



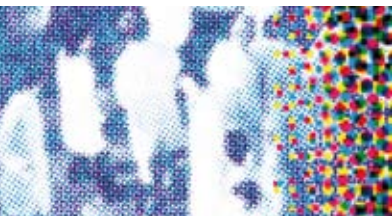
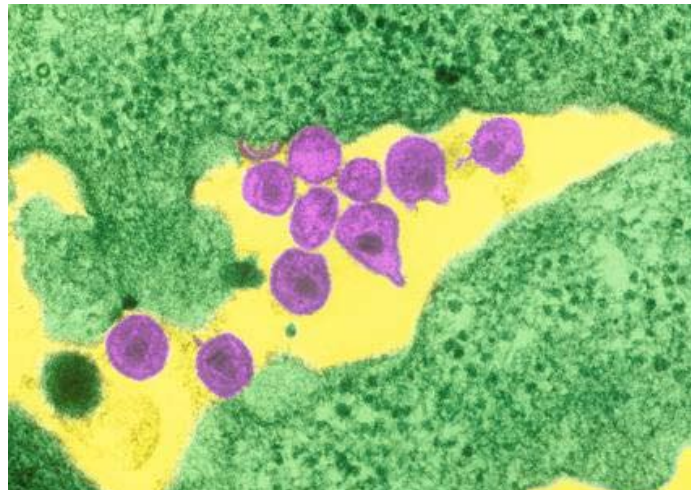
Pathologies

Institut Pasteur  
Institut Pasteur  
International Network

**HIV/AIDS**

*"Knowledge belongs  
to all mankind"*

Louis Pasteur



# Fighting infectious disease



The Institut Pasteur works 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 their resources on research into infectious pathologies (HIV/AIDS, tuberculosis, malaria, etc.) and emerging diseases (SARS, influenza, dengue fever, West Nile fever, etc.).

## > Spreading knowledge

To ensure that the results of the research benefit the people concerned, the Institut Pasteur works in close partnership with other research institutions and major public and private institutions at the national and international level. The aim is to contribute to improving human health through basic research, monitoring, and surveillance and by developing new diagnostic tools, medicines and vaccines.

### GLOSSARY

**Virus** : infectious agent invisible under an ordinary optical microscope. Viruses are distinguishable from bacteria because they have only one type of nucleic acid, RNA or DNA.

**Bacterium**: unicellular micro-organism without a nucleus, visible 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 environment and may cause disease (aspergillosis, mycoses, etc.).



# HIV/AIDS

## HIV in the world

- **33 million people** are living with HIV
- **Over 2 million** deaths per year
- **2.7 million** new cases per year, including **400,000 children** under the age of 15
- In low and middle-income countries, only **31% of people** eligible for treatment actually receive it

Source: UNAIDS 2008

HIV/AIDS is one of the leading causes of death in low income countries, especially in Africa. From the discovery of the virus responsible for AIDS in 1983 to the search for candidate vaccines and the development of antiretroviral drugs, huge advances have been made in the fight against this disease.

## > The virus and its pathophysiology

Teams at the Institut Pasteur and in the International Network are working on many different aspects of the infection and ways to control viral spread in the body:

- replication mechanisms of the virus
- HIV mutation
- genetic recombination of different strains
- the immune system's response
- innate protection against the virus
- natural control of the infection in the body
- animal models
- improving treatments

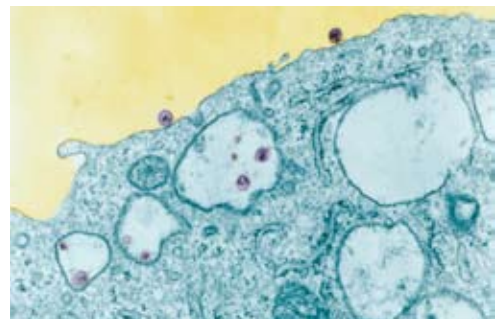
## > Advances in screening and monitoring

The Institut Pasteur International Network operates prevention and patient monitoring programmes on every continent. In Africa and southeast Asia, member institutes perform screening tests and take part in medical follow-up of HIV-positive patients (viral load, investigating antiretroviral drug resistance...). They are also involved in the prevention of mother-to-child transmission of the virus, treatment and care for infected children, and follow-up of people co-infected with HIV/AIDS and tuberculosis.

## > The challenge of finding a vaccine

The extreme variability of the virus is one of the main difficulties that researchers must contend with in the quest to develop a vaccine. Vaccine research therefore focuses on finding viral fragments capable of consistently activating HIV-specific humoral and cellular immunity. Two candidate vaccines are being developed simultaneously:

- ✓ a preventive "HIV-measles" candidate vaccine, with clinical trials beginning in late 2009
- ✓ a therapeutic candidate vaccine designed to restore HIV-positive individuals' immune defences.



*The HIV-1 virus entering a macrophage*

## GLOSSARY

**Retrovirus:** an enveloped virus with genetic material consisting of RNA. After transforming the RNA into DNA, the virus inserts itself into the chromosomes of the host cell where it then replicates

**Opportunistic infections:** HIV-positive individuals are vulnerable to contagions that persons with normal immunity can typically fight off, due to their weakened immune systems

## The disease

AIDS (Acquired Immunodeficiency Syndrome) is a chronic immune system deficiency caused by infection with the Human Immunodeficiency Virus (HIV). The virus attacks CD4+ T lymphocytes, one of the body's vital cells.

After HIV enters the bloodstream, an asymptomatic period is followed by a collapse of immune defences, leaving the body vulnerable to opportunistic infections. In the absence of treatment, AIDS is fatal in the vast majority of cases.

With more than 30 million people infected and over 2 million deaths each year, AIDS remains one of the major pathologies of the current era.

### > Routes of infection

The epidemic first spread in Africa among heterosexuals before appearing in 1981 in North America among members of the gay community. HIV then moved on to Europe, where it was discovered that the virus infected people receiving blood transfusions, haemophiliacs and drug users who shared needles, proving it could be transmitted via blood. Later, the disease was shown to be transmissible from mother to child during pregnancy, birth or breastfeeding.

### > Treatments

Since the first antiretroviral drug, AZT, was put on the market in 1996, HIV/AIDS treatments have evolved considerably. Today, the standard treatment is known as triple therapy since it combines three molecules that control the infection by intervening at different stages in the virus' replication.

The treatment reduces the circulation of HIV in the blood and leads to an increase in CD4+ T lymphocyte count. These drugs provide enhanced protection against opportunistic infections but can also cause side effects of varying severity.

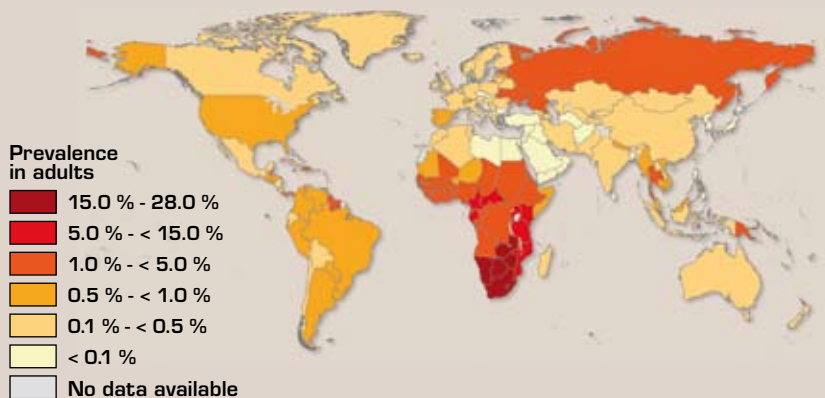
### Principal symptoms

The symptoms usually associated with AIDS are actually due to opportunistic infections resulting from lowered immune defences (weight loss, frequent fever, wasting...).

Tuberculosis is one of the most common causes of death among AIDS sufferers, especially in Africa. Cryptococcal infection, the causative agent of meningitis, is the second deadliest infection for patients with HIV.

### HIV in the world

Source : UNAIDS 2008





### **Nobel Prize for the discovery of HIV**

In October 2008, the Nobel Prize for Medicine was awarded to Françoise Barré-Sinoussi and Luc Montagnier of the Institut Pasteur for their work leading to the discovery of the AIDS virus.

In 1983, their research team was the first to isolate HIV, “a discovery that has been vital for our current understanding of the biology of this disease and for antiretroviral treatment for the disease,” according to the Nobel committee.

### **Diagnosing VIH-1**

In April 2007, the Institut Pasteur and NIH (National Institutes of Health), a network of agencies working on health in the United States, renewed their collaboration agreement aimed at improving HIV-1 diagnosis.

## **Research**

Scientists at the Institut Pasteur and in the International Network are studying many different aspects of HIV infection. Research programmes carried out in conjunction with France’s National AIDS Research Agency (ANRS) aim to understand how the virus enters human cells and the molecular mechanisms involved in HIV’s spread throughout the body.

### **> The virus in the body**

Many different teams are studying the body’s immune response, particularly the ways in which cells create barriers to defend themselves against viral attack. Researchers are also trying to understand how HIV-1 multiplies and remains dormant in macrophages (specialised immune defence cells).

How does HIV pass from one cell to another? How does a cell create its own antiviral barriers? Describing HIV’s replication mechanisms and the immune system’s response will give us a better understanding of the potential for infection and the processes involved in the virus’ spread.

### **> Research on transmission**

Several studies aimed at improving the prevention of mother-to-child transmission of the virus are currently underway. Particular attention is being paid to the placenta’s natural resistance and innate maternal immunity, two avenues that could lead to combating transmission in utero.

Researchers are also looking into the increased risk of transmission in cases where mothers have viral or parasitic co-infections.

### **The International Network and clinical research**

**The Pasteur Centre in Cameroon** has launched a programme aimed at preventing mother-to-child transmission of HIV. It has also begun a study looking into ways of improving therapeutic management of HIV-positive children (treatment and response to vaccination).

**In Cambodia**, research is focusing on HIV-tuberculosis co-infections, treatment protocols for antiretroviral medicines, drug interactions, and immune system mechanisms.



## > Natural protection against the virus

There are a certain number of people who, despite having been exposed to HIV on one or more occasions, do not become infected. There are also a handful of patients who have been HIV-positive for ten years or longer but whose immune systems manage to control the virus' multiplication naturally. Unsurprisingly, these two groups of people attract considerable attention from researchers. For example, studies have demonstrated the vital role played by CD4+ and CD8+ T lymphocytes in these "HIV-controllers."

The Unit on the Regulation of Retroviral Infections headed by Françoise Barré-Sinoussi at the Institut Pasteur is studying the importance of so-called "natural killer" cells, which are capable of controlling infected cells. Other research, carried out using an animal model (monkeys), aims to provide a better understanding of the mechanisms by which the disease progresses or fails to progress to advanced stages.

## > Mechanisms of immunodeficiency

The Institut Pasteur's Viral Immunopathology Laboratory is working on the interactions between CD8+ T lymphocytes and HIV-1 as part of immune system restoration in HIV-positive patients undergoing antiretroviral treatment. Other areas of research include the virus' interaction and control of its environment, its capacity to replicate, and the processes by which the immune system is undermined by HIV.

### The International Network and basic research

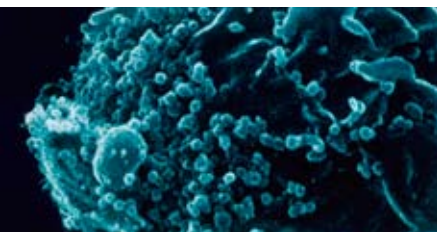
The Institut Pasteur Korea, inaugurated in April 2004, is currently working to identify new therapeutic targets. The HKU-Pasteur Research Centre in Hong Kong and the Institut Pasteur Shanghai specialise in genetic diversity and antiretroviral drug resistance. At the Institute Pasteur-Cenci Bolognetti Foundation in Italy, researchers are developing new reverse transcriptase and integrase inhibitors to treat the disease.

*Researchers at the Institut Pasteur in Korea are working to identify new therapeutic targets*

**The Institut Pasteur's Unit on the Regulation of Retroviral Infections, headed by Françoise Barré-Sinoussi, is studying in utero transmission of HIV-1, particularly the increased risk induced by viral or parasitic co-infections such as malaria.**

→ **The Institut Pasteur in Bangui** is henceforth a World Health Organisation Collaborating Centre (WHOCC). It serves as microbiological observatory for communicable diseases and takes part in collaborative projects within the WHO network.

→ Since 2003, **the Institut Pasteur in Algeria**, a regional reference laboratory, has run a programme to observe antiretroviral drug resistance.



*The HIV-1 virus on the surface of a lymphocyte*



*Africa at the forefront of clinical research*

## GLOSSARY

**HIV-measles vaccine:** based on an attenuated live measles vaccine, it is known as a “recombinant vaccine” because HIV genes have been introduced into the measles genetic code

**CD4+ T lymphocytes:** cells in the body involved in cellular immunity that are targeted by the HIV virus

**Resistance:** resistance to antiretroviral drugs can be found in some as yet untreated patients (primary resistance) and some HIV-positive individuals already undergoing treatment (secondary resistance)

## Future prospects: new drugs and vaccines

### > Drug treatments

Several clinical trials aimed at improving existing treatments are currently underway. The Institut Pasteur’s Viral Immunopathology Laboratory and Immunoregulation Unit are involved in clinical trials financed by the French National AIDS Research Agency (ANRS).

### > The vaccination route

The foremost difficulty in developing a vaccine against HIV lies in the virus’ extreme variability. It is essential to identify viral sequences that are common to as many strains as possible in order for the vaccine to protect against the majority of existing viruses.

An “HIV-measles” candidate vaccine, developed over the past few years in the Institut Pasteur Viral Genomics and Vaccination Laboratory, will undergo clinical trials in 2009-2010. If proven effective, children and adolescents will receive priority vaccination.

A second candidate vaccine, this one for therapeutic use, is designed to restore infected patients’ immune defences. It has been developed by the Institut Pasteur’s Molecular Virology and Vectorology Laboratory. Encouraging results in animals offer hope that clinical trials will soon be possible in humans.

Several laboratories are also involved in an ANRS programme exploring other possible avenues for vaccine development.



*Triple therapy is the standard treatment for patients with HIV/AIDS*

### Units working on HIV/AIDS at the Institut Pasteur

- Virus and Immunity
- Viral Pathogenesis
- Regulation of Retroviral Infections
- Molecular Retrovirology
- Enzymatic Regulation of Cellular Activities
- Viral Immunopathology Laboratory
- Cellular Immunology and Immunogenetics
- Lymphocyte Cell Biology
- Immunoregulation
- Antiviral Cell Immunology
- Viral Genomics and Vaccination Laboratory
- Molecular Virology and Vectorology Laboratory

### Institutes working on HIV/AIDS in the International Network

- Pasteur Centre in Cameroon
- Hong Kong University-Pasteur Research Centre
- Institut Pasteur in Algeria
- Institut Pasteur in Bangui
- Institut Pasteur in Cambodia
- Institut Pasteur Korea
- Institut Pasteur in Côte d’Ivoire
- Institut Pasteur in Dakar
- Institut Pasteur – Cenci Bolognetti Foundation, Rome
- Institut Pasteur in Ho Chi Minh City
- Institut Pasteur in Madagascar
- Institut Pasteur in Saint Petersburg
- Institut Pasteur Shanghai – Chinese Academy of Sciences

The Institut Pasteur and the International Network work in close collaboration with the WHO.



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# Institut Pasteur: a worldwide presence

A not-for-profit private foundation, the Institut Pasteur performs research, education and public health activities in the public interest since its creation in 1887.

At the nexus of several disciplines, including microbiology, immunology, and molecular biology, it is recognized worldwide for its contributions to biomedical science.

The Institut Pasteur is open to the world and is at the core of an International Network of some thirty institutes on all five continents, most of which are independent entities governed by their national authorities.

Animated by the International Affairs Department of the Institut Pasteur, the institutes of the International Network are associated in partnerships and cooperation agreements covering scientific research, training and public health services, and they share common values and objectives.

