malaria species, but the initial attack may start with lassitude, headache, anorexia, and occasional nausea and vomiting. The fever comprises a cold stage (shivering and a feeling of intense cold), a hot stage (distressing heat, dryness, burning, intense headache, nausea and vomiting), and finally a profuse sweating stage. The typical attack often begins in the early afternoon and lasts from eight to twelve hours. **Persons experiencing these symptoms and having been in an area with malaria should see a doctor immediately.**

What are the Specific Clinical and Pathological Characteristics of the Disease?

Plasmodium vivax

- Infects new red blood cells
- Incubation period: eight to 27 days (nine to 10 months recorded)
- **Primary attack lasts eight to 10 hours**
 - Sudden, shaking chill often for several hours
 - Headache, back pain, nausea, malaise
 - Irregular fever first two to four days; up to 104 to 105° F
 - Fever terminates by crisis with drenching sweat, up to several hours
- Series of fevers every 48 hours with diminishing intensity for two weeks
- Red cell destruction leads to anemia
- Latent period of two weeks
- Secondary attacks (less intense) for two months
- Second latent period of six to nine months
- Long term relapses two and one-half to three years
- Infection dies out

Plasmodium malariae

- Clinical symptoms similar to *P. vivax*, but may be more severe
- Untreated infection may have relapses 30 to 50 years later

Plasmodium ovale

- Clinical symptoms similar to *P. vivax*
- Spontaneous recovery common and fewer relapses

Plasmodium falciparum

- Infects **all** red blood cells
- Incubation period nine to 14 days
- **Primary attack (36 to 48 hours)**
 - Headache, back pain, prostration, chill, nausea, vomiting or mild diarrhea
 - Few parasites may be present
 - Fever may be low but this is critical time for diagnosis, symptoms depend on immunity
- Symptoms intensify, higher temperature, anxiety, mental confusion common
- Temperature may reach 105 to 110° F
- Delirium or coma without hyperpyrexia
- Cerebral manifestations of excitation, depression, behavioral changes with psychotic tendencies
- Fever irregular and no distinct periodicity
- Sweating may be present even when fever is low
- Pulse and respiration rates are rapid
- Nausea, vomiting and diarrhea increase; frequently a cough
- Spleen and liver enlargement
- If untreated, "pernicious malaria" may develop suddenly
- Severe dehydration and anemia
- **Symptoms may take various forms**
 - Bilious form: vomiting, gastric distress, jaundice
 - Algid form: high internal heat, body cold and clammy
 - Choleraic form: stools loose (rice water)
 - Acute hemolysis of erythrocytes (hemoglobinuria) with dark, mahogany-red urine (blackwater fever)

- Renal failure
- Frequent recrudescence first month
- After three to five months, latent periods are longer between attacks
- Radical cure in about 10 months

In summary, imported *P. falciparum* cases can be fatal in infants, young children, and nonimmune adults if not diagnosed correctly and timely. Unfortunately, most U.S. doctors have never seen a patient with malaria, and it has been wrongly diagnosed as dysentery, dengue, influenza, hepatitis, heat stroke, nephritis and other diseases.

How do you Detect the Malaria Parasite in Humans and Mosquitoes?

Blood Films stained with Giemsa stain.

A thorough search of one or several thick blood films should demonstrate parasites in humans. Nonimmunes with symptoms, especially those taking or having recently taken antimalarial drugs, may have fewer detectable parasites. Detection of parasites in thick films requires some experience. Thin blood films are used to assist in species identification of doubtful cases of malaria.

Serological tests

A number of tests are available that can identify and measure the parasite or the antibody: immuno-precipitation, immuno-fluorescence (IFA), indirect (IHA) or passive (PA) hemagglutination, indirect enzyme-linked immunosorbent assay (ELISA), radio-immuno assay (RIA), and merozoite inhibition in culture. These highly sensitive techniques are now used for research and epidemiological surveillance but not generally for diagnosis. In the future, these tests may replace the blood films.

Mosquito dissections

The presence of the parasite can be confirmed in mosquitoes by dissecting in saline the gut and salivary glands of the adult female and examining the tissue under a compound microscope for the presence of oocysts and sporozoites, respectively. These forms are relatively easy to find. However, unlike the blood

forms, the oocysts and sporozoites of all four species of human malaria, as well as other animal malaria species appear similar morphologically and can only be distinguished using the above serological tests. Although there are questions to be answered, the ELISA is very useful for determining infection rates when they are low and large numbers of mosquitoes need to be examined. With the ELISA, mosquitoes can be tested in pools of 10.

How do you Treat the Disease?

Several drugs are available to prevent and cure malaria, depending on which species and its sensitivity. The most common drug is chloroquine, which is used to treat the acute infection and as a chemoprophylaxis to prevent symptoms of the disease. An additional drug, primaquine, is also required to eliminate the latent forms in the liver tissue of *P. vivax* and *P. ovale*. Unfortunately, *P. falciparum* has become resistant to chloroquine in all countries except the Dominican Republic, Haiti, Central America west of the Panama Canal, the Middle East, and Egypt. In addition, *P. falciparum* is resistant to both chloroquine and Fansidar®, (another antimalaria drug) in Thailand, Burma, Cambodia, the Amazon basin area of South America, and sub-Saharan Africa. A new drug, mefloquine (Lariam®) is highly effective against both chloroquine and Fansidar®-resistant *P. falciparum* infections (Centers for Disease Control, 1990c).

What are the Vector Species?

Worldwide, there are approximately 400 described species of *Anopheles*, of which 60 are vectors of malaria, but only 30 of them are of major importance. In Florida, there are ten *Anopheles* species, all of which are potentially capable of transmitting malaria (Freeborn, 1949):

Anopheles quadrimaculatus

- Principal malaria-carrier
- Found in every Florida county, more abundant in the north
- Complex of at least four sibling species (Narang et al., 1989)

- Breeds in alkaline ponds, lakes and gum swamps in the limestone and red clay regions of north and western Florida

An. crucians

- Breeds in acid ponds and cypress swamps

An. punctipennis

- A winter breeder
- Breeds in slow-flowing alkaline streams of north and west Florida

An. perplexens

- A rather rare mosquito in north-central Florida

An. atropos and An. bradleyi

- Salt marsh breeders

An. albimanus

- Major malaria vector in Central America
- Now a very rare species in Florida (Lounibos, in press), but in 1946 fairly common in the Florida Keys (Haeger, 1949)
- Breeds in sunlit pools

An. walkeri

- More common in central Florida
- Breeds in heavily vegetated lakes

An. georgianus

- Rare species
- Breeds in seepage areas

An. barberi

- Tree-hole breeder

Origin and Impact of Malaria in the United States and Florida

Considerable evidence suggests that malaria has been present since prehistoric man in the Old World, probably originating in Africa (Bruce-Chwatt, 1980). However, its origin in the New World is controversial. Some suggest that malaria in the Americas, especially North America, was imported by the Spanish conquistadors and later by the colonists. Others believe that malaria existed in Central and South America long before the Europeans arrived.

According to Russell (1968), malaria did not exist in North America before the European colonial settlements. *Plasmodium vivax* and *P. malariae* were probably introduced by the Spanish, English, Dutch and French, and *P. falciparum* mostly by African slaves. In 1526, about 500 Spanish colonists, including a number of black slaves, sailed from present day Dominican Republic to Cape Fear River in North Carolina, then included in the name Florida, which included most of the southeastern coastal United States. This colonization attempt apparently failed partly due to malaria. The English brought *P. vivax* malaria with them, along with slaves infected with *P. falciparum* malaria, to Jamestown in the early 1600s, where it became one of the most fatal diseases of the colonies. During the 18th and 19th centuries, malaria spread the length and breadth of the United States and even into southern Canada. Russell (1968) mentions instances where both settlers and native Americans were decimated from malaria epidemics. Malaria probably reached its peak in 1875 (Bradley, 1966) and then declined in the North while remaining an important health hazard in the South well into the 20th century (Russell, 1968).

In Florida, both *P. vivax* and *P. falciparum* occurred in all 67 counties and was once a major scourge, causing misery, poverty, and general economic distress. Data collected from 1917 to 1944 by the Bureau of Vital Statistics and summarized by Provost showed 24 counties having annual death rates from malaria of 100 per 100,000. Eight had rates of over 200, and Dixie county, in 1930, over 300. According to the usually accepted ratio of 200 malaria cases per death, these rates mean 20 percent, 40 percent, and 60 percent or better of the populations

involved had malaria. Malaria mortality reports for Florida show a steady decrease since 1934 with no large outbreak since 1937. This reduction in malaria in Florida, as elsewhere in the United States, was probably due to adult mosquito sprays, more and better screening, use of repellents, agricultural and other drainage practices, and the use of antimalarial drugs. Residual spraying of walls in houses with DDT was introduced in 1945 in the 10 counties with the highest malaria death rates. In the following year, a DDT oil mist was used as a larvicide. Until recently, the last case of malaria from a bite of a naturally infected mosquito occurred in 1948.

Can Malaria be a Problem Again?

Probably not, at least not in a major way. However, the number of known imported cases into the United States has been generally increasing since 1973 (Centers for Disease Control, 1991a). During 1980 to 1988, 1,534 cases of *P. falciparum* malaria among U.S. civilians were reported. Of these, 80 percent were acquired in sub-Saharan Africa, 7 percent in Asia, 7 percent in the Caribbean and South America, and 7 percent in the rest of the world. Of the 37 fatal infections during this same period, 27 were from sub-Saharan Africa (Centers for Disease Control, 1990c).

A few years ago, one may have expected that malaria would never be a problem again in the United States. However, there may be occasional small outbreaks within the United States, including Florida, since malaria in some areas of the world is increasing. Each year over seven million U.S. business persons and tourists are traveling to areas where malaria is present (Oaks et al. 1991), and more visitors and grant workers are coming to the U.S. from these malarious areas.

The first Florida case of human malaria (*P. vivax*) in 42 years was acquired presumably through the bite of a mosquito in Gulf County that may have become infected after biting an unknown grant worker with malaria (Centers for Disease Control, 1991b). The woman who came down with malaria had no history of foreign travel, blood transfusion, or IV-drug use. She had spent the nights of May 19 and 27 sleeping outdoors at a fish camp at Willis Landing, Gulf

County. The mosquito-biting activity at night was reportedly intense. No secondary cases were reported. Efforts to trace and survey grant workers employed at a large fish farm adjacent to the campsite were unsuccessful. Mosquito collections at the presumed site of infection (June 14 to August 22, 1990) following the malaria diagnosis included *An. quadrimaculatus* attempting to bite humans after sunset. It, along with *An. crucians* and *An. punctipennis*, were collected in CO₂-baited light-traps (Nayar, Baker, and Clements, unpublished).

The recent three California *P. vivax* outbreaks since 1986 have the following similarities (Centers for Disease Control, 1990b):

- a limited access to medical care for grant workers with malaria, resulting in delays in identifying and treating the parasitemic persons and the application of control measures;
- a lack of adequate sanitary water and wastewater disposal facilities and adequate shelter for the workers; and
- the presence of an effective *Anopheles* mosquito vector and a susceptible human population.

Specific sources of infection could not be identified in the California outbreaks, but agricultural workers from countries with endemic malaria had been present in the affected areas. Similar conditions occur in Florida, especially in the northern areas of the Panhandle. The cryptic malaria case in Florida in 1990 may have occurred for similar reasons.

In addition in Florida, many of the wetlands originally drained and ditched for malaria control (*i.e.* around Tallahassee, where malaria was extremely intense) are now being restored back to wetlands. Anopheline populations may be expected to increase in these newly available habitats, some near larger population centers.

Moreover, malaria is basically a "poor person's" disease. Economic downturns increase poverty, resulting in more people sleeping in temporary, makeshift shelters, abandoned buildings, outdoors under bridges and overpasses, or in large culverts. These same sites, while providing some protection to

the homeless, are also excellent resting sites for *Anopheles* mosquitoes. Thus, now and probably for the first time since the depression years of the thirties, a larger segment of our population, including legal and illegal grants and visitors with imported malaria, have an opportunity for increased contact with anopheline mosquitoes, which prefer to blood feed during sunset and evening hours.

How Should we be Prepared for Small Malaria Outbreaks in Florida?

Florida's state health and related agencies should:

- remind physicians and public health workers annually about the importation of malaria among travelers, visitors, and grant workers, and the danger of not clinically diagnosing malaria from the more common febrile illnesses; and
- inform all county health officers, mosquito control directors, and the Director of the Florida Medical Entomology Laboratory in Vero Beach of all imported malaria cases by county in Florida.

Mosquito control agencies should:

- identify the locations of all actual and potential anopheline breeding sites in the county or district;
- annually survey with a dipper all larval habitats during the *Anopheles* breeding season;
- from landing rate and trap collections, identify and record the seasonal abundance of all *Anopheles* in the county;
- identify grant working and living areas and possible potential imported malaria cases; and
- be informed of all imported and introduced malaria cases in the county and Florida

What Should be Done if there is a Malaria Case?

Any malaria case that is not readily explained by foreign travel, visitors, grant workers, or by induced artificially, is strongly suggestive of possible local transmission. Thus, the threat of additional cases in the near-term is substantial for a small localized area. When one case of malaria has been verified, the local public should be warned to report immediately any fever to their physician or county public health unit (CPHU). The physician or county health worker should take and examine a blood film of all individuals suspected of having malaria.

Depending on the number of cases (two or more), the CPHU should conduct a blood film survey of grant workers and local residents (family and neighbors) in the immediate area where the malaria cases occurred to identify possible carriers. In the unlikely event of additional cases, further immunodiagnosis and serological tests should be done in the local area. Local residents should be informed and educated by fact sheets, door-to-door visits, and by the press on how malaria is transmitted and how to avoid being bitten at night by staying indoors, wearing protective clothing, and applying insect repellent. It is very important that local residents report any fever to their physician or CPHU immediately; *P. falciparum* can be fatal.

In the unlikely event of a major outbreak of malaria, the application of appropriate larvicides at known *Anopheles* breeding sites and adulticides at resting sites is warranted to reduce the human-*Anopheles* contact. In addition, primary efforts should continually be made to reduce the opportunity for *Anopheles* to take a human blood meal by educating the public on the use of protective clothing, screens on windows and doors, repellents, and fans to keep mosquitoes away.

Postscript

Since this paper was submitted for publication a woman, 22, from Belleair, Florida, died February 12, 1992, in Clearwater, Florida, from *P. falciparum* malaria contracted during a trip to Mali in West Africa as part of a Baptist missionary program. She was hospitalized on January 30, 1992.

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References

Bradley, G.H. 1966. A review of malaria control and eradication in the United States. *Mosquito News* 26:462-470.

Boyd, M.F. (ed.) 1949. *Malariology*, 2 vols. Saunders, Philadelphia, Pennsylvania.

Bruce-Chwatt, L.J. 1980. *Essential Malariology*, William Heinemann Medical Books Ltd. London.

Centers for Disease Control. 1989. Malaria Surveillance Annual Summary 8. Issued November 1989.

Centers for Disease Control. 1990a. Summary of Notifiable Diseases, United States. *MMWR* 38:1-54.

Centers for Disease Control. 1990b. Transmission of *Plasmodium vivax* Malaria-San Diego County, California, 8 and 9. *MMWR* 39:91-94.

Centers for Disease Control. 1990c. Recommendations for the Prevention of Malaria Among Travelers. *MMWR* 39:1-10.

Centers for Disease Control. 1991a. Summary of Notifiable Diseases, United States. *MMWR* 39:1-61.

Centers for Disease Control. 1991b. Mosquito-Transmitted Malaria; California and Florida, 1990. *MMWR* 40:106-108.

Freeborn, S.B. 1949. Anophelines of the nearctic region. In: M.F. Boyd (ed.) *Malariology*. Vol.1. pp 379-398, Saunders. Philadelphia.

Haeger, J.S. 1949. The present status of *Anopheles albimanus* in the Florida Keys. Report of the Twentieth Annual Meeting of the Florida Anti-Mosquito Association:118-121.

Lounibos, L.P. In press. Culicidae and Chironomidae. In: M. Deyrup (ed.) *Rare and*

Endangered Invertebrates of Florida. University of Florida Press. Gainesville.

Narang, S.K., P.E. Kaiser and J.A. Seawright. 9. Identification of species, a new member of the *Anopheles quadrimaculatus* species complex: A biochemical key. *J. Am. Mosq. Control Assoc.* 5:317-324.

Oaks, S.C. Jr., V.S. Mitchell, G.W. Pearson and C.C.J. Carpenter (eds.) 1991. *Malaria, Obstacles and Opportunities*. National Academy Press, Washington, D.C.

Russell, P.F. 1968. The United States and Malaria: Debits and Credits. *Bull. N. Y. Acad. Med.* 44:623-653.

Russell, P.F., L.S. West, R.D. Manwell, and G. Macdonald (Eds.) 1963. *Practical Malariology*. 2nd Edition. Oxford University Press. London.

Stürchler, D. 9. How much malaria is there worldwide? *Parasitology Today* 5:39.

Wernsdorfer, W.H. and I. McGregor (eds.). 8. *Malaria, Principles and Practice of Malariology*. 2 vols. Churchill Livingstone. Edinburgh.