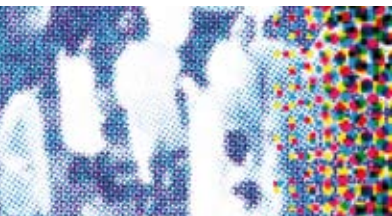
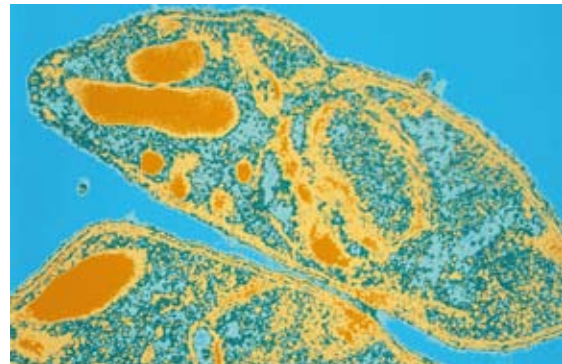




Pathologies

Institut Pasteur
Institut Pasteur
International Network
&
Malaria

*« Knowledge is
the heritage of humanity »*
Louis Pasteur



Fighting infectious diseases



The Institut Pasteur helps to prevent and treat diseases, especially infectious ones, through research, training and public health activities.

Infectious diseases caused by pathogens (**viruses**, **bacteria**, **parasites** or **fungi**) kill 13 million people worldwide every year.

> Mobilizing researchers

The Institut Pasteur and the International Network focus a large proportion of their resources on research into these infectious pathologies (Aids, tuberculosis, malaria, etc.) and emerging pathologies (SARS, avian influenza, dengue fever, West Nile fever, etc.).

> Spreading knowledge

To ensure the results of the research benefit the concerned people, the Institut Pasteur has set up close partnerships with other research institutions and with major public or private institutional players at national and international levels. The aim is to contribute to improving human health through basic research, monitoring, diagnosis and alerts and by developing new diagnostic tools, medicines and vaccines.

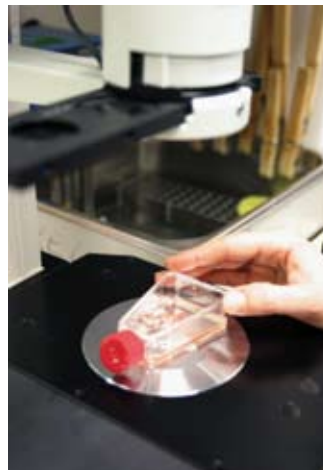
GLOSSARY

Virus : infectious agent, invisible under an optical microscope. Is distinguishable from bacterium because it has only one type of nucleic acid, RNA or DNA.

Bacterium: unicellular micro-organism without nucleus, visible only under a microscope, whose two main shapes are spherical (cocci) or elongated (bacilli).

Parasite : animal or plant organism which lives off its host.

Fungus: filamentous unicellular micro-organism that multiplies in a favourable medium and may cause diseases (aspergillosis, mycoses, etc.).



Malaria

KEEP IN MIND

- **1 to 3 million** deaths each year.
- Increasing levels of **resistance** of mosquitoes and parasites.
- **No** vaccine available.
- **Potential vaccines** undergoing trials.

KEEP IN MIND

- **40 %** of the world's population threatened.
- **Africa** is the hardest hit continent, concentrating **90% of the known cases**.
- **Epidemics** can occur when **population shift**.

Malaria, one of the deadliest infectious diseases, is transmitted to humans through the bite of a female mosquito of the *Anopheles* genus infected by a parasite of the *Plasmodium* genus.

Several species of parasites of the *Plasmodium* genus are responsible for the disease in humans (*P. falciparum*, *P. vivax*, *P. ovalae*, *P. malariae*) but *Plasmodium falciparum* is the most pathogenic species which accounts for the fatal cases. The main mosquito responsible is the *Anopheles gambiae* on the African continent.

According to the World Health Organization, malaria causes 1 to 3 million deaths per year and kills a child every 30 seconds.

> A regional risk with a planetary reach

The pathology threatens 2 billion people and infects over 500 million people per year in almost 100 countries or territories. It strikes the disadvantaged tropical areas in Asia, Latin America, and above all sub-Saharan Africa, with a major economic and social impact that reaches far beyond the consequences on health. Furthermore, travelers from malaria-free countries who visit the infected regions are highly vulnerable because they have little or no immunization.

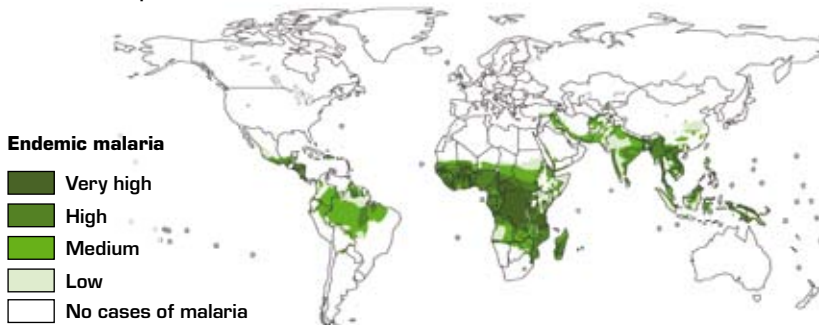
> A worrying situation

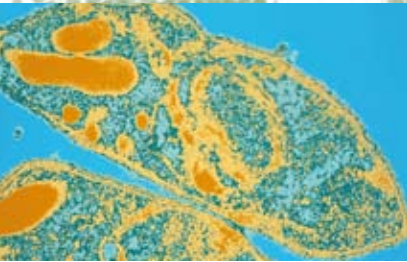
The existing means used to combat malaria, through anti-malarial drugs and eradication of mosquitoes, are becoming less and less efficient due to increased levels

of resistance to drugs and insecticides. Many teams at the Institut Pasteur and in the Institut Pasteur International Network are hence working on the disease. Besides the research on developing a vaccine, several laboratories are carrying out basic research work on humans and on the parasite and its carrier. Two potential vaccines are currently undergoing trials.

Transmission of malaria

http://rbm.who.int/partnership/wg/wg_monitoring/docs/apw_report_oxford.pdf
- accessed 5 April 2005





Plasmodium falciparum, the most virulent malaria parasite...



...is transmitted to humans by the female mosquito of the *Anopheles* genus.

KEEP IN MIND

A child dies of malaria every 30 seconds.

GLOSSARY

Artemisinin: plant native to China, containing a substance that is active against multi-resistant strains of malaria. The molecules derived from the plant have shown their efficacy: swift disappearance of the parasite from the blood, together with disappearance of the high temperature that is characteristic of malaria. To preserve the therapeutic potential of artemisinin, the WHO is coordinating its cultivation and its use as a drug.

Pathology

Malaria is due to a parasite, *Plasmodium*, which multiplies in the human liver and then attacks red blood cells.

In its milder forms, the disease is manifested by high temperatures, headaches and vomiting, which usually occur ten to fifteen days after being bitten by the insect. The serious forms can often become chronic with attacks occurring throughout the victim's life.

> Death can occur quickly

In the absence of treatment, a mild attack can worsen over a few days, or even a few hours, and lead to complications that may be fatal: coma, severe anaemia, generalized convulsions, pulmonary oedema, haemorrhages, etc.

Over a million people die of malaria every year: principally new-born infants, young children and pregnant women.

> The main weapons used to fight the disease

One must make a distinction between preventive measures — mosquito nets, insecticides, anti-malarial drugs — and curative treatments. The anti-malarial treatments prescribed depend on the levels of resistance shown by the parasite and the country in which malaria is rife, and they often involve a combination of several drugs (quinine, chloroquine, artemisinin, etc.).

However, in many regions of the world, the parasites and the mosquitoes are increasingly resistant to the treatments.



Children are highly vulnerable to the disease.

Malaria and transmission of HIV from mothers to their children

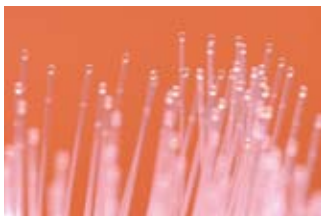
Researchers at the Institut Pasteur have published a study showing that an infection by the malaria parasite in pregnant women could increase the risk of in utero transmission of the Aids virus.

For more information:
www.pasteur.fr

Research

USEFUL FACTS

Plasmodium falciparum, which causes malaria, was first described in 1880 by Alphonse Laveran, a researcher at the Institut Pasteur, and the winner of a Nobel prize in 1907.



KEEP IN MIND

In Paris, the Centre for the production and infection of *Anopheles* (CEPIA) produces over a million females a year to enable researchers to study the interactions between the parasites responsible for malaria and their hosts.



Collection of adult *Anopheles* mosquitoes in CEPIA.



Major basic and biomedical research programmes are currently ongoing at the Institut Pasteur and in the Institutes of the International Networks.

These research programmes cover:

✓ The biology of the infectious agent

Although the parasite responsible for malaria was discovered in the late 19th century, much still remains to be learned about its biology (transmission, biodiversity) to identify new therapeutic and vaccine targets.

✓ The biology of the carrier mosquito

Not all the species are equally likely to be infected: within a given population of the most widespread African carrier, *Anopheles gambiae*, many mosquitoes show natural resistance.

It is important to understand their defence mechanisms, by working on laboratory models and also in the field in Africa. As the insect is the only malaria carrier, the chain of transmission can be broken by taking steps to attack the females that carry the parasite.

The Units working on malaria at the Institut Pasteur in Paris

- Biology of host-parasite interactions
- Malaria biology and genetics
- Center for the production and infection of *Anopheles*
- Genetics of the response to infections in humans
- Genetics and genomics of insect vectors
- Parasite molecular immunology
- Structural immunology
- Immunophysiology and intracellular parasitism
- Malaria transgenesis laboratory
- Parasite vaccinology laboratory
- Biomedical parasitology
- Early response to parasites and immunopathology

In particular, these units are continuing to study the parasite and the carrier mosquito, the factors governing the virulence of malaria, the epidemiology of the disease, infection by *Plasmodium falciparum* and research on a vaccine.

For more information: www.pasteur.fr

GLOSSARY

Pathogenesis: mechanism governing the triggering and evolution of a pathological process.

Physiopathology: study of functional problems in an organism or an organic system and its reactions during a disease.

Antigen: substance which prompts the generation of antibodies when introduced into the organism.

Immune response: activation of the immune system when an organism is attacked, including by vaccination in humans, which enables efficient defence mechanisms to be developed to ward off a pathogenic agent.

✓ Studies of transmission, pathogenesis and epidemiology of the disease in humans

One of the particular aspects of infection by *Plasmodium falciparum* is sequestration of infected red blood cells in the vessels of vital organs such as the brain, heart and lungs. Two lines of exploration are being pursued:

- A study of the physiopathology and the immune response to better understand the disease;
- A study of the surface antigens on the parasite to better grasp their interaction with their receptors on the host cells or with the antibodies produced during the immune response.

✓ Exploration of therapeutic targets and development of new therapeutic approaches to malaria

✓ The search for potential vaccines

International cooperation

Several institutes in the Institut Pasteur International Network are currently working on malaria research:

African Zone

- Institut Pasteur in Côte d'Ivoire
- Institut Pasteur in Madagascar
- CERMES, Niamey, Niger
- Institut Pasteur in Bangui, Central African Republic
- Institut Pasteur in Dakar, Senegal

Americas Zone

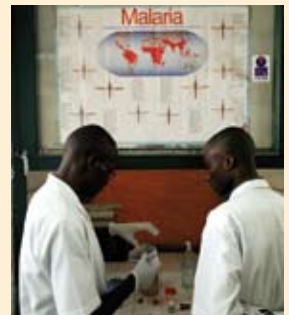
- Institut Pasteur in Guadeloupe
- Institut Pasteur in French Guyana: National Reference Centre for malaria chemo-resistance for the Antilles and French Guyana region

Asia-Pacific Zone

- Institut Pasteur in Cambodia
- Institut Pasteur in Korea
- National Institute of Hygiene and Epidemiology, in Hanoi, Vietnam

For more information: www.pasteur-international.org

Institut Pasteur in Madagascar has organized a **Malaria Workshop** each year since 2003. On the strength of its success, a similar workshop in English was set up in Tanzania in 2007 (www.pasteur.mg/Atelier-Palu).



Since 1990, the populations in the villages of Dielmo and Ndiop have been followed by the Institut Pasteur in Dakar, in collaboration with the Institute of Research for Development (IRD) and the Senegalese authorities. The aim here is to understand the mechanisms of the natural immunity to malaria acquired under various conditions of transmission. The studies have confirmed the genetic nature of sensibility to malaria and enabled identification of potential vaccines among the parasite's antigens.

GLOSSARY

Monocyte: type of large, mononuclear leucocyte (white blood cell).

Immunogenic: triggering an immune response.

Prospects: finding a vaccine, and developing new drugs

> Two potential vaccines

The Biomedical parasitology unit of the Institut Pasteur (Paris) is taking part in research to develop two potential vaccines. Studies have been carried out by comparing test samples from people who are naturally resistant to malaria and people who have been infected in the zones where the disease is endemic. The studies have established the fact that cooperation of the antibodies with monocytes is crucial to the defence mechanism.

✓ Two promising molecules

Studies of the *Plasmodium falciparum* genome have enabled researchers to identify two molecules, one that is present at the surface of the parasite during the blood cycle, and another during the hepatic stage. Both of them are undergoing vaccine experimentation.

✓ Initial results

For the blood cycle, a phase I clinical trial, carried out in Europe and Africa, has shown that the molecule is well tolerated, immunogenic and protective. Trials of the potential vaccine aimed at the hepatic stage are currently under way.

> Development of drugs

✓ Identifying new therapeutic targets

At the Institut Pasteur in Korea, advanced processes are being applied to identify new molecules with the help of broadband imaging techniques, which enable researchers to directly observe the product's effects on the infected cells.

✓ Monitoring the emergence of drug resistance in the regions where the Institutes in the International Network are located

✓ Developing new malaria diagnosis tools

✓ Studying the epidemiology, the environment and the climate

GIS (Geographic Integrated Systems) methods can be used to analyse the relations between transmission, environment and climate (and especially rainfall levels), which are essential to evaluate the impact of certain steps taken to control malaria.

The European BIOMALPAR programme

BioMalPar (Biology and Pathology of Malaria Parasite) is a network of excellence from FP7 concerning malaria research coordinated by the Institut Pasteur and covering 32 institutes worldwide, in 10 countries in Europe, five in Africa, and India (www.biomalpar.org).



Mosquito nets still provide essential protection



A set of data gathered in Niger using the GIS method

Institut Pasteur: a worldwide presence




A non-profit private foundation, the Institut Pasteur contributes to the prevention and treatment of infectious diseases through research, education and public health activities since it was created in 1887.

At the source of several disciplines — microbiology, immunology, and molecular biology — it is one of the most efficient centres of biomedical research in the world.

Open to the world, it is at the core of an International Network of about thirty Institutes on five continents; most of them are independent entities that are governed by the authorities in their country.

Linked by the International Affairs Department, these institutes are associated in partnerships and cooperation agreements covering scientific research, training and public health services, and they share common values and objectives.

Several laboratories in the Institut Pasteur International Network provide expertise for the WHO, either as Cooperating Centres or as National Reference Centres recognized by the WHO.



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