

ALEXANDER YERSIN – YERSINIA PESTIS ALEXANDER YERSIN – YERSINIA PESTIS ALEXANDER YERSIN – YERSINIA PESTIS

do

https://doi.org/10.56238/arev7n11-200

Submission date: 10/17/2025 Publication Date: 11/17/2025

Francisco Prado Reis¹, Raissa Pinho Morais², Felipe Matheus Sant'Anna Aragão³, Iapunira Catarina Sant'Anna Aragão⁴, Francisco Guimarães Rollemberg⁵, Vera Lúcia Correa Feitosa⁶, José Aderval Aragão⁷

ABSTRACT

This article describes the history of plague, contextualizing the three major pandemics: the Plague of Justinian (541 CE), the Black Death (1347 CE), and the Third Pandemic (1894 CE). The Black Death is presented as the most devastating, responsible for the death of up to 50% of the European population and a catalyst for significant social and economic transformations. Recent research, utilizing paleoecology, questions the uniformity of the Black Death's demographic impact, suggesting regional variations in mortality and agricultural growth. The central focus is Alexandre Yersin, a Swiss-French scientist from the Pasteur Institute. In 1894, during an outbreak in Hong Kong, Yersin isolated and identified the bacillus causing the plague, subsequently named Yersinia pestis. The text narrates his arduous journey, his rivalry with Kitasato Shibasaburo, and how, despite unfavorable conditions, his discovery was crucial and formally recognized decades later. Yersin's contribution was fundamental to understanding the disease's epidemiology and to the development of treatments. The article concludes that, although plague is now more controllable, sporadic cases still occur globally, and there are concerns about potential resurgences, accidental or intentional, highlighting the continued relevance of research into the disease.

Keywords: Black Death. Pandemics. *Yersinia pestis*. Alexandre Yersin. Demographic Impact.

¹ Professor. Universidade Tirandentes. E-mail: franciscopradoreis@gmail.com

Orcid: https://orcid.org/0000-0002-7776-1831 Lattes: http://lattes.cnpq.br/6858508576490184

² Master's student in the Health and Environment. Universidade Tirandentes.

E-mail: raissa.pinho@souunit.com.br Orcid: https://orcid.org/0000-0001-5860-1712

Lattes: http://lattes.cnpq.br/1694249681084583

³ Cardiology Resident. Instituto do Coração (INCOR). Universidade de São Paulo (FMUSP).

E-mail: felipemsaragao@hotmail.com Orcid: https://orcid.org/0000-0001-9211-7000

Lattes: http://lattes.cnpq.br/4619345212343744

Internal Medicine Specialist. Hospital Municipal Dr. Munir Rafful (HMMR)

E-mail: icatarinasaragao@hotmail.com Orcid: https://orcid.org/0000-0002-5298-537X

Lattes: http://lattes.cnpq.br/6291628187714859

⁵ Urological surgeon. E-mail: rollembergchico@icloud.com

Orcid: https://orcid.org/0009-0009-3972-1669

⁶ Professor of Molecular Biology. Universidade Federal de Sergipe. E-mail: vera_feitosa@uol.com.br Orcid: https://orcid.org/0000-0001-5705-6433 Lattes: http://lattes.cnpq.br/3337321488338686

⁷ Professor of Clinical Anatomy. Universidade Federal de Sergipe. E-mail: adervalufs@gmail.com Orcid: https://orcid.org/0000-0002-2300-3330 Lattes: http://lattes.cnpq.br/6911783083973582



ISSN: 2358-2472

RESUMO

Este artigo descreve a história da peste, contextualizando as três grandes pandemias: a Peste de Justiniano (541 d.C.), a Peste Negra (1347 d.C.) e a Terceira Pandemia (1894 d.C.). A Peste Negra é apresentada como a mais devastadora, responsável pela morte de até 50% da população europeia e catalisadora de importantes transformações sociais e econômicas. Pesquisas recentes, utilizando paleoecologia, questionam a uniformidade do impacto demográfico da Peste Negra, sugerindo variações regionais na mortalidade e no crescimento agrícola. O foco central é Alexandre Yersin, um cientista suíço-francês do Instituto Pasteur, que em 1894, durante um surto em Hong Kong, isolou e identificou o bacilo causador da peste, posteriormente denominado Yersinia pestis. O texto relata sua trajetória, sua rivalidade com Kitasato Shibasaburo e como, apesar das condições adversas, sua descoberta foi essencial e reconhecida décadas mais tarde. A contribuição de Yersin foi fundamental para compreender a epidemiologia da doença e para o desenvolvimento de tratamentos. O artigo conclui que, embora a peste seja atualmente mais controlável, ainda ocorrem casos esporádicos no mundo e há preocupações sobre possíveis ressurgimentos, acidentais ou intencionais, destacando a relevância contínua da pesquisa sobre a doença.

Palavras-chave: Peste Negra. Pandemias. *Yersinia pestis*. Alexandre Yersin. Impacto Demográfico.

RESUMEN

Este artículo describe la historia de la peste, contextualizando las tres grandes pandemias: la Peste de Justiniano (541 d.C.), la Peste Negra (1347 d.C.) y la Tercera Pandemia (1894 d.C.). La Peste Negra se presenta como la más devastadora, responsable de la muerte de hasta el 50% de la población europea y catalizadora de importantes transformaciones sociales y económicas. Investigaciones recientes, utilizando paleoecología, cuestionan la uniformidad del impacto demográfico de la Peste Negra, sugiriendo variaciones regionales en la mortalidad y en el crecimiento agrícola. El enfoque central es Alexandre Yersin, un científico suizo-francés del Instituto Pasteur, quien en 1894, durante un brote en Hong Kong, aisló e identificó el bacilo causante de la peste, posteriormente denominado Yersinia pestis. El texto narra su trayectoria, su rivalidad con Kitasato Shibasaburo y cómo, a pesar de las condiciones adversas, su descubrimiento fue esencial y reconocido décadas después. La contribución de Yersin fue fundamental para comprender la epidemiología de la enfermedad y para el desarrollo de tratamientos. El artículo concluye que, aunque la peste es actualmente más controlable, aún ocurren casos esporádicos en diferentes partes del mundo y existen preocupaciones sobre posibles resurgimientos, accidentales o intencionales, lo que resalta la relevancia continua de la investigación sobre la enfermedad.

Palabras clave: Peste Negra. Pandemias. *Yersinia pestis*. Alexandre Yersin. Impacto Demográfico.



1 INTRODUCTION

The Black Death, which devastated Europe, Western Asia, and North Africa between 1347 and 1352, stands as the most catastrophic pandemic in human history. Historians estimate that up to 50% of Europe's population perished during this period and attribute profound religious, political, and social transformations to the pandemic — changes that even paved the way for major cultural and economic developments such as the Renaissance. The origin of the medieval Black Death pandemic (1346–1353 AD) has long been the subject of research, owing to its massive demographic impact and enduring historical consequences (Benedictow, 2004).

The millennia-long history of pandemics that have afflicted humanity reveals that we are faced with cyclical and recurring phenomena that profoundly shape human life. In the biblical Book of 1 Samuel, written around 1000 BC, the Phillistines are said to have suffered from an outbreak of tumors associated with rodents — possibly an early account of bubonic plague. Similarly, in 627 BC, the prophet Jeremiah described a devastating calamity of his time, proclaiming: "Hear, O women, the word of the Lord; receive the words from His mouth, and teach your daughters wailing, and every one her neighbor lamentation." "For death has climbed through our windows, entered our palaces, to cut off children from the streets and young men from the squares. Corpses of men will fall like dung on the open field, like sheaves behind the reaper, with no one to gather them." (Jeremiah 9:20–22)

John Kelly (2021), in his book *The Great Death*—as it was known to medieval Europeans—classified it as one of the seminal events of the last millennium, a catastrophe that cast a vast shadow over the centuries that followed and remains deeply embedded in the collective memory of the West. Glatter and Finkelman (2021), along with numerous historians, have described it as one of the deadliest and darkest chapters in human history. The devastating onslaught swept across Europe and Asia in the mid-1300s and is regarded as one of the most infamous pandemics in recorded history. Many scholars estimate that it claimed the lives of around 50 million Europeans—roughly half of the continent's population. From the ports along the China Sea to the fishing villages on the coast of Portugal, the Black Death unfolded with an almost apocalyptic intensity, inflicting suffering and death on a scale so immense that, even after two world wars and 27 million deaths from AIDS worldwide, it continues to haunt the human imagination.

First identified as *Bacterium pestis* and later renamed *Pasteurella pestis*, the Gramnegative, rod-shaped bacillus isolated by Alexandre Yersin and Kitasato Shibasaburo in 1894



was officially reclassified in 1967 as *Yersinia pestis*, designating a new genus distinct from other *Pasteurella* species. *Y. pestis* is an aerobic, Gram-negative coccobacillus belonging to the family *Enterobacteriaceae*.

Most historians agree that the causative agent of the plague, *Yersinia pestis*, originated in China or Central Asia—along the Silk Road—and spread through fleas parasitizing rats, which were common pests at the time and thrived in the holds of ships. As Ujvari (2021) noted, the trajectory of plague outbreaks closely followed established human trade and travel routes.

Spyrou et al. (2022), after performing genetic analyses on the teeth of individuals buried in cemeteries near Lake Issyk-Kul in Kyrgyzstan—dating to eight years before the Black Death reached Europe—identified an ancient strain of Yersinia pestis. Approximately thirty skeletons were examined, and DNA extracted from their teeth revealed genetic traces of the bacterium. The researchers concluded that these remains represented the most ancient known lineage of the pathogen, potentially pinpointing the origin of the Black Death, more than 600 years after it decimated tens of millions of people across Europe, Asia, and North Africa. University of Stirling historian Dr. Philip Slavin, a member of the team, was instrumental in the historic discovery. He said: "Our study puts an end to one of the biggest and most fascinating questions in history and determines when and where the most notorious and infamous killer of humans emerged." The principal objective of this article is to acknowledge and highlight the figure of Alexandre Yersin, one of modern medicine's heroes, and his fundamental contribution to the discovery of Yersinia pestis, the etiological agent of plague, thereby correcting the historical oversight of his due recognition. To achieve this, an overview of the major plague pandemics and the impact of his discoveries will be provided.

2 THE THREE GREAT PANDEMICS

John Frith (2012), reporting on the history of the plague, described that there were three major global pandemics of plague recorded, in 541, 1347, and 1894 CE, each causing devastating mortality of people and animals across nations and continents. These three great plague pandemics had different geographical origins and paths of spread. The Justinian Plague of 541 began in central Africa and spread to Egypt and the Mediterranean. The Black Death of 1347 originated in Asia and spread to the Crimea, then to Europe and Russia. The third pandemic, in 1894, originated in Yunnan, China, and spread to Hong Kong and India, then to the rest of the world. This is why John Kelly (2021) called the plague the most



successful example of a wandering disease recorded in history, and an extraordinary feat for a disease that does not even originate in humans.

The first major bubonic plague pandemic in recorded history, characterized by the appearance of buboes and septicemia, was the Justinian Plague of 541 CE, named after Justinian I, the Byzantine emperor at the time. The epidemic is believed to have originated in Ethiopia, Africa, before spreading to Pelusium, Egypt, in 540 CE. From there, it advanced westward to Alexandria and eastward to Gaza, Jerusalem, and Antioch, eventually traveling aboard ships along the Mediterranean maritime trade routes. By the autumn of 541 CE, the plague had reached Constantinople (modern-day Istanbul).

The Byzantine court historian Procopius of Caesarea, in his monumental work *History* of the Wars, provided one of the earliest and most detailed eyewitness accounts of the epidemic. He described individuals suffering from fever, delirium, and painful swellings (buboes), remarking that the plague was an affliction "by which the whole human race was almost annihilated." Procopius further described the symptoms in vivid detail:

"... with most of them, it happened that they were struck by the disease without realizing what was happening, whether through waking vision or a dream. They experienced a sudden fever—some upon waking, others while walking, and still others while engaged in their daily tasks—without any regard for what they were doing. The body showed no change from its previous color, nor was it hot as would be expected in fever, nor did any inflammation immediately appear. The fever was so languid at first that neither the sufferers nor the physicians who examined them suspected any danger. It was natural, therefore, that none of those who contracted the disease expected to die from it. Yet on the same day in some, on the following day in others, and in the remainder within a few days, a bubonic swelling developed—not only in the area below the abdomen, known as the *boubon*, but also in the armpits, behind the ears, and even on the thighs." (*Procopius of Caesarea, History of the Wars*, Book II).

The epicenter of the Justinian pandemic was Constantinople, where the outbreak reached its peak in the spring of 542 CE, claiming an estimated 5,000 lives per day—with some contemporary reports suggesting as many as 10,000 daily deaths. Ultimately, it is believed that more than one-third of the city's population perished. The devastation was not confined to the Byzantine capital: successive waves of the plague spread across Europe, the Middle East, and North Africa, marking one of the earliest and most devastating pandemics in recorded history. Other major outbreaks of the Justinian Plague occurred across Europe



and the Middle East over the following two centuries — striking Constantinople in 573, 600, 698, and 747 CE; Iraq, Egypt, and Syria in 669, 683, 698, 713, 732, and 750 CE; and Mesopotamia in 686 and 704 CE.

The Black Death arrived in Europe in the 1340s. The second Black Death pandemic reached Messina, Sicily, probably from Central Asia, via Genoese ships carrying flea-infested rats in October 1347. In 1347, the plague was brought from Asia Minor to Crimea by the Tatar armies of Khan Janibeg, who besieged the city of Kaffa (now Feodosya in Ukraine), a Genoese trading city on the shores of the Black Sea. A wave of plague infections began that quickly spread across most of Europe in a relentless manner. It was the first major European outbreak of the second great Eastern European pandemic that occurred throughout the 14th to 18th centuries. In 1348, the disease reached Marseille, Paris, Germany, Switzerland, and Austria, and then Spain. It spread to England and Norway in 1349. It decimated London in 1349 and reached Scandinavia, northern England, and Eastern Europe in 1350. The Tatars left Kaffa and carried the plague with them, spreading it further to Russia and India.

The term "Black Death" was not used until much later in history; in 1347, it was simply known as "the pestilence" or "pestilentia." Several explanations exist for the origin of the later term. One theory suggests that it referred to the hemorrhagic purpura and ischemic gangrene of the limbs that sometimes resulted from septicemia. According to Ziegler (1969), the expression derives from the Latin translation pestis atra or atra mors—with atra meaning "terrible" or "dreadful," a word whose connotation also implied "black," and mors meaning "death." Thus, atra mors came to be translated as "Black Death."

For a person struck by the Black Death in the 14th century, the disease was effectively a death sentence, as no cure existed. The bubonic plague was the most common form of the illness. Its name originates from one of its most recognizable symptoms: the painful swelling of lymph nodes, which formed pus-filled swellings known as buboes (hence the term "bubonic") —typically appearing in the groin or armpits. Much like HIV, the pathogen responsible for the Black Death possessed an extraordinary ability to evade and confuse the body's immune system. By the time the immune defenses began to respond, the infection had usually progressed beyond control. As a result, the plague proved devastatingly lethal, capable of killing nearly any host it infected—including rats, marmots, gerbils, squirrels, camels, chickens, pigs, dogs, and cats. It thus earned its reputation as an adaptable and indiscriminate killer.



In his diary, the Italian writer and poet Giovanni Boccaccio (1313–1375) vividly described the symptoms of the plague, noting "the appearance of gavoccioli [buboes] in the groin or armpits, some of which grew as large as a common apple, others as large as an egg." He further observed that "the deadly gavoccioli spread indiscriminately to all parts of the body; then, after that, the symptoms of the disease changed to black or livid spots appearing on the arms and thighs, and on all parts of the body."

Between 1347 and 1350, the Black Death claimed the lives of approximately one quarter of Europe's population—more than 25 million people—and an additional 25 million in Asia and Africa. Mortality was particularly devastating in urban centers such as Florence, Venice, and Paris, where more than half the population succumbed to the plague. A second major epidemic, known as the *pestis secunda*, struck in 1361, killing an estimated 10–20% of Europe's population. During this period, other virulent infectious diseases with high mortality rates—such as smallpox, infantile diarrhea, and dysentery—also plagued the population. By 1430, the population of Western Europe remained smaller than it had been in 1290, and demographic recovery to pre-1348 levels only occurred at the beginning of the 16th century. By 1349, most of Europe had been infected by the Black Death, but the deadly bacterium continued its relentless spread, reaching various regions of the Middle East and North Africa by 1350. The ferocious *Yersinia pestis* bacteria even reached Mecca, the holy city of Islam, carried by pilgrims performing the Hajj.

Although the initial pandemic waned toward the end of the 14th century, recurrent outbreaks continued to devastate Europe over the next four centuries (*Bramante; Stenseth; Walløe, 2016*). By 1351, the pace of the contagion had slowed considerably, marking the end of the initial and most catastrophic phase of the pandemic. By around 1353, the Black Death had been suppressed. The final death toll is unknown, but it is estimated that the outbreak claimed more than 200 million lives. In Europe alone, between 25 and 50 million people died. The plague also led to the massacres of 210 Jewish communities across the continent. In total, medieval Europe lost about 50% of its population. Between 1656 and 1657, two-thirds of the populations of Naples and Genoa died from the disease. In 1665–1666, London lost about a quarter of its citizens—approximately 100,000 people—and a similar number died in Vienna in 1679. Moscow recorded more than 100,000 deaths from the plague during 1770–1771. The bubonic plague of the 14th century transformed European society and economies, leading to a severe shortage of labor in agriculture and skilled crafts. The geopolitical impact



included a decline in the power and international status of the Italian states. The plague had circled Europe in just under four years.

The third plague pandemic, often referred to as the modern pandemic, emerged in the mid-19th century. It began in Yunnan Province, in southwestern China, around 1855, where recurrent outbreaks had been documented since 1772, and later spread to Taiwan (*Bramanti, Stenseth, & Walløe, 2016*). The disease spread to the Americas and Europe via maritime trade routes, with the first known European cases reported in London in 1896. It struck Canton (Guangzhou) in 1894, causing approximately 70,000 deaths, and soon after reached Hong Kong. From there, ships carried the plague to Japan, India, Australia, and North and South America between 1910 and 1920. It is estimated that 12 million people died of plague in India between 1898 and 1918. Merchant rats brought the disease to San Francisco's Chinatown in 1900 (*Perry & Fetherston, 1997*). Although only a few cases of plague have been reported in Europe since 1950, sporadic outbreaks continue to occur worldwide. In total, it is estimated that more than 200 million people have died from plague throughout human history.

The third pandemic fluctuated in intensity across the globe for the next five decades, officially subsiding only in 1959. By then, the disease had caused over 15 million deaths, the vast majority occurring in India. Later outbreaks were recorded in China and Tanzania (1983), Zaire (1992), and India, Mozambique, and Zimbabwe (1994). In Madagascar, during the mid-1990s, a multidrug-resistant strain of *Yersinia pestis* was identified. Currently, about 2,000 cases of plague occur annually, primarily in Africa, Asia, and South America, with a global case-fatality rate ranging from 5% to 15%. According to Deschutes County Health Services, a handful of human plague cases still appear each year in the United States and around the world, although the disease today is much rarer and far more treatable. In February 2024, a rare human case was confirmed in rural Oregon.

More than just a historical oddity, outbreaks of plague continue to occur and occasionally cause deaths around the world. Since the 1990s, despite health surveillance efforts, bubonic plague has been considered a re-emerging disease by the World Health Organization (WHO). In the 21st century, cases of plague have been reported in Africa, Asia, and the Americas (Yuan *et al.*, 2020).

In Brazil, bubonic plague arrived during the third pandemic of the disease in 1899. The physician, public health specialist, bacteriologist, and epidemiologist Oswaldo Cruz contributed to the fight against the plague in Brazil by organizing teams to eliminate rats and



encouraging the population to capture the animals by offering cash rewards. The most significant outbreaks were recorded in the states of Ceará and Paraíba in 1980, with 76 reported cases and 3 deaths. The main risk areas are located in mountainous regions, namely the Uruburetama, Macaco, Baturité, Ibiapaba, Matas, Pedra Grande, and Chapada do Araripe mountain ranges. The last reported case occurred in 2005 in the state of Ceará, in the municipality of Peste Branca.

3 DEMOGRAPHIC IMPACT OF THE BLACK DEATH IN EUROPE

Estimates of the number of people who died from the Black Death vary widely, but most historians generally believe that between 75 and 200 million people perished. In Europe, the Black Death killed approximately 30–50% of the population, or between 50 and 75 million people, with the most affected areas possibly losing up to 80% of their inhabitants. Across Eurasia, it is estimated to have killed between 75 and 200 million people, and worldwide, around 75 million deaths occurred during the 14th century, when the global population was still below 500 million.

Recent research has questioned whether the Black Death truly decimated half of Europe's population. A new approach—Big Data Paleoecology (BDP)—has used palynology (the study of pollen) to assess the demographic impact of the Black Death on a regional scale across Europe, independently of written sources and traditional archaeological materials. The analysis of 1,634 pollen samples from 261 sites reflects changes in landscape and agricultural activity. Findings suggest that mortality from the Black Death varied considerably among European regions. While the pandemic was immensely destructive in some areas, in others it had a much milder impact. Surprisingly, the BDP identified a sharp agricultural decline in several regions of Europe, independently corroborating historical analyses suggesting high mortality in Scandinavia, France, western Germany, Greece, and central Italy, thereby providing strong validation for this approach. At the same time, there was substantial evidence of continuity and uninterrupted agricultural growth in Central and Eastern Europe, as well as in several parts of Western Europe, particularly Ireland and the Iberian Peninsula. The present territory of the United Kingdom and northwestern Europe were the regions that suffered the least.

Thus, the BDP invalidated traditional narratives of the Black Death that assumed *Y. pestis* was uniformly prevalent—or nearly so—throughout Europe and that the pandemic had a universally devastating demographic impact. Although these findings suggest that the Black



Death was not as catastrophic as many historians have argued, the authors of this study did not propose a new estimate for the actual number of pandemic victims. "We don't feel comfortable taking a guess," stated Timothy Newfield, a disease historian at Georgetown University and one of Dr. Izdebski's collaborators. This indicates that the mortality associated with the Black Death was neither universal nor uniformly catastrophic. If it had been, the sedimentary records of the European landscape would reflect it.

Other experts were not convinced by the findings of the new study. John Aberth, author of *The Black Death: A New History of the Great Mortality in Europe, 1347–1500*, stated that the research did not alter his view that approximately half of Europe's population perished during the pandemic. He expressed doubt that the plague could have spared entire regions of the continent while devastating neighboring ones, emphasizing that European societies were highly interconnected even during the Middle Ages through trade, travel, commerce, and migration. Aberth concluded by noting his skepticism that any large region could have escaped unscathed.

It is often said that Europe took more than two centuries to restore its population to pre-plague levels. Yet the losses extended beyond demography: during this period, the continent also suffered profound setbacks in labor, art, culture, and the economy.

Today, this form of the disease has been largely eradicated. However, according to the World Health Organization, between 2010 and 2015 there were 3,248 reported cases worldwide, resulting in 584 deaths. With modern medical treatments, the plague can now be effectively controlled and managed, reducing both mortality and transmission risks.

The plague can be found on every continent except Oceania. Although the risk of infection remains low, it still exists. The regions with the highest concentration of cases are located in Africa, Asia, and South America, with most occurrences since the 1990s reported in the Democratic Republic of Congo and Peru.

During MEDTROP 2024, Dr. Alzira Almeida, Emeritus Researcher at the Oswaldo Cruz Foundation, explained that despite the disease maintaining a low mortality rate since the 1990s and being under control in Brazil since 2005—according to the Ministry of Health—it has not yet been completely eradicated. She cited a report from *BBC News Brasil* noting that cases of plague continue to be recorded in other countries, such as the United States, where 14 deaths occurred between 2000 and 2020, with an average of seven cases per year.

Dr. Almeida also highlighted that both African and European countries have reported cases in recent years. According to her, a resurgence of the Black Death pandemic could



occur in two ways: first, through the intentional reintroduction of the pathogen via bioterrorism; and second, unintentionally, through the accidental spread of infection by people, fleas, rodents, or other animals, including domestic species.

4 ALEXANDRE YERSIN AND THE MODERN HISTORY OF THE BLACK DEATH

According to Butler (2014), the modern history of the plague began in 1894, when Alexandre Yersin successfully isolated the causative bacterium in culture and identified it under a microscope. Other major milestones in modern plague research include the development of the first anti-plague serum by Yersin, Émile Roux, Albert Calmette, and Armand Borrel in 1895, as well as more recent studies suggesting that the Black Death was transmitted not only by rats but also by lice and fleas. These advances established the plague as a laboratory-confirmed bacterial disease, enabling accurate diagnosis, the creation of effective antibiotic treatments, and a deeper scientific understanding of its pathogenesis. In 1980, the genetic relationship between *Yersinia pestis* and *Yersinia pseudotuberculosis* was identified, and in 1981, researchers discovered three plasmids associated with virulence in *Y. pestis*, marking important progress in molecular bacteriology.

Alexandre Émile Jean Yersin was born in 1863 in Aubonne, in the canton of Vaud, Switzerland, the posthumous son of Jean-Alexandre-Marc Yersin and Fanny-Isaline-Emilie Moschell. His father, a teacher, died just weeks before his birth. Yersin began studying medicine in Lausanne, Switzerland, in 1883, continued his studies in Marburg, Germany, in 1884, and later transferred to Paris (1884–1886).

The young Alexandre Yersin grew up during a tumultuous period in medicine and politics. The Franco-Prussian War (July 1870–January 1871) culminated in the defeat of Napoleon III (Treaty of Frankfurt, May 1871) and in the coronation of Prussian King William I as Emperor of a unified Germany in the Hall of Mirrors at Versailles—all under the strategic direction and intellectual influence of Otto von Bismarck.

The Swiss scientist Alexandre Yersin joined the Pasteur Institute in 1885, at only 22 years of age, and worked under the supervision of Émile Roux. In 1886, he entered Louis Pasteur's laboratory at the École Normale Supérieure, and in 1889 he became part of the newly founded Pasteur Institute as a research collaborator of Roux, who introduced him to Pasteur. Together, Yersin and Roux contributed to the development of anti-rabies serums and co-discovered the diphtheria toxin produced by the bacillus *Corynebacterium diphtheriae*. At 25 years old, three years after his arrival in Paris, Yersin wrote and defended his doctoral



thesis, earning a bronze medal, which he later gave to his mother. In this work, he described a new experimental form of tuberculosis, which he called "typhus bacillus" or "typhus bacillosis." This became known in medical literature as "Yersin's type of tuberculosis." Such an achievement alone would have secured his name in the history of medicine. At that time, however, Yersin was not yet a licensed physician, nor a French citizen, as the practice of medicine was legally restricted to citizens of the French Republic. The case was quickly resolved, as Yersin's mother was of French ancestry.

Roux warned Calmette that Yersin was a unique individual, a solitary spirit who aspired to become a sailor or an adventurer. Pasteur and Roux eventually accepted the inevitable—Yersin could not be confined to the laboratory bench. More than that, he possessed an insatiable curiosity and a profound aversion to routine. In 1889, Yersin acquired French citizenship, but his unease with academic lecturing soon reawakened his restless, exploratory nature. In 1890, he left France for indochina, joining the Compagnie des Messageries Maritimes as a ship's physician on the Vietnam passenger line.

In his biographical novel *Plague and Cholera*, Patrick Deville (translated by Marília Scalzo, 2017) described Yersin as an individualist, as altruists so often are—an ascetic who single-handedly built an empire within an empire. Yersin was 26 years old when he wrote the Rimbaudian phrase: "Life is not worth living without movement." Pasteur's own maxim seemed to resonate in his mind: "I would feel like I was committing a crime if I spent a day without working." Another statement attributed to Yersin reveals his temperament: "Life in a laboratory seems impossible to me once you have experienced freedom and life in the open air."

In 1892, at the age of 29, Yersin joined the colonial health service, and at 31, in 1894, he was sent to Hong Kong, where a plague epidemic had broken out in May. It was in this city that the race to identify the causative agent of the Black Death unfolded, represented by two young scientists from rival schools of thought: the French Pasteur Institute, founded by Louis Pasteur, and the German school led by Robert Koch. Koch's representative, Shibasaburo Kitasato, appeared to hold an advantage, having access to modern laboratory equipment and the support of a large research team. Pasteur's representative, in contrast, was considered disconnected and under-resourced, having traveled alone from French Indochina. On June 15, 1894, Yersin arrived in Hong Kong, which had been established as a British colony following the First Opium War in 1841.



Possessing a keen sense of observation, Yersin recorded his initial impressions through both photographs and written notes: pestilential corpses scattered in the streets, floating in puddles of stagnant water, lying in gardens, and even aboard moored boats. In his notes from that first night, he wrote: "I noticed many dead rats scattered on the ground and decomposition in the sewers. British soldiers emptied and burned houses, piled up belongings, threw lime and sulfuric acid, and erected red brick walls to block access to infected neighborhoods." Lawson, a Scottish physician appointed by the British Colonial Medical Service, had established several leprosariums throughout Hong Kong—facilities that soon became veritable death traps. Straw mats were thrown on the floors for patients, only to be later burned along with their occupants. Under the tropical rains, carts laden with stacked corpses passed through the streets.

Shibasaburo Kitasato, the world-renowned bacteriologist, was received with admiration and full honors by Dr. James Lawson, who directed Hong Kong's hospitals. Provided with ample equipment, Kitasato was granted immediate access to a laboratory at Kennedy Hospital, where all plague victims' corpses had been reserved for his exclusive use. When Alexandre Yersin arrived three days later, he was completely ignored by Lawson, who dismissed him as "the Frenchman," claiming he had never heard of him. Yersin was allotted only precarious accommodations—an open corridor at Kennedy Hospital—and was denied access to the plague corpses, all of which had been assigned to the Japanese delegation. What ensued began to resemble a Scottish–French rivalry (Solomon, 1997). This entire mission was meticulously documented by Yersin himself in his Hong Kong diary (Yersin, 1894). From the very beginning, the circumstances were deeply unequal. It was a moment when Yersin might well have abandoned his efforts; under those conditions, as historians later observed, he was clearly the underdog.

On June 14, 1894, one day before Alexandre Yersin's arrival in Hong Kong, Shibasaburo Kitasato announced that he had identified and isolated the etiologic agent of the plague from patients' blood samples. His results—more precisely, those communicated by his collaborator James Lowson, followed by Kitasato's own detailed article on August 25 (*Kitasato*, 1894). Kitasato had arrived in Hong Kong three days before Yersin, supported by a team of six assistants, while Yersin had traveled alone from French Indochina, carrying only a microscope, sterilizer, and basic culture materials in his luggage.

During his first five days of investigation, Yersin faced repeated frustration working solely with blood samples from infected patients, the only material initially available to him.



ISSN: 2358-2472

Although he already suspected that the buboes were the key anatomical sites to be examined, this required access to corpses, which he lacked. With the assistance of his local guide and interpreter, Father Vigano, Yersin eventually obtained bubo samples from deceased individuals, having secured them by bribing English sailors responsible for corpse disposal. From these specimens, he successfully stained and isolated short rod-shaped bacilli, which he cultured and subsequently used to inoculate mice and guinea pigs—all of which died within 24 hours, each presenting a typical bubo. Because the open corridor where Yersin had been placed was neither suitable nor safe for laboratory work, he decided to construct his own facility. With the assistance of Father Vigano, he built a small straw-andbamboo hut in just two days, near the Alice Memorial Hospital—itself a larger, though equally rudimentary, straw structure. Within a week of his arrival, Yersin successfully isolated the causative agent of the plague, sent samples of buboes to Paris, and formally reported his findings to the British authorities. Following his complaint to these authorities, he finally obtained official access to plague corpses, which allowed him to detect the same microorganism not only in human victims, but also in dead rats and in the soil of infected neighborhoods across Hong Kong.

His specimens were sent to Albert Calmette and Amédée Borrel at the Pasteur Institute, who confirmed his discovery and began developing a therapeutic antiserum using the bacterium. Yersin also forwarded material to James Lowson, who hastily shared the results with Kitasato's Japanese team. Upon examining Yersin's preparations, Lowson reportedly advised the Japanese to search for the microbe in the buboes, acknowledging privately to Yersin that the organism previously isolated by Kitasato was not the same. The situation soon escalated: Kitasato claimed priority for the discovery, igniting a scientific and political controversy that persisted for decades. Historical vindication came only in the 1970s, when the plague bacillus was officially renamed *Yersinia pestis*, thereby recognizing Alexandre Yersin as its true discoverer.

With the end of the epidemic, Yersin decided to return to Saigon on August 3, 1894. Meanwhile, his findings had already reached France: on June 30, his letter announcing the discovery was presented verbally to the French Academy of Sciences by Émile Duclaux, then acting director of the Pasteur Institute (1895–1904). In September 1894, Yersin's complete report appeared in the *Annales de l'Institut Pasteur* (Yersin, 1894), officially establishing him as the first scientist to observe and describe the plague bacillus responsible for the Black Death. Within a single week, Yersin had written the article that sealed his place in medical



ISSN: 2358-2472

history. In his laboratory notebook, he summarized his conclusions with remarkable lucidity: "The plague is therefore a contagious and inoculable disease. Rats are likely to be its main vehicle, but I have found that flies catch the disease." In just two months, Yersin had unraveled the mystery of one of humanity's deadliest epidemics. His discoveries in Hong Kong were fundamental to understanding the epidemiology of plague, laying the foundation for modern public health and vector control strategies that would endure for decades.

Against all odds, Yersin succeeded in identifying the true causative agent of the plague, producing results that were both accurate and reproducible. His connections with the Pasteurian network in Paris further ensured that his reputation and priority in the discovery were ultimately recognized and preserved. During his first autopsy in Hong Kong, Yersin meticulously described his experimental procedures: he aspirated fluid from a bubo, observed Gram-negative bacilli under the microscope, and inoculated laboratory animals, which subsequently died exhibiting the same bacterial invasion in their tissues. He then sealed a sample of the bubo in a glass tube and immediately dispatched it to Paris (*Hawgood*, 2008). With this body of evidence, as Patrick Deville notes, Yersin—who never knew his father and would never become one himself—at least attained the paternity of his discovery: Yersinia pestis.

But who was truly correct? The answer, paradoxically, came from the Japanese themselves. As early as 1895, Aoyama, the pathologist who had assisted Kitasato in Hong Kong, expressed doubts about the nature of the bacilli identified in the blood, suspecting that they were actually systemic streptococci. Later, in 1900, Tatsusaburō Yabe, chief physician of the Japanese Navy, examined the cultures preserved in Kitasato's laboratory and confirmed that they were, in fact, a species of pneumococcus.

"The honor of discovering the plague bacillus belongs solely to Yersin, and we sincerely regret that our distinguished microbiologist made an unbelievable mistake regarding the plague microbe." In the end, Kitasato appeared uncertain, as he later issued contradictory statements concerning his own findings. It is reported that Kitasato declared at the Sixth Biennial Conference of the Far Eastern Association of Tropical Medicine, held in Tokyo in 1925, that "the discovery of the plague bacillus is due to the great Yersin."

However, these quotations cannot be found in either the official conference proceedings or in the speech Kitasato delivered as president of the Association. The question of who was right or wrong was thoroughly analyzed by Bibel and Chen (1976), whose



examination of the published records demonstrated that Kitasato had misidentified the plague pathogen, although he never formally acknowledged his error.

How, then, did Yersin succeed in identifying the correct pathogen where Kitasato failed? The difference likely lies in their methodological approaches: Yersin examined bubonic material, which contained abundant bacilli, whereas Kitasato analyzed blood samples, where such bacteria are nearly absent. Furthermore, Kitasato cultured his samples at 37°C in a heated incubator, while Yersin, lacking such equipment, was forced to culture at ambient temperature (30–32°C) —a range that appears to be more favorable for the growth of the plague bacillus.

With the resurgence of bubonic plague in Hong Kong, Canton, and Amoy in the spring of 1896, Yersin left for China once again, but this time with his antiserum. As this antiserum had never been tested on humans, Yersin was reluctant to use it for ethical reasons. However, in Canton, Catholic Bishop Monsignor Chausse begged Yersin to treat Tisé, his 18-year-old Chinese seminarian, who had a fever and symptoms typical of the plague. Less than 12 hours after treatment, in the presence of the French consul in Canton, the patient miraculously recovered from the disease. Like Pasteur before him in Paris with his rabies vaccine (1885), Yersin now treated a patient with an antiserum whose efficacy and safety had only been proven in animals. In Amoy, he successfully repeated his treatment on 23 patients, with only two deaths.

After spending five years, having started his research in Paris in 1890 at the age of twenty-nine, he abandoned science, microbiology, and research, and became a physician on the ships of the French company *Messageries Maritimes* in Asia, sailing the Saigon–Manila and Saigon–Haiphong routes. He would never live in Paris again. After only two years at sea, he began to grow bored. The last day of May 1940 was also Yersin's last voyage, and he would never return to France. In 1891, he decided to settle in the city of Nha Trang, in Indochina (now Vietnam), where he spent almost half a century living and working until his death on March 1, 1943.

In the afterword to his book *Doctors & Discoverers: Lives That Created Modern Medicine*, John Galbraith Simmons (2004) made a statement that amounted to a retraction: an unforgivable omission evident to every reader of the book is that of Alexandre Yersin, a Swiss bacteriologist who became a naturalized French citizen and who can be considered one of the heroes of modern medicine. This omission would have condemned Yersin to die



as an unknown explorer among thousands of other forgotten explorers. This motivated me to write this article.

REFERENCES

- Aberth, J. (2023). The Black Death: A new history of the great mortality in Europe, 1347–1500. Speculum, 98(1).
- Benedictow, O. J. (2004). The Black Death, 1346–1353: The complete history. Boydell & Brewer.
- Bibel, D. J., & Chen, T. H. (1976). Diagnosis of plague: An analysis of the Yersin-Kitasato controversy. Bacteriological Reviews, 40(3), 633–651. https://pmc.ncbi.nlm.nih.gov/articles/PMC413974/
- Bramanti, B., Stenseth, N. C., Walløe, L., & et al. (2016). Plague: A disease that changed the course of human civilization. Advances in Experimental Medicine and Biology, 918, 1–26. https://doi.org/10.1007/978-94-024-0890-4
- Butler, T. (2014). Plague history: Yersin's discovery of the causative bacterium in 1894 enabled, in the subsequent century, scientific progress in understanding the disease and the development of treatments and vaccines. Clinical Microbiology and Infection, 20(3), 202–209. https://doi.org/10.1111/1469-0691.12540
- Deville, P. (2017). Plague and cholera (M. Scalzo, Trans.). Editora 34. (Original work published in French)
- Frith, J. (2012). The history of plague Part 1: The three great pandemics. Journal of Military and Veterans' Health, 20(2). https://jmvh.org/article/the-history-of-plague-part-1-the-three-great-pandemics/
- Glatter, K. A., & Finkelman, P. (2021). History of the plague: An ancient pandemic for the age of COVID-19. The American Journal of Medicine, 134(2), 176–181. https://doi.org/10.1016/j.amjmed.2020.08.019
- Hawgood, B. J. (2008). Alexandre Yersin (1863–1943): Discoverer of the plague bacillus, explorer, and agronomist. Journal of Medical Biography, 16(3), 167–174. https://doi.org/10.1258/jmb.2007.007017
- Izdebski, A., Guzowski, P., Poniat, R., & et al. (2022). Palaeoecological data indicate land-use changes across Europe linked to spatial heterogeneity in mortality during the Black Death pandemic. Nature Ecology & Evolution, 6, 297–306. https://doi.org/10.1038/s41559-021-01652-4
- Kelly, J. (2021). The great mortality: An intimate history of the Black Death, the most devastating plague of all time (C. W. Galindo, Trans.; 2nd ed.). Bertrand Brasil.
- Kitasato, S. (1894). The bacillus of bubonic plague. The Lancet, 144(3704), 428–430. https://doi.org/10.1016/S0140-6736(01)58670-5
- Perry, R. D., & Fetherston, J. D. (1997). Yersinia pestis: Etiologic agent of plague. Clinical Microbiology Reviews, 10(1), 35–66. https://doi.org/10.1128/CMR.10.1.35-66.1997



- Salomon, T. (1997). Hong Kong, 1894: The role of James A. Lowson in the controversial discovery of the plague bacillus. The Lancet, 350, 59–62.
- Simmons, J. G. (2004). Discovering doctors (R. Vinagre, Trans.). Houghton Mifflin Harcourt.
- Spyrou, M. A., Musralina, L., Gnecchi Ruscone, G. A., & et al. (2022). The source of the Black Death in 14th-century central Eurasia. Nature, 606, 718–724. https://doi.org/10.1038/s41586-022-04800-3
- Ujvary, S. C. (2021). History of epidemics (2nd ed., 2nd reprint). Contexto.
- Yersin, A. (1894). La peste bubonique à Hong-Kong. Annales de l'Institut Pasteur, 8, 662–667.
- Yuan, Y., & et al. (2020). The characteristics and genome analysis of the novel Y. pestis phage JC221. Virus Research, 283, Article 197982. https://doi.org/10.1016/j.virusres.2020.197982
- Ziegler, P. (1969). The Black Death. The John Day Company.