# La lettre de l'Institut Pasteur

QUARTERLY NEWSLETTER

#129-130
NOVEMBER
2025


EDITORIAL

## Breaking new ground


**Prof. Yasmine Belkaid,**
President of the
Institut Pasteur


**Today, antimicrobial resistance poses a major public health problem. The growing number of antibiotics that have become ineffective is indicative of this alarming trend.**

The risk is enormous: common infections could once again become fatal. We could find ourselves powerless against certain infections, whether bacterial, viral, fungal or parasitic.

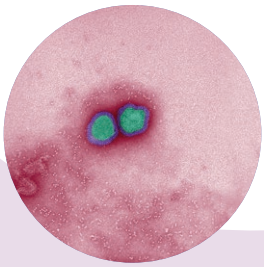
In these pages, you will discover how the fight is being organised, thanks to the work of our researchers and international collaborations in which the Institut Pasteur is fully engaged.

Now more than ever, a comprehensive and coordinated approach is essential to designing, testing, and implementing therapeutic alternatives, in order to ensure safer and more sustainable treatments for infectious diseases. Understanding antimicrobial resistance means highlighting the complexity of pathogens and addressing one of the major challenges facing global health. By supporting the Institut Pasteur, you enable our researchers to take action and innovate, paving the way for promising solutions. Thank you for sharing this commitment with us.


**At the end of the 19th century, Louis Pasteur demonstrated that microbes are everywhere – in water, in the air, on objects, on skin – and that some of them cause disease.** These pathogenic microbes are classified into four major families, each comprising thousands of species: bacteria, viruses, parasites, and fungi. To combat the diseases they carry, antimicrobial drugs and treatments have been developed by scientists and pharmaceutical companies. The best known are **antibiotics** against bacterial diseases.

CONTINUED ON P. 2

## In this issue



Influenza viruses.

Observation at the Institut Pasteur of an antibiogram to test the sensitivity of a bacterial strain to different antibiotics.

Foot of a man infected with a dog hookworm larva (dog intestinal worm).

But the antimicrobial family also includes **antivirals** (against viruses), **antiparasitics** (against parasites or protozoa) and finally **antifungals** (against fungi). Saving millions of lives each year, antimicrobials have played an essential role in the quality of human health.

## Pathogenic microbes are becoming increasingly resistant

Antimicrobial resistance (AMR) occurs when bacteria, viruses, fungi, and parasites evolve over time and no longer respond to drugs, making it more difficult to treat infections and increasing the risk of disease spread. With regard to antibiotics, resistance has become a major public health problem since their introduction in the 1940s and their widespread use.

This antibiotic resistance has accelerated with the overuse of antibiotics in human medicine, veterinary medicine, and agriculture. Bacteria have developed formidable strategies to survive these drugs: destruction or modification of the antibiotic by enzymes, protection of the targeted part of the bacterium, expulsion of the antibiotic by pump systems, etc.: an entire arsenal that bacteria can pass on to each other, allowing 'superbugs' to spread. While antibiotic resistance is an inevitable phenomenon, its current explosion is largely due to human activity. Today, AMR goes far beyond the scope

UNDERSTANDING

### *The main antimicrobials and the diseases they combat*

- ***Antibiotics against bacterial diseases***
  *Pneumonia, bronchitis, ear infections, meningitis, urinary tract infections, septicaemia, chlamydia, gonorrhoea, syphilis, Lyme disease, tuberculosis, leprosy, etc.*
- ***Antivirals for viral diseases***
  *HIV, influenza, herpes, chickenpox-shingles, cytomegalovirus, hepatitis B and C, RSV bronchiolitis, Covid-19, etc.*
- ***Antimalarials** for malaria, **antihelminthics** for intestinal worms, and **antiprotozoals** for diseases caused by amoebas, giardia, leishmania, trypanosomes, toxoplasma, etc.*
- ***Antifungals against fungal diseases Fungal infections**, especially common on the skin, hair, nails, mucous membranes and genitals; numerous diseases affecting agricultural production, etc.*

WHOOPING COUGH

ACTION PASTEUR

# Unprecedented resistance **to antibiotics**

In 2024, France experienced a major whooping cough epidemic, with an estimated 150,000 cases, a level not seen in several decades.

According to **Sylvain Brisse**, head of the National Reference Centre (CNR) for Whooping Cough at the Institut Pasteur , *"this outbreak can be explained by several interconnected factors: the cyclical effect of the disease and antigenic variations facilitating immune escape.*
*This epidemic has revealed an even more worrying phenomenon with the emergence of strains resistant to macrolides, the main class of antibiotics used."*
Of the 400 strains analysed at the CNR, around 15 were resistant. *"We discovered that the three French lineages had very close ancestors among the Chinese strains."* This observation suggests multiple introductions from China, where the situation is now dramatic:
*"Nearly 100% of pertussis strains there are resistant to macrolides, and this resistance also extends to other pathogens, no doubt reflecting excessive and inappropriate use of antibiotics."*
To better detect these resistances, the CNR has developed a rapid molecular test (qPCR) targeting the mutation responsible.
*"This test has enabled us to estimate that the resistance rate in France has remained low, at 2 to 3%."*
Vaccination remains the essential defence against whooping cough. Among adults and the elderly, delays in recommended booster shots persist and can lead to serious complications.

***"This pertussis epidemic reminds us that infectious diseases never really disappear: they return in new forms, especially when our vigilance wanes."***

• • •

of antibiotics. The phenomenon threatens all treatments: antivirals (with resistant strains of HIV), antifungals (against the emerging fungus *Candida auris*), and antimalarials (such as artemisinin, which is ineffective against certain forms of malaria).

### The threat of a major global health crisis is now a reality

The consequences of this resistance are serious and constitute a major global health issue. Antimicrobials are losing their effectiveness and infections are becoming increasingly difficult, if not impossible, to treat. Many medical procedures rely on antimicrobials: major surgery (prostheses, transplants); cancer treatments (chemotherapy); intensive care or neonatal care, etc. Without effective antimicrobials, these procedures become much more dangerous.

This health crisis already causes 4.95 million deaths annually (*The Lancet*, 2024) and could reach 10 million per year by 2050. Among other things, we risk entering a post-antibiotic era, where common bacterial infections would once again become deadly. This worrying prediction has raised awareness at the highest levels, as resistance is spreading rapidly through travel, trade, and agriculture. A resistant microbe that appears in one part of the world can quickly spread everywhere. It affects all countries, rich and poor alike, and thus threatens global health security.

### The example of the Monkeypox virus and resistance to Tecovirimat

Mpox (formerly monkeypox or simian smallpox) is an infectious disease caused by the Monkeypox virus. It is mainly transmitted from rodents to humans, but can also spread between humans. Since 2022, specific strains have been causing major epidemics that are spreading outside the endemic areas of Central and West Africa. A drug called Tecovirimat can be used to treat infected patients.

However, this drug is ineffective against certain resistant viruses. In 2022, in the United States, approximately 1% of patients treated with Tecovirimat developed resistance to the drug. Research carried out at the Institut Pasteur has helped to understand how variants carrying certain mutations render the antiviral treatment ineffective. Using molecular structure data from the viral protein targeted by Tecovirimat, researchers at the Institut Pasteur, led by Pablo Guardado-Calvo, are developing new antivirals that could act on resistant viruses.

• • •

ACTION PASTEUR

## *Candida auris*: the invisible enemy of hospitals

Identified in South Korea in 1996 but described as a new species in 2009, *Candida auris* is now one of the most worrying pathogenic fungi. ***"Its almost simultaneous emergence on several continents, with no epidemiological link, is striking,"*** explains **Alexandre Alanio**, deputy director of the National Reference Centre for Invasive Fungal Infections and Antifungals (CNRMA) at the Institut Pasteur.

The first traces of it in France date back to 2007, identified retrospectively after the genomic databases were updated by Marie Desnos (deputy director of the CNRMA). Since then, it has spread worldwide, with outbreaks reported as early as 2011, particularly in India and the Middle East. ***"In Europe, cases are still imported, but there has been a worrying increase, especially in Southern and Eastern Europe, with nosocomial transmission" (hospital-acquired infections).***

*Candida auris* is notable for its ability to colonise hospital environments, persisting on surfaces despite disinfection. In 2024, a French hospital experienced an outbreak involving 25 patients infected with the same strain, revealing active transmission. Intensive care units are particularly vulnerable, as the fungus adheres to equipment and is resistant to standard cleaning methods. ***"Even with enhanced protocols, it is difficult to eradicate,"*** confirms **Fanny Lanternier** (head of the CNRMA), highlighting its role as an environmental reservoir promoting reinfection, especially in immunocompromised patients.

Therapeutically, *Candida auris* is resistant to several antifungal agents, particularly azoles. ***"In France, strains remain sensitive to echinocandins, but resistance is emerging elsewhere, such as in South America and the United States,"*** warns Fanny Lanternier. The risk would further complicate treatment.

The CNRMA plays a key role in surveillance and research. ***"We systematically sequence genomes to trace strains and understand how they are transmitted,"*** explains Alexandre Alanio. This data, combined with that provided by hygienists, enables protocols to be adapted. ***"Our priority is to develop rapid diagnostic tools, especially for countries in the Global South, where resources are lacking,"*** he insists. Fanny Lanternier adds: ***"Research into resistance mechanisms is crucial for anticipating crises."***

"Candida auris ***reminds us that pathogenic fungi know no borders. Its emergence is linked to global factors, requiring a coordinated response,"*** concludes Alexandre Alanio. For Fanny Lanternier, ***"Investing in research and surveillance is essential to prevent it from becoming unmanageable."*** Urgent action is needed to preserve the effectiveness of treatments and limit the spread of this insidious pathogen.

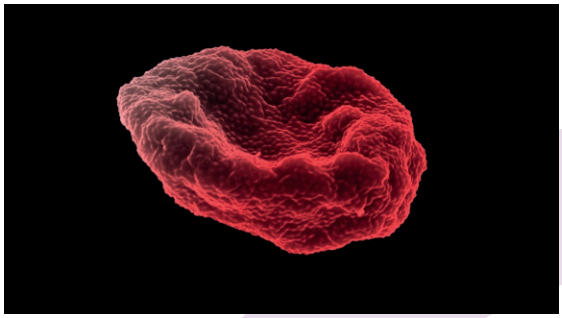
**Culture of *Candida auris* on chromogenic medium.**

### The example of the fungus *Aspergillus*: resistance from the fields

The fungus *Aspergillus fumigatus* is responsible for serious lung infections and is developing increasing resistance to azole antifungal treatments (the standard drugs). Indeed, infections with resistant Aspergillus (up to 10% of cases in Europe) increase mortality in frail patients (those who have undergone transplants or are undergoing chemotherapy). The work of Alexandre Alanio (Institut Pasteur/AP-HP), who participated as an expert in the recent report by the EFSA (European Food Safety Authority), reveals that this resistance largely emerges from the environment: the widespread use of azole fungicides in agriculture selects for resistant mutant strains in soil, air, and compost. These strains are then inhaled by humans, compromising the effectiveness of treatments in immunocompromised patients. This resistance is monitored at the national level by the National Reference Centre for Invasive Fungal Infections and Antifungals (CNRMA) by Fanny Lanternier (director of the CNRMA), Dea Garcia-Hermoso and Alexandre Alanio (deputy directors of the CNRMA).

### Artemisinin struggling against increasingly resistant malaria parasites

*Plasmodium falciparum,* responsible for the most deadly form of malaria, now poses a major challenge: growing resistance to antimalarial drugs, particularly artemisinin, the central component of combination therapies that constitute the standard treatment. This



Human red blood cell infected with *Plasmodium falciparum* at the schizont stage observed by scanning electron microscopy. Colourised image.

phenomenon, which first appeared in Southeast Asia in the 2000s, is now also being observed in Africa, where 90% of malaria cases are reported, due to the local emergence of resistant parasites.

This resistance, identified through the discovery of the K13 genetic marker, poses a growing threat: mutations in this gene slow down the elimination of the parasite from the blood, reducing the effectiveness of treatments. In French Guiana, the only territory with active indigenous transmission (a few hundred cases annually), the National Malaria Reference Centre is closely monitoring these mutations to prevent their emergence and spread in forest areas. In the French overseas departments and regions (Martinique, Guadeloupe, Mayotte), where malaria had been eliminated, resistance poses a risk of reintroduction via imported cases from Africa or Asia, combined with the presence of competent mosquito vectors.

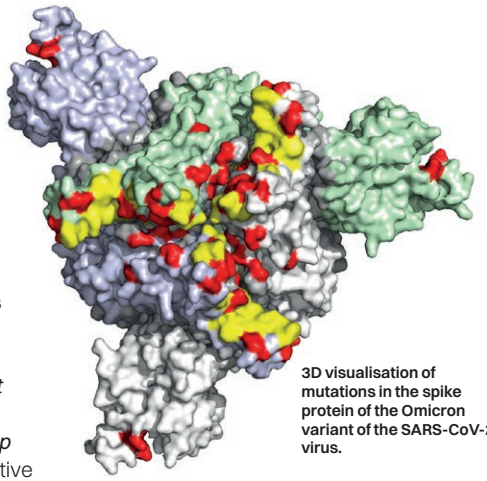
**Continued on p. 6**

ACTION PASTEUR

# **Resistance to antivirals:** a danger underestimated?

Resistance to antiviral drugs, which receives less media coverage than resistance to antibiotics, is a growing and underestimated challenge in the fight against viral infections. As **Olivier Schwartz**, Head of the Virus and Immunity Unit at the Institut Pasteur, explains, *"it is an equally crucial issue, especially for viruses such as HIV or SARS-CoV-2, which evolve rapidly."* Viruses accumulate mutations under the pressure of treatment, thereby escaping its action. This phenomenon is particularly worrying for HIV, which requires lifelong treatment, and for SARS-CoV-2, whose variants have rapidly rendered the first antiviral monoclonal antibodies ineffective. "*A single mutation can be enough to induce resistance,"* emphasises the researcher, stressing the need for real-time monitoring.

To limit this risk, strategies rely on combinations of molecules, such as triple therapy for HIV. Genomic sequencing also makes it possible to detect resistant mutations early on and adapt treatment protocols. Artificial intelligence offers new prospects by predicting resistance and designing more robust antivirals. Olivier Schwartz insists: *"Without a detailed understanding of viral biology, it is impossible to develop sustainable treatments."* A proactive approach is essential to preserve the effectiveness of these essential treatments. *"We must anticipate these resistances by diversifying our therapeutic tools and strengthening the surveillance of viral strains",* sums up Olivier Schwartz.



3D visualisation of mutations in the spike protein of the Omicron variant of the SARS-CoV-2 virus.

*"Viruses accumulate mutations under the pressure of treatments. A single mutation can be enough to induce resistance."*

# Guilhem **Janbon**

Head of the Fungal Pathogen RNA Biology Unit and Director of the Mycology Department at the Institut Pasteur

*"Fungal infections deserve more attention, as they can be serious and difficult to treat."*

### Pathogenic fungi are often overlooked. How important are they to human health?

Some fungi cause serious infections in humans.
Every year, 1.6 to 2.6 million people worldwide die from fungal infections, and billions more are affected by skin or systemic infections. These figures are comparable to those for tuberculosis or certain cancers, yet pathogenic fungi remain one of the poor relations of research: less than 3% of the global budget for infectious diseases is dedicated to them.

These infections affect everyone. Pathogenic fungi are everywhere: in the air we breathe, on our skin, and even in our digestive system. They are part of our environment, but can become dangerous under certain conditions.

### Which fungi are of most concern today?

Four species stand out for their dangerousness and their impact on public health. ***Cryptococcus neoformans*** is a fungus that my laboratory has studied closely. It is responsible for severe meningitis, particularly in people whose immune systems is weakened. Without treatment, these infections can be fatal.
***Candida albicans*** is a natural part of our microbiota, particularly on the skin, in the digestive tract and on the mucous membranes. Under normal circumstances, it is harmless, but if our microbial flora becomes unbalanced, it can cause severe infections, such as candidemia (blood infections) or deep infections that are difficult to treat.
***Aspergillus fumigatus*** is a fungus that we breathe in daily in the form of spores, which are harmless to most of us.

However, in vulnerable individuals, it can cause pulmonary aspergillosis, a serious infection that destroys lung tissue and is often resistant to conventional antifungal treatments.
Finally, ***Candida auris*** is a fungus that is of great concern to the scientific and medical community. It only appeared after 2005 and was not known to be pathogenic before that date. Today, it is responsible for nosocomial epidemics (hospital-acquired infections) in many countries.

### How do fungi become resistant to antifungal drugs?

Resistance to antifungal drugs is a complex phenomenon based on two main mechanisms. The first is natural resistance. This means that fungi possess genetic characteristics that protect them from the outset. The second mechanism is acquired resistance. This develops over time, particularly in patients undergoing prolonged treatment with antifungal drugs. Under this pressure, fungi mutate and become resistant. Another factor exacerbates the problem: the widespread use of antifungal drugs in agriculture. The same classes of molecules are used to protect crops and treat humans. This intensive use promotes the emergence of resistant strains, which can then infect humans.

### What treatments are available for fungal infections?

Currently, there are four main classes of antifungal agents available to treat fungal infections: polyene antifungals; azole antifungals; echinocandins; and 5-fluorocytosine. New molecules are under development, but these molecules are also likely to be used in agriculture, which could accelerate the emergence of new resistances.

The big gap in our therapeutic arsenal is vaccines.

Unlike bacteria or viruses, there is currently no vaccine to prevent fungal infections.

### Does climate change influence fungal infections?

Yes, and that is one of our main concerns. Global warming could expand the geographical distribution of certain fungi. *Candida auris* is a case in point. Its sudden appearance in several countries suggests that it may have adapted to higher temperatures, perhaps due to global warming.

If this hypothesis is confirmed, we could see the emergence of other pathogenic fungi in the coming years.

### Should we fear a fungal pandemic, like the one we experienced with Covid-19?

A fungal pandemic on the scale of Covid-19 is unlikely, as fungi do not spread as easily as viruses. The most worrying scenario would be the emergence a fungus that is resistant, virulent, and transmissible. Although this remains unlikely, scientists and doctors are closely monitoring fungal outbreaks, as such a situation could pose a major challenge to public health.

> ***Candida auris*** **is a real challenge for hospitals and laboratories, as it is able to persist on surfaces despite cleaning protocols."**

MALARIA

ACTION PASTEUR

# Monitoring **resistance markers**

Resistance to artemisinin, a key treatment for malaria, is mainly due to mutations in the Kelch13 gene. These mutations reduce the parasite's ability to absorb haemoglobin, thereby limiting the release of ferrous iron ($Fe^{2}$), which is essential for activating the drug. By blocking this mechanism, the parasite weakens the effect of artemisinin, as if it were *'defusing a bomb',*

according to **Didier Ménard**, professor at the University of Strasbourg and researcher at the Institut Pasteur.

But the resistance does not stop there: *"Even within a genetically identical population, there is heterogeneity among subpopulations. Some of them adopt a specific cellular programme that gives them the ability to resist exposure to artemisinin."*

Contrary to initial fears, the resistance observed in Africa is not linked to the importation of Asian strains, but is the result of a local and independent emergence. *"What is worrying is that these resistances appear without any link between regions, which complicates their control,"* the researcher points out.

**With 600,000 deaths annually, mainly among children under 5 and pregnant women, malaria remains one of the deadliest infectious diseases.**

Study of malaria transmission. Banizoumbou village, Niger..

Another challenge is the loss of the HRP2 gene in some parasites, preventing them from producing the HRP2 protein, which is the target of rapid diagnostic tests. As a result, tests may give negative results in infected individuals, delaying or preventing appropriate treatment.

To overcome this therapeutic impasse, several approaches are being deployed: diversification of treatments with drug combinations, and increased surveillance through early detection of resistance via molecular markers and in vitro tests.

***"Without new treatments and innovative strategies, the progress made could collapse."***

**Continued from p. 4**

## How can we reverse the trend of antimicrobial resistance?

The fight against antimicrobial resistance (AMR) requires a coordinated approach by researchers, doctors and veterinarians. Human, animal and environmental health are closely linked and must be protected together to prevent disease, a concept known as 'One Health' or Global Health. Faced with the global spread of resistance genes (e.g. via waste water or international trade) and without a holistic response, we risk a return to an era where common infections will once again become deadly, warns the WHO (World Health Organisation). Cutting-edge multidisciplinary research and integrated approaches are being implemented – epidemiology, genomics, evolutionary biology, modelling, structural and chemical biology – to decipher how resistance emerges and spreads in microorganisms, as well as their interaction with the host organism. Through its early warning centres (including National Reference Centres), the Institut Pasteur contributes to the surveillance of emerging resistance, with the development of nano-electronic sensors to detect antibiotic resistance in three minutes and genomic tests to anticipate HIV or malaria resistance. Researchers are also studying therapeutic escape strategies that promote resistance, particularly within biofilms (communities of microbes that aggregate and attach themselves to a living or inert surface, producing a protective matrix of viscous substances). Microbes in a biofilm can be 100 to 1,000 times more resistant to antimicrobials than in their free state. Finally, researchers are developing therapeutic alternatives (phage therapy, antimicrobial peptides, drug combinations, bispecific antibodies).

The aim is to contribute tirelessly to the development of innovative therapeutic strategies (antibiotics, antiparasitics, antifungals, antivirals, antivectors) in order to ensure safer and more sustainable treatments for infectious diseases. ■

**REPORT BY THE EDITORIAL TEAM**

PROFILE

Fluorescence microscopy of *Aspergillus fumigatus* mycelium.

# Sarah Dellière

## Dual experience in hospitals and laboratories, beneficial to patients

*"I draw inspiration from the problems encountered in the hospital to fuel my work at the Institut Pasteur."*

***"In life, there is nothing to fear, everything to understand."*** **This quote from Marie Curie could well sum up Sarah Dellière's philosophy and career path. Determined, optimistic, and adventurous, she likes to step outside her comfort zone to enjoy new experiences and continually hone her knowledge.**

Sarah Dellière was born in a small village near Saint-Nazaire. ***"My mother was a schoolteacher and my father was a general practitioner."*** The fields surrounding her house were an incredible playground for an explorer equipped with a Swiss Army knife, an insect box, and a snack in her backpack. ***"It was in this environment that I decided, at a very young age, to become a doctor myself."***

Her parents still laugh about this anecdote today: the first time Sarah was allowed to go and buy a magazine on her own at the local newsagent's, she didn't bring back Mickey Mouse magazine, but a special issue of Sciences et Vie Junior

"Plague in the Middle Ages". Seeking to understand infectious diseases quickly became her "hobby".

As a teenager, she concluded that studying medicine would not be enough to answer all her questions about life, so she began to consider a career in research as well.

At 17, with her graduation certificate in hand, she won an academic and sports scholarship to attend an American university in New Jersey.
Her academic results were excellent and she joined the tennis team at Fairleigh Dickinson University, where she began a degree in biology, required for enrollment for medical school in the United States.

***"I clearly wasn't going to become a professional tennis player; there were girls who were much stronger than me. The university chose me mainly because of my excellent academic results, which raised the level of the team."***

The cost of American university led to her return to France, where she enrolled in medical school in Nantes, completing her studies with a Master's degree in microbiology. She did her internship in microbiology in Paris at the AP-HP and took a gap year to complete a Master's degree in Infectious Diseases and Immunology, with a specialisation in mycology, at Paris Descartes University, then flew off again to do a ten-month research internship at McGill University in Canada (working with Dr Don Sheppard's team) on her favourite fungus: *Aspergillus fumigatus.*

At the Institut Pasteur, she is attempting to understand the underlying mechanisms between human immunity and the fungus *Aspergillus fumigatus*.
She currently divides her time between the Institut Pasteur and the hospital, where she performs diagnostics in parasitology and mycology.

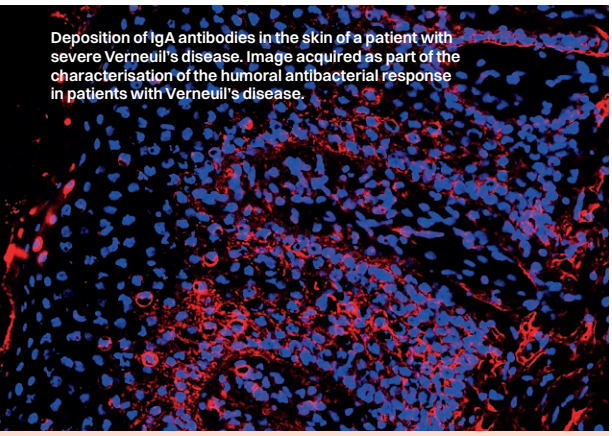
***"In the environment, fungi such as* Aspergillus fumigatus *are ubiquitous, contributing to the breakdown of dead matter and coexisting very well with the human immune system. But when a patient is immunocompromised, such as after a transplant or certain types of chemotherapy, and more recently in patients with severe Covid-19, this fungus becomes pathogenic. Initially, it colonises the lungs, multiplies and attacks the tissues, destroying them. The mortality rate is 50%."***

Thanks to this translational approach, she was able to compare samples from uninfected and infected patients. Her observations revealed that certain immune proteins were missing in infected patients compared to others.

National Reference Centre for Invasive Fungal Infections and Antifungals (CNRMA) at the Institut Pasteur. From left to right: Déa Garcia-Hermoso (research engineer at CNRMA), Sarah Dellière (researcher in the Aspergillus Immunobiology Unit), Fanny Lanternier (head of CNRMA).

Today, she is attempting to answer various questions: Is the fungus capable of destroying these immune proteins? Was the patient's immune system already compromised prior to infection? Are these proteins completely consumed during the interaction between the immune system and the pathogen, leaving insufficient quantities? One of these proteins, surfactant protein D, is already used in premature babies to help them breathe better.

***"Thanks to my dual training as a doctor and researcher, I hope to be able to bridge the two worlds with a comprehensive vision of what we need to do to meet the challenges posed by infections."***



Deposition of IgA antibodies in the skin of a patient with severe Verneuil's disease. Image acquired as part of the characterisation of the humoral antibacterial response in patients with Verneuil's disease.

# Towards a new treatment for Verneuil's disease

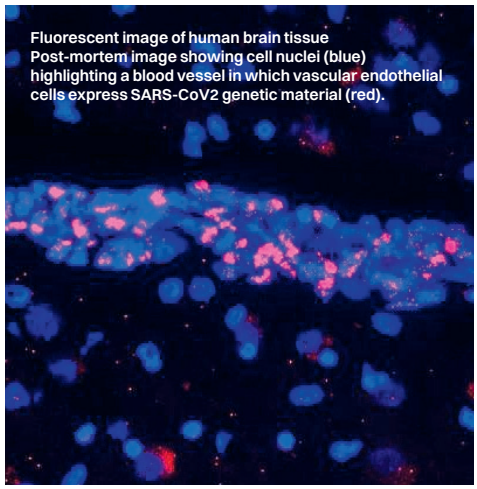
**Verneuil's disease is a dermatological condition that causes painful abscesses in the folds of the body.**

There are three stages of the disease, and unfortunately for patients, many diagnostic uncertainties. Even if correctly diagnosed, there is no definitive treatment for this disease. Certain antibiotics, biotherapies, and even surgery on the lesions can control flare-ups, but ongoing maintenance treatment seems essential to prevent relapses. Hence this new clinical trial, called ABCESS2, led by the Institut Pasteur.

** Therapeutic trial led by Dr Maïa Delage and Dr Aude Nassif, two dermatologists practising at the Institut Pasteur Medical Centre.*

LONG COVID

# SARS-CoV-2 persists in the brain stem over the long term



Fluorescent image of human brain tissue Post-mortem image showing cell nuclei (blue) highlighting a blood vessel in which vascular endothelial cells express SARS-CoV2 genetic material (red).

**Several months after contracting Covid-19, some patients suffer from persistent symptoms known as "long Covid". Researchers at the Institut Pasteur have discovered, through a study on animal models, that the SARS-CoV-2 virus infects the brain and persists for up to 80 days in the brain stem, even after the acute phase of the disease.**

This "low-level" viral presence (with a low viral load but active replication) has been observed in several variants (Wuhan, Delta, Omicron). It is associated with symptoms such as anxiety, depression, and memory problems. Analyses reveal that the virus disrupts the activity of genes linked to brain metabolism and neuron function, with mechanisms similar to those of neurodegenerative diseases such as Parkinson's. In particular, the production of dopamine – a neurotransmitter crucial for mood and cognition – is impaired. These findings provide a biological explanation for some of the neurological symptoms of long Covid and open up avenues for future therapies targeting deregulated genes.

** Work led by Guilherme Dias de Melo, lead author of the study and researcher in the Lyssavirus, Epidemiology and Neuropathology Unit at the Institut Pasteur.*

STUDY

# New insights into steroid hormones

**A large-scale study conducted by the Institut Pasteur over 10 years involving 1,000 people reveals unprecedented variations in steroid hormones (such as cortisone, oestrogens, androgens and progestogens), which play a crucial role in regulating metabolism, the immune system, reproduction, and stress resistance.**

The study, based on mass spectrometry analysis of 17 steroids, shows that genetics, gender and age strongly influence steroid hormones, but that lifestyle (smoking, diet) also plays a key role, impacting hormonal balance and long-term health. These data provide a reference for understanding hormones and their implications for health. This study paves the way for more personalised medicine, taking into account the specific hormonal characteristics of each individual.

**In women,** oral contraception significantly reduces 12 hormones (to levels lower than in menopausal women), while increasing certain corticosteroids.

**In men,** smoking disrupts several steroids, and the decline in androgens (such as testosterone) with age is linked to increased risks of disease.

An unexpected link has been observed between fast food consumption and high levels of cortisone and cortisol, hormones involved in stress and metabolism.

The team already plans to explore the links between hormonal variations and the development of diseases.

** Study led by Darragh Duffy, head of the Translational Immunology Unit, and Molly Ingersoll, director of the joint unit (with the Cochin Institute) on Inflammation and Mucosal Immunity.*

FOOD SAFETY

# Botulism in France

**Botulism, a rare but serious neurological disease, periodically makes headlines in France, often in connection with poorly prepared homemade preserves.**
**Recent episodes serve as a reminder of the importance of constant vigilance.**

In September 2024, in Indre-et-Loire, five young adults were hospitalised after eating wild garlic pesto during a meal with friends. Four of them required months of treatment to overcome the effects of the toxin, while the authorities worked to quickly remove

600 jars were suspected of being contaminated, sold at local markets. An investigation was launched to understand the circumstances of this contamination.

A few months later, in July 2025, a new cluster of cases occurred in Maine-et-Loire: six people fell ill after eating improperly preserved food.

Despite rapid treatment, one of them did not survive, highlighting once again the risks associated with inadequate sterilisation.

Between these events, a case detected in Isère in November 2024 shows that the danger can affect all types of artisanal food products. A pork terrine, sold directly at a farm, is identified as the source of contamination. Tests confirm the presence of the toxin, leading to the immediate recall of the affected preserves.

Since 2018, France has had around 100 cases of botulism, including one death. These situations, although rare, often follow the same pattern: local products, inadequate preservation, and avoidable consequences. Health authorities regularly remind the public of best practices: rigorous sterilisation of preserves and caution with non-industrial products.

Symptoms – visual disturbances, difficulty swallowing or dry mouth – should be treated as a warning sign, as early treatment is essential. With around 20 outbreaks recorded each year, botulism remains an exceptionally rare disease, but its severity warrants special attention, particularly for high-risk foods. These episodes serve as a reminder that food safety, even in the simplest of tasks, must never be neglected.

# Counterfeit medicines

FOCUS

**In 2025, the WHO (World Health Organisation) warned of an explosion in counterfeit medicines, a growing global threat. These products, whose identity, composition or origin have been fraudulently altered, pose a major threat to public health. They may contain toxic substances (such as antifreeze), incorrect dosages, or no active ingredients, making their consumption extremely risky.**

The WHO is sounding the alarm after dramatic cases of poisoning, such as the deaths of 300 children in Gambia, Uzbekistan and Indonesia in 2022-2023, who were victims of contaminated paediatric syrups. These cases illustrate the urgent need for action against trafficking that affects every continent and every therapeutic area, from antidiabetic drugs to anticancer drugs, antibiotics to anxiolytics.

Illegal online sales are the main driver of this scourge, with a proliferation of unregulated websites offering medicines without prescriptions. Operation Pangea XVII, conducted by Interpol between 2024 and 2025, revealed the scale of the problem: 50.4 million doses seized in 90 countries, worth €56 million, and nearly 800 arrests. However, penalties are often less severe than for drug trafficking, which encourages criminals.

Counterfeit medicines are not only ineffective: they aggravate diseases, and can cause death. The WHO also highlights their impact on drug resistance, a critical issue for global health. Traffickers are now targeting the most in-demand medicines, such as those for diabetes and obesity, in response to the rise in self-medication.

Faced with this danger, the WHO and health authorities are calling for vigilance: it is essential to purchase medicines only from approved pharmacies or certified platforms, and to report any doubts about a product. Suspicious packaging, abnormally low prices or the absence of a package leaflet should raise alarm bells.

This scourge also reveals flaws in international regulation, with distribution channels that are sometimes flawed, especially in developing countries. However, even rich countries are not spared, due to the ease of access to these products online.

The WHO insists: a counterfeit medicine is not a medicine, it is poison. Awareness among everyone – patients, healthcare professionals and governments – is essential to combat this problem effectively.

LASSA FEVER

# A candidate vaccine in clinical trials

**After more than 20 years of research on Arenaviruses, a team from the Institut Pasteur led by Sylvain Baize has created an original vaccine platform called MOPEVAC, which will strengthen the institute's pandemic preparedness initiatives.**

The first vaccine candidate developed using this platform targets Lassa fever, a haemorrhagic fever that causes 5,000 to 6,000 deaths each year in West Africa.

*"To achieve long-lasting and effective protection, we needed to work on a vaccine vector that could be administered in remote areas and, ideally, be effective with a single injection, as is the case with yellow fever, for example. The Phase 1a trial will involve 72 healthy volunteers, whose safety and immune responses will be monitored for over a year. The first enrolment is scheduled for early 2026,"* explains the researcher.

Beyond the expected results for the Lassa fever vaccine candidate, the MOPEVAC platform has been transformed to obtain a more universal expression vector, thereby enabling a response to viral outbreaks with vaccine candidates that are effective against other pathogens with very high mortality rates.

** Study led by Sylvain Baize. The MOPEVAC project trials are funded by France 2030 as part of the "Emerging Infectious Diseases and CBRN Threats" strategy led by the Health Innovation Agency and operated on behalf of the French government by Bpifrance, which already supports pre-clinical studies.*

PLAGUE

# A new model for understanding the seasonality of epidemics

**Plague, an endemic disease in Madagascar, reappears every year, mainly between October and March. New mathematical models (combining field surveys and supercomputer analysis), developed through collaboration between the Institut Pasteur in Paris and the Institut Pasteur de Madagascar, now provide a better understanding of the seasonal dynamics of plague in Madagascar.**

*"Thanks to our extensive data collection, we have observed that flea density increases on rats even as rat populations decline. Even if the rat population is declining, due to the increase in the number of fleas, the risk of transmission to humans is higher during the wet season,"* explains Fanohinjanaharinirina Rasoamalala.
The aim is to move from reacting to epidemics to anticipating them, via an early warning system, in collaboration with local authorities.

** Study led by the Plague Unit of the Institut Pasteur of Madagascar and the Mathematical Modelling Unit for Infectious Diseases of the Institut Pasteur in Paris, supported by the Armed Forces Biomedical Research Institute and the French Agency for International Technical Expertise.*

HISTORY

# Leprosy existed in America long before the arrival of Europeans

**A recent study has revealed that a second species of bacteria responsible for leprosy, recently identified as *Mycobacterium lepromatosis*, has been infecting humans in America for at least 1,000 years, several centuries before the arrival of Europeans.**

This study analysed the DNA of nearly 800 samples, including ancient human remains (from archaeological excavations) and recent clinical cases presenting symptoms of leprosy. The results confirm that *M. lepromatosis* was already widespread in North and South America long before European colonisation and provide a better understanding of the current genetic diversity of pathogens of the *Mycobacterium* genus.

***"This discovery transforms our understanding of the history of leprosy in the Americas,"*** said Dr. Maria Lopopolo, first author of the study and researcher in the Microbial Paleogenomics Laboratory at the Institut Pasteur.

***"This study clearly illustrates how ancient and modern DNA can rewrite the history of a human pathogen and help us better understand the epidemiology of contemporary infectious diseases,"*** said Nicolás Rascovan, lead author of the study and head of the Microbial Palaeogenomics Laboratory at the Institut Pasteur.

The project was carried out in close collaboration with indigenous communities, who were involved in decisions regarding the use of ancestral remains and the interpretation of results.

** Study led by scientists from the Microbial Paleogenomics Laboratory at the Institut Pasteur , the CNRS and the University of Colorado (United States), in collaboration with various institutions in America and Europe.*

EXHIBITION

# Portrait of Louis Pasteur on display in Bayonne

**To mark the reopening of the Bonnat-Helleu Museum scheduled for autumn 2025, the Institut Pasteur is loaning the famous painting created in 1886 by Léon Bonnat (1833–1922) depicting Louis Pasteur and his granddaughter Camille Vallery-Radot (1880–1927). The sober background and meticulous attention to detail emphasise both the solemnity of the portrait and a rare family intimacy.**

When Louis Pasteur filed his patent for pasteurisation in 1871, Carlsberg Breweries, founded in 1847 by Jacob Christian Jacobsen (1811–1887), were the first in Denmark to adopt this method, which revolutionised the brewing industry. Jacobsen, who had immense admiration for Pasteur, commissioned the painter Léon Bonnat to paint a portrait of Louis Pasteur for his wife, Marie Pasteur (1826-1910), as a token of gratitude for his work. However, it was ultimately his son Carl Jacobsen (1842-1914) who presented the painting to the scientist in 1888, during an exhibition in Copenhagen.

This gesture symbolises the deep friendship between the two men, as well as Carlsberg's commitment to science, which led to the creation of the Carlsberg Research Laboratory in 1875, whose work was directly inspired by Pasteur's discoveries.

Pasteur's sittings at Bonnat's studio gave rise to cordial exchanges, as evidenced by the letters and telegrams that have been preserved. The addition of Camille to the composition, which was done after the fact, was a challenge for the artist, who asked the family to return to pose. Presented at the 1886 Salon, the portrait was praised by critics, although some saw a certain rigidity in it. Yet it is precisely this solemnity that makes it a major work, both an official portrait and an emotional testimony. The painting was also presented at the 1889 World's Fair.

**The painting will be returned to the large living room of Louis and Marie Pasteur's apartment in autumn 2028 for the museum's reopening.**

**Louis Pasteur with his granddaughter Camille Vallery-Radot, Léon Bonnat (1833-1922), 1886.**

**From left to right: François Jacob, Jacques Monod, and André Lwoff, Nobel Prize winners in Medicine in 1965. Jacques Monod presents a set of dice illustrating the basics of symmetry in the allosteric model.**
*Jacques Monod's office, two days after the Nobel Prize announcement.*

SYMPOSIUM

# Societal commitment of researchers in the spotlight

**The Institut Pasteur is delighted to invite you to save the date of 10 December 2025 for an international symposium organised to mark the 60th anniversary of the Nobel Prizes awarded to François Jacob (1920-2013), Jacques Monod (1910-1976) and André Lwoff (1902-1994).**

This symposium will not only be a celebration of history, but also a manifesto of researchers' ongoing commitment to the common good, through a rich programme bringing together scientists in the life sciences and the humanities and social sciences.

*This anniversary project was conceived in 2022 on the initiative of President Christian Vigouroux, who approached the Defence Historical Service. The three researchers who won the Nobel Prize in 1965 are former members of the Armed Forces Health Service (SSA).*

*This day will be an opportunity to broaden the discussion to other lesser-known figures and groups from the Institut Pasteur who were nevertheless linked to the Resistance and the Liberation, notably women such as Hélène Sparrow and researchers from the Pasteur Network.*

**Event details**

- **Date** **December 10, 2025** *(day of the Nobel Prize award ceremony in Stockholm in 1965)*
- **Location** Duclaux Amphitheatre, Institut Pasteur, 28 rue du Docteur Roux, Paris
- **Time** 9h30 – 17h00

**Registration required**
*https://colloqueinstitutpasteur10decembre.eventbrite.com*

# Pasteur and you

**WE ARE AT YOUR SERVICE**

Donor Relations: **33 1 40 61 33 33**
Legacy: **33 1 40 61 32 03**

Medical center, international vaccinations, and travel medicine : **33 1 45 68 80 88**

Don en Confiance – VOTRE DON, NOTRE ENGAGEMENT


## 19th edition of PasteurDon :

# A huge thank you for your commitment!

**From October 8-12, 2025, many of you supported our researchers during the 19th edition of Pasteurdon. Your donations keep research alive and enable the Institut Pasteur to pursue its mission: putting science at the service of everyone's health.**

Alongside Julia Vignali and Kad Merad, the Institut's patrons, and our 50 media partners, the public was made aware of the importance of the work carried out by our 1,600 researchers. Among the topics highlighted were the increase in cancer among young people, the emergence of new microbes linked to climate change, and understanding epidemics.

The funds raised directly finance our research programmes without any intermediaries. Several patrons and partner companies also became involved:

### Fondation Le Roch-Les Mousquetaires

A loyal partner of Pasteurdon for over 15 years, it is renewing its commitment in 2025. Thanks to the involvement of the Intermarché and Bricomarché chains, eight shared products were offered from 8 to 19 October, with a portion of the sales donated to the Institut Pasteur.

### AG2R La Mondiale

A long-standing patron, AG2R La Mondiale supported the Institut Pasteur through its "Vivons vélo pour l'Institut Pasteur" (Let's cycle for the Institut Pasteur) programme. In September in Strasbourg and October in Paris, guided bike rides of around 15 km were organised in the form of treasure hunts. AG2R La Mondiale made a donation to the Institut Pasteur for each participant.

### ASSU 2000

A partner of Pasteurdon for the 12th consecutive year, ASSU 2000 renewed its support for research on the gut microbiota. A "product-sharing" operation was set up in 300 branches and on its website. Starting in September, two euros were donated to the Institut Pasteur for each insurance policy taken out (car, motorcycle, health, life insurance).

**Thanks to everyone's generosity, the 2025 edition was a success and resonated widely with the general public. Your donations are a tremendous encouragement to our researchers. THANK YOU!**

## Relive the PasteurDon conferences available for replay!

During Pasteurdon, you may have been able to attend our conferences on October 9, and if not, you can watch them again. Professors Arnaud Fontanet and Sylvain Brisse share their fascinating work on an essential topic:

***Understanding past and present epidemics to better anticipate those of tomorrow.***

**A captivating event for everyone interested in research and public health issues.**

***"Pandemic preparedness"***

**Arnaud Fontanet**
Head of the Emerging Diseases Epidemiology Unit

***"The resurgence of forgotten diseases"***

**Sylvain Brisse**
Head of the Biodiversity and Epidemiology of Pathogenic Bacteria Unit

**Access the conference replays *via* :**
*https://youtube.com/live/rtmGNXSG9Q4*
**or by scanning this QR code**

## Subscription and/or support form

INSTITUT Pasteur

**I am making a donation of:**

☐ **30€** ☐ **45€** ☐ **60€** ☐ **75€** ☐ **100€** ☐ Other amount.....**€**

☐ **On www.pasteur.fr**

☐ **By bank check made payable to the Institut Pasteur**

☐ I wish to continue receiving the Institut Pasteur Newsletter and I am enclosing the amount for a one-year subscription: 4 issues at the price of €6 (non-deductible).

☐ I would like to receive, in complete confidentiality and without obligation, information on the possibilities of bequests, donations, and life insurance benefiting the Institut Pasteur.

The personal data collected on this form are intended for the Institut Pasteur and its subcontractors for the purpose of processing your donation, your **subscription to *the Lettre de l'Institut Pasteur***, issuing your tax receipt, soliciting your generosity, and sending you information about the Institut Pasteur. They are kept for the period strictly necessary to achieve the aforementioned purposes. In accordance with the Data Protection Act, you may object to their use and have the right to access, rectify, limit, port, or delete them. To do so, please contact our Donor Relations Service - Institut Pasteur, at 25 rue du Docteur Roux, 75015 Paris, France or via email at **dons@pasteur.fr.** You can also contact our Data Protection Officer by email at **dpo@pasteur.fr** or by mail at: Data Protection Officer, Institut Pasteur, Legal Department, 28 rue du Docteur Roux, 75724 Paris Cedex 15, France. In case of difficulty, you can also file a complaint with the CNIL (French Data Protection Authority). Your contact details may be shared with other organisations soliciting public donations, unless you object by checking the box here ☐) or sent outside the European Union for mailing production, unless you object by checking the box here ☐).

**MY CONTACT DETAILS**

*Last name* .....

*First Name* .....

*Adress* .....

.....

.....

.....

.....

1IFL130


La lettre de l'Institut Pasteur — INSTITUT Pasteur

**Quarterly newsletter published by the Institut Pasteur**

**Publication Director:** Yasmine Belkaid • **Editorial Directors:** Antoine Bogaerts, Constance Derely • **Editor-in-Chief:** Valérie Caro, Denis Allard • **Contributors to this issue:** Aurélien Coustillac, Laurence Isnard, Emma Leprêtre, Margaux Provot, Agnès Rastoin • **Art Direction and Production:** BRIEF/Caribara • **Photo Credits:** Institut Pasteur / François Gardy / Jean-Marc Panaud / François Rodhain / Sylvain Brisse / Camille Picard / Fanny Lanternier / CNRMA / Aurélie Claës et Jean-Marc Panaud / Olivier Schwartz et Félix Rey / Guilhem Janbon / Olivier Ménard / Valérie Zeitoun / Immunobiology of Aspergillus-Vishukumar Aimanianda et Sarah Dellière / Immunobiologie et Thérapie-Ayawavi Viviane Agbogan / Krees Raharison ; Vincent Prévot/Inserm ; Alexandre Darmon / Art in Research ; Olivier Ménard ; André Rau-H&K / François Roealants ; OneHeart / Institut Pasteur / P. Sordoillet ; Getty Image ; D.R • **Printing:** Imprimerie Bulls Market Group • **Press Commission Number:** 0127 H 88711 • **ISSN :** 1243-8863 • **Subscription:** 6 euros pour 4 numéros par an • **Contact :** Institut Pasteur - 25 rue du Docteur Roux - 75015 Paris - Tel. +33 1 40 61 33 33

*This newsletter was printed on paper and using manufacturing processes that respect the environment.*


**www.pasteur.fr** ✉ dons@pasteur.fr