The discovery of the plague bacillus in Hong Kong, 1894

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THE SITUATION TODAY

Although the plague has claimed the lives of millions of people over the centuries, it no longer poses a major risk to public health. Spread by fleas, the disease mainly infects small animals, and can occasionally be transmitted to humans. According to figures released by the World Health Organization, 2,118 cases of human plague were reported in 2003, of which 182 were fatal.[1]

How, in the space of a century, did this notorious disease go from being the scourge of humanity to a rare and relatively well-controlled pathology? Key to this advance was the detailed description of the bacteria by the Franco-Swiss doctor Alexandre Yersin: the bacteria was named *Yersinia pestis* in his honour. Following Yersin's work, research was oriented towards antiserum[2] treatment, the administration of antibiotics, and the prevention of infection through the development of vaccines.

Thanks to these measures, the plague is no longer in the news. Yet the methodology that led Yersin to make his discovery remains relevant whenever scientists are confronted with a new epidemic and attempt to identify its causes. In recent years, the same type of approach has been used to study emerging diseases such as AIDS, SARS, Chikungunya and the Ebola virus.

ANALYSIS

The text considered here is recorded in the annals of the Institut Pasteur. It is a statement by Dr Alexandre Yersin[3] relating the discovery of the microbe

1. In general, only small mammals are hosts of the plague. Humans are only "accidental" victims. For more information on the plague today, see the WHO website.
2. Antiserum treatment involves injecting a patient suffering from a disease with serum taken from an animal that has been immunised against the same disease. This serum – a blood sample from which the red blood cells have been removed – contains antibodies that recognise the specific infectious agent and fight against it. The most common sera are those used against tetanus and diphtheria. They are obtained by vaccinating horses with increasing quantities of the tetanus or diphtheria toxin. Antiserum treatments can, however, produce serious allergic reactions. They are a fallback option used when no preventative vaccine exists, or to help the body fight against venom after a bite.
3. The Franco-Swiss doctor and bacteriologist Alexandre Yersin (1863–1943) is relatively unknown in Europe but venerated in Vietnam, where he spent most of his life. In addition to discovering the plague bacillus, he also

causing the bubonic plague. The statement describes the different stages – spanning a period of three weeks – that led to the identification of the cause of this centuries-old affliction.

***Figure 1:* Portrait of Alexandre Yersin.**
(Institut Pasteur photograph library)

This statement, running to only a few pages in length, is remarkable for the author's scientific rigour and gift for synthesising information. In it, Yersin provides a fine example of the Pasteurian School's approach to medical microbiology (see pane). Certain passages from this work were shared by Émile Duclaux[4] of the Académie des Sciences in a note recorded in the minutes of 30 July 1894.[5]

The Institut Pasteur and the Pasteurian School of microbiology

The Institut Pasteur was founded in Paris in 1887, financed by funds raised by an international subscription. Louis Pasteur, who had just developed the rabies vaccine (1885), had three aims: to make the vaccine accessible to as many people as possible; to develop the study of infectious diseases; and to disseminate knowledge.

From its very beginnings, this non-profit foundation has focused its energy on three complimentary fields of work. These were: 1) the Pasteur Hospital, home to anti-rabies vaccination campaigns (which

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introduced *Hevea* (the rubber tree) into Indochina, which still provides a significant financial windfall for Vietnam through its latex exports. A chronology of Yersin's life is available (in French) on the Institut Pasteur website.

4. The doctor, biologist and chemist Émile Duclaux (1840–1904) worked closely with Louis Pasteur for most of his career, mainly in the fields of bacteriology and agriculture. In 1895 he succeeded Pasteur as director of the eponymous institute.

5. *Comptes-rendus de l'Académie des Sciences, 1894, 119, p. 356*. *Sur la peste de Hong-Kong.* "Note de M. Yersin". Type "Yersin" into the search bar to go to page 356.

were later extended to other diseases) as well as antiserum treatments for rabies patients; 2) the research centre, where Pasteur's colleagues studied the agents of numerous diseases such as tuberculosis, diphtheria and malaria; and 3) the "technical microbiology" course, which instilled in young scientists the theoretical concepts and practical study of microorganisms that Louis Pasteur had pursued throughout his career.

In no time at all, researchers trained at the Pasteurian School could be found all over the world, leading to the creation of a network of Instituts Pasteur on all five continents. This network bolstered the implementation of strategies to combat infectious diseases in the very regions where they were developing.

***Figure 2:* Map showing the international network of Instituts Pasteur in 2008**

CONTEXT

Though a few serious outbreaks of plague have stood out over the centuries, this disease still remains endemic[6] in some areas of the world. South East Asia was – and still is – one such area. As was wont to happen, cases of plague on the Mongolian plateaux shifted from endemic to epidemic status in the early months of 1894. The disease had reached Yunnan.

> *In March that year, it* [the plague] *appeared in Canton and, within a few weeks, had caused 60,000 deaths in the city. The busy trade routes between Canton and Hong Kong on one hand, and Hong Kong and Tonkin on the other, coupled with the difficulties in imposing effective quarantine measures along the coast of these regions, aroused concerns within the French government of Indochina being overrun by the epidemic.*

6. Endemic diseases have a long-term presence in a region, whereas epidemics break out intermittently and then recede.

Upon reaching Canton, the plague quickly spread to the neighbouring British colony of Hong Kong. The strategic position of this port, situated at a busy trading crossroads between East and West, raised the very real spectre of the disease spreading to the rest of the world. Later events would confirm that the risks had not been underestimated: the epidemic, known as oceanic plague, spread to all five continents, with the most severe outbreaks occurring in trading ports.

> *I received the order from the Ministry for the Colonies to travel to Hong Kong to study the nature of the disease and the conditions in which it spreads, and to research the most effective means to prevent it reaching our possessions.*

Fearing that the plague would break out in their overseas possessions, the French authorities dispatched Dr Yersin, then a colonial doctor posted to Indochina, to the scene. The aim of this study was to determine the causes of the epidemic in the hope of preventing a similar outbreak on French soil. Although Yersin maintains here that he received orders from the Ministry for the Colonies, in reality, his trip was organised at his own request.

Why Yersin?

The naturally curious and adventurous Alexandre Yersin was a young French doctor of Swiss extraction. After completing his medicine thesis on tuberculosis under the supervision of Émile Roux,[7] and contributing to pioneering research on diphtheria, he worked alongside Robert Koch[8] in order to enhance his knowledge of microbiology. Upon his return to Paris, he was asked by Émile Roux and Louis Pasteur[9] to teach the first "technical microbiology" course at the Institut Pasteur. Yet his desire to undertake more field-based work in new lands led him to request a posting to the colonies as an army doctor. In his diary he writes:

> *I had always dreamed of discovering new places, of exploring; when one is young, nothing seems impossible…*

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7. Among other things, the doctor Émile Roux (1853–1933) is famous for his role in developing the rabies vaccine with Louis Pasteur. He was also director of the Institut Pasteur from 1904 until his death.
8. The German doctor Robert Koch (1843–1910) discovered the tuberculosis bacillus (1882).
9. The French chemist Louis Pasteur (1822–1895) was a pioneer of microbiology. His extensive work famously included refuting the concept of the "spontaneous generation" of microorganisms and developing the rabies vaccine. Among his many interests, he studied alcoholic fermentation and numerous diseases affecting humans and pets (anthrax, silkworm pebrine, fowl cholera, etc.). In 1887 he founded the eponymous Institut Pasteur in Paris.

Below is the letter of recommendation that Louis Pasteur sent to the Ministry of Foreign Affairs in 1890, in support of his young colleague's departure to Indochina:

> *His extensive knowledge of medicine has earned him the title of doctor. His future as a scientist promised brilliance. But, of all of a sudden, after much reading, he has been overcome with a desire to travel to faraway lands and nothing can retain him among us. I can vouch that Dr Yersin is the most serious of men, unfailingly honest, extraordinarily brave, possessed of varied and precise knowledge: in a word, capable of bringing great honour to our country.*

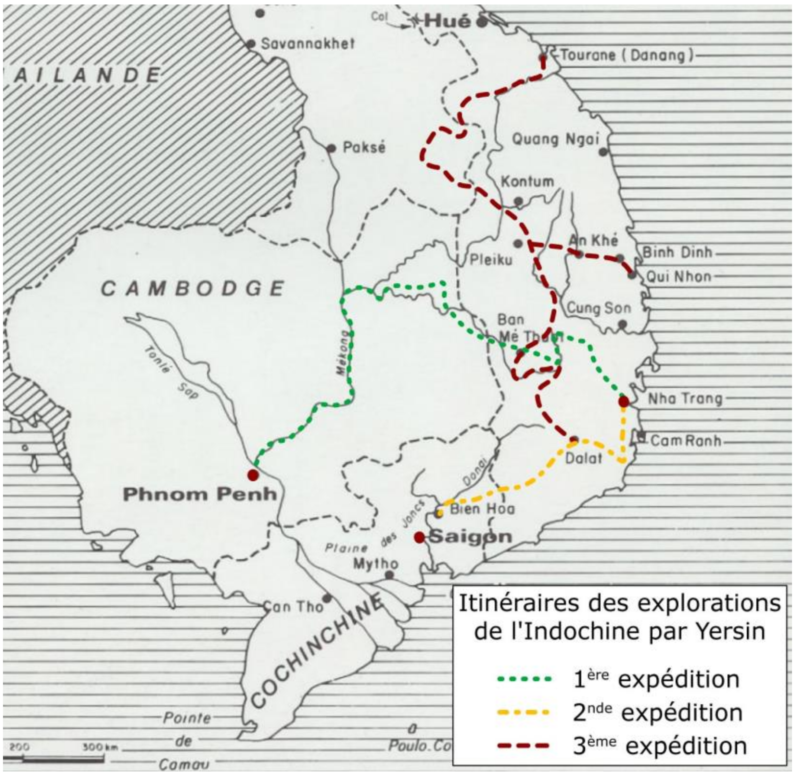

***Figure 3:* Map showing the itineraries of Alexandre Yersin's three exploratory expeditions in southern Indochina.**

Yersin served for a time as a doctor with the Messageries Maritimes cargo company on the Saigon–Manila line. This was followed by several expeditions in the Indochinese jungle (Figure 3). In March 1892 he moved to Nha-Trang – a city on the south-eastern coast of Vietnam – where he set up a branch laboratory of the Institut Pasteur of Saigon, directed by Albert Calmette.[10]

10. The doctor and bacteriologist Albert Calmette (1863–1933) gave his name to the tuberculosis vaccine (BCG, Bacillus Calmette–Guérin), which he developed with Camille Guérin (1872–1961) at the beginning of the 20th century.

<u>Figure 4:</u> Self-portrait of Alexandre Yersin in Nha Trang, on his return from his final expedition (March 1892).
(Institut Pasteur photograph library)

When plague broke out in Hong Kong, Yersin's desire to explore a new place, coupled with his scientific curiosity, led to his asking permission to study the epidemic on the ground. To advance his cause, his contacts in France petitioned the government on his behalf. Despite the support of Louis Pasteur and Émile Roux – which won Yersin a grant from the Ministry of Public Education – Yersin had difficulty obtaining permission from the general governor of Indochina to travel to Hong Kong.

Settling in

<u>Figure 5:</u> Alexandre Yersin in front of his straw hut in Hong Kong, in June 1893.
(Institut Pasteur photograph library)

I moved myself and my equipment into a straw hut that I'd had built with the permission of the English government in the grounds of the main hospital.

This short paragraph gives only the briefest of insights into the conditions that awaited Yersin in Hong Kong. Nor does Yersin mention the presence of a Japanese team led by a student of Robert Koch, Shibasaburo Kitasato.

Yersin, who had arrived with a servant on 15 June, had great difficulty obtaining the necessary permissions from the English authorities to study the disease. Eventually he built a temporary straw hut close to the hospital, where he set up his equipment (a microscope and an autoclave to sterilise contaminated equipment). Lacking credibility, he initially had to the bribe the gravediggers to gain access to bodies. The situation improved in time, however, and he was given access to patients in the hospital and allowed to take the biological samples he needed for his study.

Kitasato, for his part, arrived on 12 June and was provided with a full team of scientists and a laboratory at the English hospital.

***Figure 6:* Shibasaburo Kitasato (1853–1931)** *is above all known for his research into the tetanus agent. A pioneer of Japanese medical microbiology, he founded an eponymous institute in Tokyo in 1914.*

Description of the disease: The Bubonic Plague

History of the disease

The plague had long been one of the great scourges of humanity. This highly contagious disease was nearly always fatal until the discovery of treatments (antisera and antibiotics) at the turn of the 20th century. The three pandemics[11] of the Christian era were the Justinian Plague of the 6th century in Africa and Europe; the Black Death of the 14th and 15th centuries, which broke out in Asia and ravaged Europe and North Africa; and lastly, the Oceanic Plague. The latter, which provides the basic framework of study for our text, began in Mongolia at the end of the 19th century and quickly spread from China right across Asia, infecting 77 ports on five continents. Though rapidly brought under control in the West, this outbreak proved particularly devastating in India, right up until the mid 20th century.

Symptoms

Yersin took pains to describe the symptoms very precisely, from their early stages until remission, or – in most cases – death.

Here are the symptoms of the disease:

Sudden appearance after an incubation of four and half to six days: severe fatigue, prostration.

The patient suddenly succumbs to intense, often delirious fever. On the first day a single bubo appears. 75 times out of a 100, this bubo is found in the groin; 10 times out of 100 in the armpit; rarely on the neck or in other areas.

The lymph node[12] rapidly grows to the size of a hen's egg. Death comes 48 hours later, often earlier. When the patient is still alive after five or six days, the prognostic is better and the bubo softens; an operation can be performed to remove the pus.

This description closely echoes observations recorded over the centuries, leaving no doubt as to the diagnosis. Aside from the fever, the most recognisable symptom of plague is the appearance of a bubo, hence the name bubonic plague. In reality this is an acute inflammatory reaction in a lymphatic node, most often in the groin. Yersin reports that in "a few cases, the bubo does not

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11. A pandemic is a very extensive epidemic affecting several continents, or even the whole world.
12. The lymph nodes produce and differentiate immune-system cells called lymphocytes. The body contains, to name but few, inguinal nodes (groin area), axillary nodes (armpits) and occipital nodes (nape of the neck). After infection, the plague bacillus spreads via the lymphatic system to the nearest lymph nodes, and multiplies there, creating the first bubo.

have time to appear: all that is observed is the haemorrhaging of the mucous membranes". These are cases of the highly contagious, pulmonary form of the disease.[13]

Yersin reports a very high mortality rate – around 95% – in the hospitals. This figure is corroborated by historical descriptions, which indicate a mortality rate of 60–80% among patients, a rate that rises in cases of pulmonary plague. These figures give an idea of the severity of the disease and the fear it inspires. Indeed, few diseases are so highly contagious and have such a high mortality rate. The figures also reflect the total lack of means to combat the infection at the time, meaning that those infected were almost certainly doomed.

Living conditions of the affected population

After his insightful description of the factors that seem to favour the development of the disease, Yersin remarks on the insalubrious living conditions of its first victims in Hong Kong: the Chinese population. He notes in particular the inadequate and rat-infested sewage system, coupled with overpopulation in the poor districts of the city. Poor hygiene, he suggests, is the main obstacle to fighting the disease. This conclusion was all the more evident in a colony where a direct comparison between districts with different living standards was possible. In the European districts, the population – which was better off and better provided for – escaped the plague.

> *Currently few Europeans have been affected by the disease thanks to the much higher levels of hygiene in the houses and districts where they live.*

Yersin's endeavour to discover the microbe now began in earnest. To succeed, he put into action all the methods and scientific rigour he had acquired from Louis Pasteur.

Microbiological study of the origins of the disease

Analysis of the pulp of the buboes and discovery of the microbe

The first stage in microbiological study involves identifying the microbe in the infected patients. The microbe must be present in all patients if it is to be acknowledged as the agent of the disease.[14] Tests are undertaken to identify the

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13. In such cases, the disease can be spread from person to person by expectoration. When a person sneezes, the contaminated mucous is pulverised in a fine, aerosol-like spray and diffuses throughout the surrounding air, spreading the microbe across large spaces.
14. This criteria is one of what are known as Koch's Postulates (inaccurately, because the criteria were most probably formulated by Jacob Henlé). They establish a causative relationship between a microbe and a disease:

pathogen on the presumed site of infection, which varies depending on the nature of the disease: in general, the skin, the blood, or sometimes (in the case of tuberculosis, for example), the lungs.

Given the characteristic swelling of the lymph nodes produced by bubonic plague, Yersin carried out blood tests but focused his work on samples of buboes taken from patients and bodies. In the buboes he found a bacteria that he describes in the following terms:

> *The pulp of the buboes always contains masses of short, stubby, rounded bacilli, which can be easily coloured using aniline, and are not stained using the Gram method.*[15] *The tips of the bacillus are more strongly dyed than the centre, which gives it a transparent zone in the middle. Sometimes the bacilli look like they are surrounded by a capsule.*

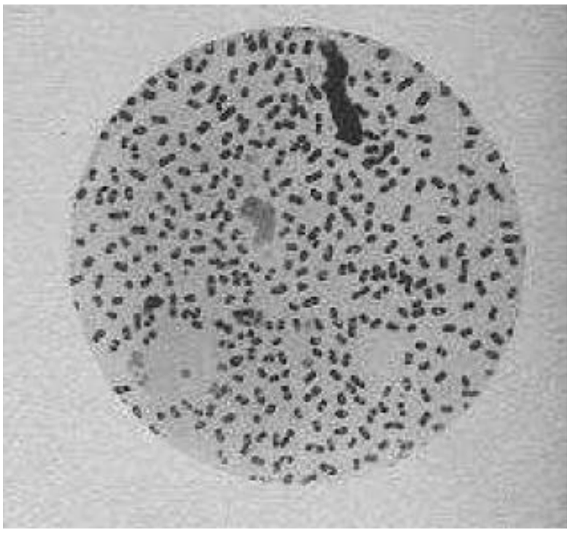

***Figure 7:* Pulp from a lymph node of a dead plague-infected rat.**
(Image 2 from Plate XII accompanying Yersin's article; see BibNum text). The proliferation of the "short, stubby, rounded" bacilli is plain to see.

We now know that this bacteria belongs to the enterobacteria family: it is called *Yersinia pestis* after its discoverer. Yersin also observes that the bacteria "is sometimes found in the blood, but in much smaller quantities: it is only present in very serious, brief and fatal cases". These sudden deaths are probably

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a) The microorganism must be found in all organisms suffering from the disease, but should not be found in healthy organisms.
b) The microorganism must be isolated from a diseased organism and grown in pure culture.
c) The cultured microorganism should cause all the symptoms of the disease when introduced into a healthy organism.
d) The microorganism reisolated from the inoculated experimental host must be identical to the original agent.

Although these postulates can be supplemented with other restrictions, they provide a reliable analytical tool for studies of this type. Here, Yersin followed the approach quite closely.

15. Gram staining is a classic technique in microbiology. It separates bacteria into two categories thanks to the different properties of their cell walls. In a Gram stain test, gram-positive bacteria retain the crystal violet dye, which is fixed by an iodine solution. Gram-negative bacteria – such as *Yersinia pestis* – do not retain this dye. They are revealed by a counterstain (fuchsine), which gives all gram-negative bacteria a pink colouring.

due to septicaemia,[16] which is one of the possible outcomes of the disease in 10–20% of cases.

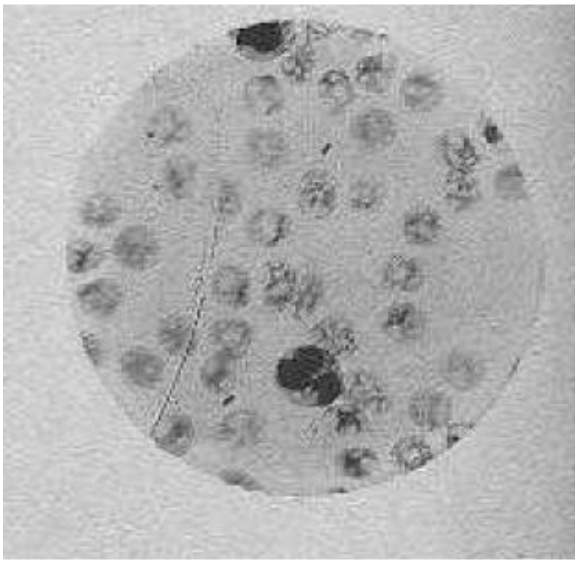

***Figure 8:* "Blood taken from a man dying of sudden plague, a quarter of an hour before his death"** *(Image 5 from Plate XII accompanying Yersin's article; see BibNum text). Only two bacilli can be seen in the blood (in the middle of the top half of the image, and below, slightly to the left). Cf. the large number in the buboes (Figure 7).*

Accounts of Kitasato's work suggest that, unlike Yersin, he was mainly interested in the septicaemic form of the disease, i.e. the blood microbe. It is likely he also successfully isolated the plague bacillus in his samples. However, it seems that his cultures were later contaminated by a pneumococcus,[17] invalidating a portion of his conclusions. The scale of his error is difficult to evaluate in retrospect, given the absence of conclusive evidence on the source of the contamination and the exact moment it occurred. The codiscovery of the plague bacillus by Yersin and Kitasato has long been a source of controversy.[18]

The bacillus culture

After identifying the bacillus, Yersin observed "Koch's Postulates" by attempting to isolate and cultivate it. Unexpectedly, the precarious conditions in

16. Septicaemia (literally, "septic blood") is a serious and general bacterial infection in an organism. Its symptoms include those caused by the microbe itself and the violent inflammation of the patient's body in reaction to the infection.

17. Pneumococcus – derived from its scientific name *Streptococcus pneumonia* – is the bacteria that causes pneumonia. This spherical bacterium (known as "coccus" in microbiological terms) is very different from the plague bacillus, which is the shape of a stick. Kitasato's initial descriptions of the plague agent were not very detailed, but resemble those of Yersin. However, his later reports provide a detailed description of a germ resembling the pneumococcus. Putting to one side the hypothesis that the cultures had been contaminated, it is also possible that the Japanese doctor had taken samples from patients suffering from acute pneumonia or from a coinfection, rather than from pulmonary plague alone.

18. For more details on the controversy, see "Diagnosis of plague: an analysis of the *Yersin-Kitasato* controversy". D. J. Bibel and T. H. Chen; *Bacteriol Rev*, September 1976, 40(3): 633–651.

the straw hut worked in Yersin's favour: as Yersin did not have access to laboratory ovens with which to reproduce the temperate of the human body, his experiments were carried out at room temperature, which, it turned out, provided optimal conditions for the microbe's development. He also identified which culture media optimised the development of the bacillus, thereby enabling others to reproduce the same conditions in their laboratory to study the microorganism.

This was followed by a circumstantial description of the colonies formed by the microbe in a culture, and its microscopical appearance.[19] These details were extremely important because, when patients presented symptoms of the plague, doctors at the diagnosis stage were able to ascertain whether they were infected by the same type of bacillus.

Reproduction of the disease in animals

Yersin observed that humans were not the only victims of the plague, but that it also affected animals, and rats in particular (this had already been noted). Drawing on this observation, he attempted to identify the causes of the disease by experimenting on animals.

> *The particular aptitude of certain animals to contract plague provided good conditions for me to undertake an experimental study of the disease.*

Yersin sought to reproduce the symptoms of the disease in laboratory animals (mice, rates and guinea pigs) using the isolated bacillus, again in strict observance of Koch's Postulates. This was a crucial stage in the microbiological study, for the bacteria in the buboes could well have been due to cross infection rather than being the actual cause of the disease.[20] This meant it would not be possible to reproduce the symptoms of the disease when the bacteria was inoculated in an animal.

In the event, the experiment proved that symptoms of the plague can be reproduced using bacteria taken from infected humans or animals as well as from bacteria from cultures:

19. Photograph 3 on Plate XII shows a microscope image of the small chains of bacteria in the culture broth.
20. Cross infection is one hypothesis that might explain Kitasato's error: his patients were perhaps infected with a pneumococcus. Infection by a pneumococcus is fatal for an organism, but the symptoms of the disease are different from those of the plague.

The first culture produced from a bubo proves challenging in peptone-agar.[21] Nevertheless, it does develop, and kills just as quickly as bubonic pulp.

This last observation is direct proof that the previously isolated bacteria is the cause of the disease: this is not a case of coinfection by another infectious agent picked up from patients.

Inoculation and contagion

Yersin tested several inoculation methods, using either injection or oral medicines. Both methods of introducing the pathogenic agent produced lesions characteristic of the disease, with microscopical examination revealing the bacillus to be present in the lymph nodes.

Inoculating mice, rats and guinea pigs with the pulp from buboes causes [the animals] to die, and autopsy reveals the characteristic lesions as well as many bacilli in the lymph nodes, spleen and blood.

He also observes that the disease can be transmitted from animal to animal:

I placed healthy mice in the same container as inoculated mice: the inoculated mice died first, but over the following days the healthy mice all succumbed to the disease one after another, with the plague bacillus present in their organs.

Observing the high number of dead, plague-infected rats in the patients' homes, Yersin speculated that they must be vectors of the disease. Yet he notes that flies in his laboratory are also infected:

I noticed that there were lots of dead flies in the laboratory where I performed my autopsies on animals. I [ground down one of these flies] into a broth and inoculated a guinea pig with it. The inoculation liquid contained a large quantity of bacilli similar in all respects to the plague bacillus, and the guinea pig died 48 hours later, displaying the lesions typical of the disease.

Unlike bacilli taken from the floor of infected houses, the bacilli in the flies were infectious, hinting at the possibility of transmission by insects. Yet, though very close, Yersin did not discover the real vector of the disease: fleas carried by rats. This discovery would be made four years later, in 1898, by Paul-Louis

21. Peptone-agar is a classic culture medium used in microbiology. It is a nutritional jelly on which microorganisms can develop into colonies. In addition to sugars, the gelatine also contains another nutritional supplement: peptone. This is a general term referring to various products of protein hydrolysis, which are sources of amino acids.

Simond in Karachi.[22] Like flies, fleas can incubate the disease for several months and then infect the rats, pets and humans they bite.

MEDICAL POSSIBILITIES: TOWARDS LESS VIRULENT STRAINS

After transplanting the plague bacillus into culture dishes several times (without using the bacillus to inoculate animals), Yersin noticed that less virulent[23] colonies developed.

> *It can be observed […] that some colonies develop much more than others. […] When animals are inoculated with the latter, their virulence is much weakened.*

Using a sample taken from the lymph nodes of a convalescing patient, he isolated a strain that was completely harmless for animals, including the most vulnerable mice. As this bacillus was in all other respects identical to the agent causing the disease, this result suggested that it might be possible to develop a vaccinal strain to protect the population from the plague. Yet Yersin remained on his guard, for at this stage he planned to immunise animals only:

> *These very meaningful facts allow me to think that inoculation with less virulent or non-virulent races or varieties of the specific bacillus would no doubt give animals immunity from the disease.*

In the event, Yersin's work on vaccination did not bear fruit. The task of obtaining a microbe that was harmless to humans but produced immunity from the plague proved particularly challenging.

Unable to produce a vaccine, Yersin worked alongside Albert Calmette and Émile Roux in 1895 to produce an anti-plague serum. The bacillus was injected into horses, which produced antibodies to fight the plague, thereby protecting themselves against the disease. By transfusing the protective antibodies to humans, the serum extracted from the horses' blood cured several infected patients in Canton and then in Amoy. However, it was not until the 1930s, with the work of Georges Girard and Jean-Marie Robic at the Institut Pasteur in Tananarive (Madagascar), that a successful vaccine would be developed.

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22. The biologist and army doctor Paul Louis-Simon (1858–1947) is remembered for his research into fleas as vectors of the plague and his work on yellow fever. Alongside his duties in the colonial army, he was also director of the Institut Pasteur of Saigon and of the Imperial Institute of Bacteriology in Constantinople. See his biography (in French) on the website of the Institut Pasteur.
23. In biological terms, the virulence of a microbe is a measure of its ability to multiply in the organism and cause a pathology.

Conclusions

In terms of scientific methodology, the work Yersin accomplished in the space of a few weeks remains exemplary. His discovery in a humble straw hut in Hong Kong paved the way to future research that would put an end to the plague as a public-health problem. Let's also not forget the bravery of this doctor and his colleagues, who, in order to achieve their aims, had no qualms about working in infected areas. Though it did not affect the quality of his research, the risk of contagion was always on the doctor's mind. The following letter to his mother, which gives the text we have just analysed a human dimension, attests to this:

Hong Kong, 1894

Dear Mum,

I'm sure you must be a little anxious to receive this letter, knowing I'm in a place one wouldn't exactly describe as a tourist destination!

After spending a few days in the hotel, I had a straw hut built next to the hospital for plague victims and moved in with my personal belongings and laboratory equipment.

It wasn't at all straightforward and if I hadn't had the luck to meet a kindly Catholic missionary, who agreed to accompany me everywhere and act as my interpreter, I don't know how I would have got by! The missionary's name is Father Vigano. He has been living in Hong Kong for 30 years, so he knows everybody.

I've already been able to study a dozen cases and it wasn't difficult to identify the microbe that multiplies in the bubo, the lymph nodes, the spleen, etc. It looks like a little stick, longer than it is wide, and which is difficult to stain. It kills mice and guinea pigs, which all display the lesions characteristic of the plague. It's always there; in my mind, there is no doubt.

Along with this letter I am sending a number of small sealed tubes containing pulp from plague buboes to the Institut Pasteur. The disease can then be studied in Paris. My experiments here are very limited because my laboratory is extremely poorly set up.

Hong Kong is a very picturesque city, built next to the sea on the slope of a sheer mountain 600 metres high, with houses staggered right up to the summit. The Chinese populations numbers more than 200,000 souls. It has now halved due to emigration caused by the plague. We are right in the middle of the rainy season: there are deluges of water, and after one of these the epidemic redoubles in force. Fatality is very high: 95% of cases. Up until now only 3 Englishmen have been infected. I don't count *the number of Portuguese; it's much higher. One of the days I'll try to take a little photograph of my straw hut with me standing in front and send it to you. I'm still keeping very well, aside from slight fatigue, because, as I'm on my own, I have to do everything myself.*

I could tell you much more, but there are two bodies waiting for me, and the gentlemen seem in a hurry to get to the cemetery. Farewell, darling Mum, wash your hands after you've read my letter to avoid catching the plague!

Your son, affectionately,

A. Yersin

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(March 2009)

(Translated by Helen Tomlinson, published December 2014)