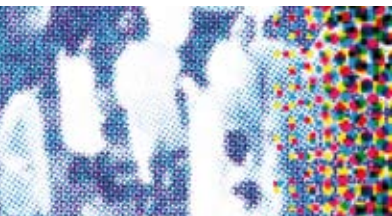
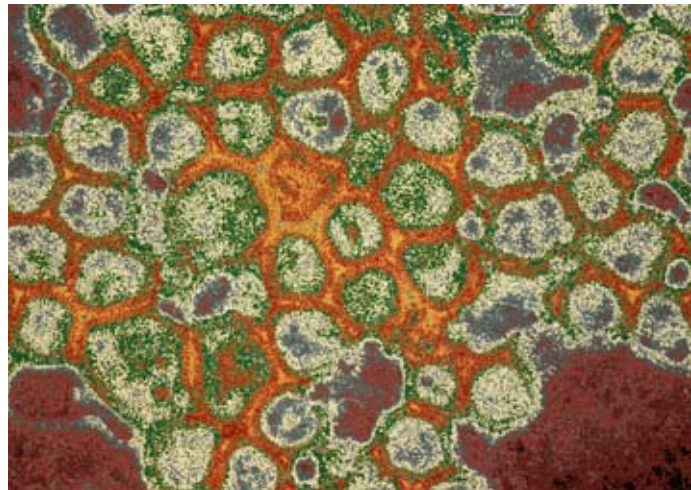




Pathologies

The Institut Pasteur
the Institut Pasteur
International Network
&
Influenza

*"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, hepatitis, 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.).



Influenza

FIGURES

Seasonal flu

- In temperate zones, flu epidemics affect **1 to 5% of the population** each year.
- According to WHO, the number of serious cases is **3 to 5 million** each year, including at least **250,000 deaths**.
- **350 million** doses of vaccine are produced every year in the absence of a pandemic.

KEY FACTS

In 1918, the "Spanish flu" spread around the world and at least **40 million people** died as a result. Other less virulent pandemics have followed: the Asian flu in 1957, the Hong Kong flu in 1968, the Russian flu in 1977 and now the H1N1_v flu in 2009.

Influenza has been described since antiquity and appears every year in the form of seasonal epidemics and sometimes in the form of pandemics, such as the Spanish flu at the beginning of the 20th century and, more recently, the H1N1_v flu.

> A variable virus

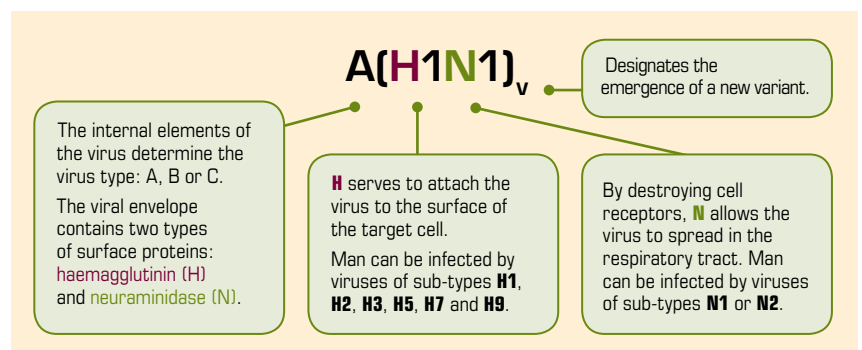
Flu is caused by three types of flu viruses; A, B and C. Viruses of type A and B, responsible for seasonal flu, exhibit the highest variability and cause most clinically significant diseases in man. One mechanism of viral variation, known as antigenic drift, leads to modifications that can inhibit recognition of the new variant by the immune system. Viral strains used for the flu vaccine therefore need to be changed regularly.

> From seasonal flu to pandemic flu

In the case of type A viruses, another kind of variation known as antigenic shift can lead to radical changes in the viral genome, resulting in the emergence of a new virus. Pre-existing immunity within the population is not protective and a vaccine prepared from seasonal strains will also be ineffective, thus contributing to the risk of a pandemic.

> Animals under high surveillance

Animal reservoirs appear to play an important role in the emergence of new flu viruses in man. Avian viruses, for example, can be transmitted directly to man. Pigs, which are susceptible to both avian and human viruses, can facilitate inter-species exchange and give rise to the emergence of viral recombinants.



Serious risks

While the majority of people recover within one or two weeks, the consequences of flu can be serious or even fatal for the elderly, immunocompromised patients and people suffering from chronic pathologies including asthma, diabetes and cancer.

KEY FACTS

- It is estimated that in healthy adults, the vaccine has a **protection rate of 70% to 90%** against the clinical disease.
- Antibiotics are agents that act against bacteria but not viruses. **They are therefore ineffective against flu.**

Seasonal flu

Flu viruses survive longer outside the human body when the weather is cold and dry, which is why seasonal epidemics occur in winter in the temperate zones of the Northern hemisphere.

> The disease

The flu virus is easily transmitted from one person to another via the respiratory route, when infected subjects expel micro-droplets by coughing or sneezing, or indirectly via skin contact, especially by one's hands.

The symptoms appear suddenly 1 to 4 days after contamination. The general symptoms, which are sometimes intense - fatigue, headaches, shivering, fever, muscle and joint pain - are associated with respiratory symptoms such as nasal congestion, pharyngitis and cough.

> Vaccination

In September and February of each year, WHO defines the composition of the flu vaccine for the following season using the most recent and virulent circulating strains. Two different vaccines are developed for the Northern and Southern hemispheres, though vaccination campaigns are relatively infrequent in Southern countries. Even though specific treatments help reduce the duration of the infection, vaccination remains the best tool to combat flu infections.

> Treatments

There are currently two classes of antiviral agents capable of preventing the replication of flu viruses. However, they may sometimes lead to serious side effects and only act on certain strains. Viruses can also become resistant, thus limiting their efficacy.

Hygiene is the primary preventive measure

In the event of a flu infection, it is necessary to wash one's hands several times a day, either with soap or an alcohol-based solution, and to cover one's mouth and nose with a paper tissue when coughing or sneezing then discard the tissue in a covered bin and immediately wash one's hands.





The US Department of Health and Human Services (DHHS) and the Institut Pasteur signed a cooperation agreement in September 2008 to control avian flu and possible flu pandemics.



Research and surveillance

Research covers many aspects of flu virus infection and mobilises a large number of research teams from the Institut Pasteur in Paris and the Institut Pasteur International Network (RIIP).

> Epidemiology and ecology

Several members of the International Network in Africa are studying the prevalence and seasonality of human flu viruses with the objective of creating serum and virus banks. These will allow researchers to improve their understanding of the epidemiology and ecology of flu viruses.

In addition, the Network is actively participating in two epidemiological research programs financed by the US Department of Health and Human Services (DHHS) in Africa and South-East Asia and by the French Ministry of Health in Africa (SURGIRA project).

The SISEA (AFD) and RIVERS (EU) projects bring together several RIIP institutes from Asia and Europe to enhance capacities to detect emerging viruses and better understand how viruses survive in the environment, including in water and food.

> Immunology

Researchers from the Institut Pasteur are working to identify cellular and viral factors that limit the replication of type A viruses in the human body. They are studying the immune response and regulation of inflammation in the presence of the virus, including the role of proteases and anti-proteases in lung inflammation. The Armand Frappier Institute in Canada is working on the various symptoms and immune defence mechanisms activated by different viral sub-types.

In Shanghai and Hong Kong, researchers are exploring the reaction of T and NK lymphocytes as they come into contact with viruses for future use in immunotherapy. They are also interested in inhibiting mechanisms of viral entry into the cell as a possible therapeutic target.

Institut Pasteur units working on flu viruses

- **National Reference Centre (CNR) for Influenza Viruses, Northern Region**
- **Unit on Molecular Genetics of RNA Viruses**
- **Laboratory for Urgent Response to Biological Threats (CIBU)**
- **Unit on Innate Host Defence and Inflammation**

GLOSSAIRE

NK Lymphocytes:

innate immune cells known as "natural killer" cells. Unlike T lymphocytes, these cells are capable of eliminating foreign cells from the body independently of antigens and without prior activation.

Viral protease:

an enzyme produced by flu viruses that degrades certain proteins in host cells. Its action can be inhibited by antiviral medicines known as anti-proteases.

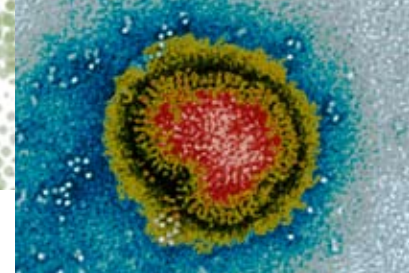
Intervention in the event of an epidemic emergency

The Institut Pasteur and the RIIP intervene in world epidemic situations via the Laboratory for Urgent Response to Biological Threats (CIBU) by responding to requests from national authorities or major international health organisations.

An expertise that can be mobilised around the clock, 7 days a week - www.pasteur.fr



A BSL-3 + laboratory at the CIBU.



Type A flu virus.

> Understanding resistance

Researchers at the Institut Pasteur have been studying flu viruses of the A(H1N1) type, representative of the viruses isolated in 2007-2008. This flu season was characterised by the worldwide emergence of H1N1 viruses resistant to oseltamivir, the main medication for the treatment of flu sold under the brand name Tamiflu®. Researchers from the Institut Pasteur have identified specific enzymatic properties of neuraminidase from recent H1N1 viruses that are likely involved in the emergence of resistant viruses and may contribute to their capacity to spread throughout the human population.

> Monitoring systems

Seasonal flu is subject to continuous surveillance via a large network of research and public health organisations across the world, including the National Reference Centres of the Institut Pasteur (Northern France) and the Institut Pasteur in French Guiana (Antilles-Guiana region). In addition, WHO has asked each country to prepare for the possibility of a pandemic. To this effect, the Institut Pasteur has an emergency intervention group, the Laboratory for Urgent Response to Biological Threats (CIBU), which can operate around the clock if needed.

Surveillance in France

Surveillance is jointly coordinated by the General Office for Health (DGS) and the Institute for Public Health Surveillance (InVS). One of InVS' missions is to estimate the magnitude of a possible pandemic in France and the epidemiological impact of the various treatment and vaccine strategies under consideration. A governmental control plan based on the expansion of the flu control committee is activated in the event of a new pandemic risk. In addition, France has intensified its microbiological surveillance of wild birds in order to gain a better understanding of the circulation of avian flu viruses.

EISN and EuroFlu

In Europe, flu surveillance is performed by EISN (European Influenza Surveillance Network) under the aegis of ECDC, as well as EuroFlu under the aegis of WHO Europe. The Institut Pasteur and several institutes in the International Network are among their active members. These bodies publish weekly epidemiological bulletins.

The WHO Global Network for flu surveillance

This network includes 128 national flu centres from 99 different countries in charge of monitoring human viruses and quickly identifying new strains in circulation in order to design an appropriate vaccine for the following season. Thirteen institutes in the RIIP belong to this network:

Other institutes in the RIIP working on influenza:

Hong Kong University – Pasteur Research Centre, CERMES (Niamey, Niger), IP in Ho Chi Minh City and IP in Nha Trang (Vietnam), Institut Pasteur in Shanghai – Chinese Academy of Sciences, IP in Tunis (Tunisia) and IP in Morocco.



From animals to humans

The examples of avian flu and the H1N1_v flu pandemic in 2009 have demonstrated that animal viruses can be directly responsible for cases of flu in humans.

> Avian flu (H5N1)

The avian influenza virus H5N1 was identified for the first time in 1997 in Hong Kong as being the cause of 18 human cases, including 6 deaths. It is characterised in poultry by the manifestation of a highly transmissible disease (hence the drastic livestock slaughtering measures) associated with a high mortality rate. Human cases have regularly been identified since 2003.

While no proof of person-to-person transmission has been found so far, there is great concern about a possible encounter of the avian virus with another human virus. This could lead to genetic exchanges that might generate a new virus capable of efficient inter-human transmission. At present, no one can predict what its virulence might be.

> The 2009 pandemic flu (H1N1_v)

A new human virus originating in pigs appeared in Mexico in the spring of 2009. The H1N1_v virus appears to infect mainly young people. The pandemic seems to be moderately serious in developed countries. However, there is reason to fear a darker picture once the virus propagates in regions with limited resources and a high prevalence of underlying medical problems. There is also concern about the development of a form that is more virulent and more resistant to treatment.

> Pasteurian mobilisation

The Institut Pasteur and the Institut Pasteur International Network are greatly involved in research and surveillance of avian flu and H1N1_v flu.

The National Reference Centre for Influenza Viruses (Northern Region) in Paris characterises the viral strains sent by the various institutes in the RIIP and conveys the results in real time to WHO.

In addition, researchers at the Institut Pasteur developed a quick diagnostic test for the 2009 H1N1_v pandemic flu just a few weeks after the beginning of the outbreak. This test was circulated within the International Network where it was used to diagnose cases in a number of countries. The various teams are ready to intervene throughout the world if a new flu virus emerges.

Certain avian viruses can be directly transmitted to humans.

FOR INFORMATION

- **The RIIP participates in the SISEA surveillance project** and in epidemiological research on emerging diseases in South-East Asia, financed by the French Development Agency (AFD). It aims to improve the diagnostic capacity of laboratories and rationalise the surveillance system on a national and regional scale.
- **The Institut Pasteur in Cambodia** now has a BSL-3 laboratory facility, allowing it to carry out more extensive virological research.

FIGURES

- **Between January 1997 and February 2009, WHO identified 405 human cases of avian flu in 15 different countries, including 245 deaths.**
- **Two months after the emergence of the H1N1_v virus, in mid-August 2009, WHO identified 160,000 cases in 168 countries, including 1,154 deaths.**

Institut Pasteur: a worldwide presence

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



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.

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The Institut Pasteur 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.

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.

