EXPLORERS IN MICROBIOLOGY

Who Changed The World

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We dedicate this book to Hon'ble Dr. Suresh Khursale (Former President of the Yogeshwari Education Society), who worked selflessly for the organization and inspired us by consistently striving to the utmost limit.

We also express our deep gratitude to the current President, Hon'ble Chandrashekhar Bardapurkar; Vice-President, Hon'ble G. B. Vyas Guruji; Secretary, Hon'ble Kamlakarrao Chousalkar; Hon'ble N. K. Golegaokar; and the Hon'ble Directors of the Yogeshwari Education Society, who are carrying forward this noble legacy with the very same momentum.

Preface-

The science of microbiology is all about microorganisms and how they work, especially the bacteria, a very large group of very small cells that have enormous basic and practical importance. Microbiology is also about diversity and evolution of microbial cells, about how different kinds of microorganisms arose. Microbiology is also about where microorganisms live on Earth, how they associate and cooperate with each other, and what they do in the world at large, in soils and waters and in animals and plants.

The science of microbiology revolves around two interconnected themes: (1) understanding the nature and functioning of the microbial world, and (2) applying our understanding of the microbial world for the benefit of humankind and planet. Microbioloists have developed a sophisticated understanding of the chemical and physical basis of life and have learned that all cells share much in common. Microbiology is at the forefront of many important breakthroughs in human and veterinary medicine, agriculture, and industry. From infectious diseases to soil fertility to the fuel you put in your automobile, microorganisms affect the everyday lives of humans in both beneficial and detrimental ways.

Microorganisms existed on Earth for billions of years before plants and animals appeared. Although microorganisms are the smallest forms of life, collectively they constitute the bulk of biomass on Earth and carry out many necessary chemical reactions for higher organisms. Microbes are masters of biosphere. They are the progenitors of all life on earth. In the absence of microorganisms, higher life forms would never have appeared and could not be sustained. Indeed, the very oxygen

we breathe is the result of past microbial activity. Moreover, humans, plants, and animals are intimately dependent on microbial activities for the recycling of key nutrients and for degrading organic matter. It is thus safe to say that no other life forms are as important as microorganisms for the support and maintenance of life on Earth.

The importance of microorganisms cannot be overemphasized. In terms of sheer number and mass—microbes contain an estimated 50% of the biological carbon and 90% of the biological nitrogen on Earth—they greatly exceed every other group of organisms on the planet. Furthermore, they are found everywhere: from geothermal vents in the ocean depths to the coldest Arctic ice. They are major contributors to the functioning of the biosphere, being indispensable for the cycling of the elements essential for life. They also are a source of nutrients at the base of all ecological food webs. Most important, certain microorganisms carry out photosynthesis, rivalling plants in their role of capturing carbon dioxide and releasing oxygen into the atmosphere. Those microbes that inhabit humans are also important, helping the body digest food and producing vitamins B and K. In addition, society in general benefits from microorganisms. Microbes are necessary for the production of bread, cheese, beer, antibiotics, vaccines, vitamins, enzymes, and many other products. Their ability to produce biofuels such as ethanol is also being intensively explored. These alternative fuels are both renewable and can help decrease pollution associated with burning fossil fuels. We have learned to fight many diseases with the knowledge of microbiology. Although most microorganisms play beneficial roles, some harm humans and have disrupted society over the millennia. Microbial diseases undoubtedly played a major role in historical events such as the decline of the Roman Empire

and the conquest of the New World. In 1347, plague (Black Death), an arthropod borne disease, struck Europe with brutal force, killing one-third of the population (about 25 million people) within four years. Over the next 80 years, the disease struck repeatedly, eventually wiping out 75% of the European population. The plague's effect was so great that some historians believe it changed European culture and prepared the way for the Renaissance. Today the struggle by microbiologists and others against killers such as AIDS and malaria continues.

Louis Pasteur, one of the greatest scientists of the nineteenth century, maintained that "Science knows no country, because knowledge be longs to humanity, and is a torch which illuminates the world.

Even before microorganisms were seen, some investigators suspected their existence and responsibility for disease. Among others, the Roman philosopher Lucretius (about 98–55 bce) and the physician Girolamo Fracastoro (1478–1553) suggested that disease was caused by invisible living creatures.

However, the first person to publish extensive, accurate observations of microorganisms was the amateur microscopist Antony van Leeuwenhoek (1632–1723) of Delft, the Netherlands.

This book focuses on the contributions of prominent figures in microbiology, such as Antonie van Leeuwenhoek, Robert Koch, and Louis Pasteur and many others. It briefly describes their major discoveries and the impact they had on the field of microbiology.

In this book, the life and times of leading pioneers in microbiology are discussed in vivid detail, focusing on the background of each discovery and the process in which they were developed.

The microscopic world, once an invisible frontier, has, over centuries, been meticulously unveiled by the insatiable curiosity and relentless dedication of remarkable individuals. From the pioneering observations of early naturalists to the sophisticated genetic manipulations of contemporary researchers, the field of microbiology is a testament to human ingenuity and the profound impact of scientific discovery on our understanding of life itself.

This book entitled, "Explorers in Microbiology- who changed the world " is an homage to these extraordinary minds, who dared to peer into the hidden realms of bacteria, viruses, fungi, and protists, and in doing so, revolutionized medicine, agriculture, environmental science, and countless other disciplines. It is a journey through their lives, their groundbreaking experiments, their triumphs, and their occasional setbacks, revealing the human stories behind the scientific breakthroughs.

Within this book, you will encounter the meticulous craftsmanship of Antonie van Leeuwenhoek, who first glimpsed the "animalcules" that swarmed in his homemade microscopes. You will witness the transformative power of Louis Pasteur's work, which debunked spontaneous generation and laid the foundation for germ theory and vaccination. We will delve into the methodical brilliance of Robert Koch, who established the postulates that govern our understanding of infectious diseases, and explore the serendipitous discovery of penicillin by Alexander Fleming, which ushered in the age of antibiotics. But beyond these giants, we have also discussed the lesser-known yet equally vital contributions of scientists whose work, though perhaps not as widely recognized, was instrumental in shaping the trajectory of microbiology.

This book is not merely a chronological recounting of discoveries; it is an exploration of the scientific process itself. It seeks to illuminate the context in which these scientists operated, the societal challenges they faced, and the ethical considerations that often accompanied their groundbreaking work.

Our hope is that by bringing these "unseen architects" into sharper focus, we can inspire a new generation of students and curious minds. The stories of these pioneers will inspire all who read them, especially young people. They can inspire young minds to creativity and further contribute to human civilization. The challenges of tomorrow, from antimicrobial resistance and emerging pandemics to climate change and sustainable food production, will undoubtedly require insights from the microbial world. Understanding the legacy of those who came before us is not just an academic exercise; it is an essential step in forging the path forward.

May the stories within these pages serve as a reminder that even the smallest forms of life hold the greatest secrets, and that it is through dedicated inquiry and unwavering passion that we continue to unlock them.

Dr. Anil P. Narsinge

Dr. Raju V. Kulkarni

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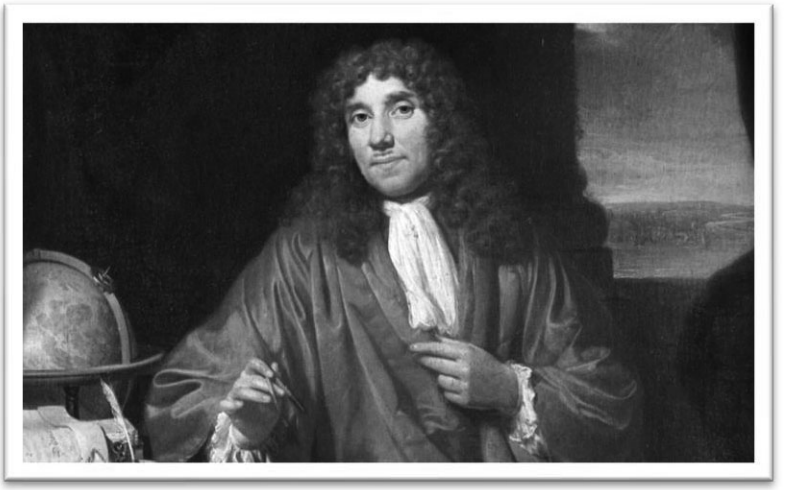


Antonie van Leeuwenhoek

Father of unimagined world of microbes

(1632-1723)

"My work, which I have done for a long time, was not pursued in order to gain the praise I now enjoy, but chiefly from a craving after knowledge, which I notice resides in me more than most other men"

➢ The Birth of The Pioneer:

History is the story of the achievements of men and women, but it records relatively few outstanding names and events. Many significant contributions were made by people whose names have been forgotten and whose efforts have been overshadowed by those who caught the fancy of the chroniclers. It is said that in science the credit goes to the one who convinces the world, not to the one who first had the idea. This

sentence highlights the importance of effective communication in science and other fields. It suggests that having an idea or discovery is not enough; one must also be able to convincingly communicate it to others in order to receive credit and recognition.

So, in the development of microbiology, the outstanding names are often of those who convinced the world—who developed a technique, a tool, or a concept that was generally adopted, or who explained their findings so clearly or dramatically that the science grew and prospered.

Antonie van Leeuwenhoek's lucid reports on the ubiquity of microorganisms enabled Louis Pasteur 200 years later to identify the role of these creatures in fermentation reactions, as well as Robert Koch, Theobald Smith, Pasteur, and many others to find the association between germs and disease. Koch is well known for isolating the germs that cause anthrax and tuberculosis, as well as the stringent requirements he imposed before a single bacterium could be identified as the cause of a disease. His fundamental contributions to microbiology earned him the Nobel Prize in 1905. Microbiology began when people learnt how to grind lenses from pieces of glass and combine them to achieve magnifications high enough to observe bacteria. Even before microbes were discovered, several researchers assumed their presence and role for disease.

The Roman philosopher Lucretius (ca. 98-55 bce) and the physician Girolamo Fracastoro (1478-1553) were among those who proposed that disease was caused by invisible living things. During the thirteenth century, Roger Bacon (1220–1292) proposed that disease is caused by invisible living organisms. However, these individuals had no proof. Athanasius Kircher (1601-1680), a monk, first mentioned "worms" in rotting

carcasses, meat, milk, and diarrheal discharges in 1658. The first microscopic investigations on bees and weevils appear to have been done between 1625 and 1630 by the Italian Francesco Stelluti, who used a microscope most likely supplied by Galileo. Robert Hooke's *Micrographia*, published in 1665, had the earliest drawing of a microorganism. However, the first person to publish lengthy, accurate observations of microbes was Antonie van Leeuwenhoek (1632-1723), an amateur microscopist from Delft, the Netherlands. Leeuwenhoek worked as a draper and haberdasher (a dealer in men's apparel and accessories), but he spent most of his free time building primitive microscopes.

Two hundred and fifty years ago, an inconspicuous man named Leeuwenhoek looked for the first time into a mysterious new world populated by a thousand distinct types of microscopic beings, some aggressive and deadly, others pleasant and useful, many of them more vital to humanity. This is the story of Leeuwenhoek, a pioneering microbiologist. It is the narrative of their constant exploration of this new and amazing world of microbiology.

Leeuwenhoek is universally recognized as the father of microbiology. He found bacteria as well as protists. He was the first to witness this unthinkable "animalcule" universe. He used his own rather basic, single-lensed microscopes to perform clever experiments out of a deep curiosity rather than just observe. Leeuwenhoek was a pioneer and an exceptional scientist.

➢ The Life of Leeuwenhoek:

On October 24, 1632, Antonie van Leeuwenhoek was born in Delft, Netherlands. When Antonie was five years old, his father passed away. Following the early death of his father,

Philips Thonisz, in 1638, Leeuwenhoek was sent to Warmond School by his mother, Grietje van den Berch. He studied the physical sciences and elementary maths in school. He never studied Latin. In 1648 he dropped out of school. He then moved to Benthuizen, a village in the centre of the Delft-Leiden-Gouda triangle, to live with his uncle Cornelis Jacobsz, van den Berch, the village's sheriff and bailiff (Schout and Baljuw), who was to teach him the fundamentals of the law. In 1648 he dropped out of school. He then moved to Benthuizen, a village in the centre of the Delft-Leiden-Gouda triangle, to live with his uncle Cornelis Jacobsz, van den Berch, the village's sheriff and bailiff (Schout and Baljuw), who was to teach him the fundamentals of the law. It quickly became apparent that Antoni's skills, which were primarily practical. In order to learn business, his mother sent him to Amsterdam when he was around sixteen years old. Among the van den Berchs were numerous merchants. Both the mother's uncle, Johan Sebastiaensz., and her grandpa, Sebastiaen Cornelisz. van den Berch, had worked in the textile industry. Her brother-in-law, Pieter Mauritsz. Douchy, was a well-connected wool merchant who lived in Amsterdam. He could have invited Antoni to stay at his home in the Rozengracht and helped him land a job with a respectable company. Leeuwenhoek returned to Delft in 1653, got married, and established himself as a draper (a fabric dealer). He also reportedly held positions as a surveyor, a wine assayer, and a lower-level city official. Only one of his six children, Maria, survived to adulthood. He was twice widowed. She cared for him till he passed away at age 91. He was he was appointed chamberlain to the Delft sheriff before turning forty. He was responsible for opening, cleaning, and locking the town's legal offices. He made a living as a haberdasher and a chamberlain, but it seemed that he spent much of his time fiddling with magnifying lenses.

➢ =Leeuwenhoek's Discoveries:

He had heard that if you carefully ground very small lenses out of transparent glass, things would appear much larger than they were to the naked eye. It would be a lot of fun to gaze through a lens and see objects much larger than your naked eye could see! He could've purchased the lenses. But that was not his nature. He made it himself. He became one of the most prolific early microscopists. This obscure and illiterate merchant developed an idiotic passion for grinding lenses used to inspect cloth for quality. He learnt how to grind and polish microscopic lenses, which he put on metal plates. He created his own lenses and small hand-held microscopes, which were more adaptable than most other instruments at the time. Leeuwenhoek discovered a means to create a tiny lens, less than one-eighth of an inch across, that was so symmetrical and perfect that it revealed small details to him with a stunning clear enormity. However, he was the only man in Holland who knew how to create those lenses.

He was the first to see and describe red blood cells, bacteria, and many other things using these devices, as well as his exceptional preparation and observation skills. He created at least 550 of them during his lifetime, the most powerful of which could magnify by 200 to 300 times. He established the world's best microscope lenses at the time. These microscopes exhibit little resemblance to modern compound light microscopes, which may magnify 1,000 to 3,000 times. Leeuwenhoek possessed the open-mindedness that is crucial for an investigator. Using his lenses, he focused on anything he could fit beneath them, such as a whale's muscle fiber, his own skin scales, rainwater, human saliva, animal excrement, fly brains, beetle eyes, spider spinnerets, frog skin, fish scales, and so forth. For hours, he studied the structure of a sheep's hairs.

He meticulously dissected a fly's head and placed its brain on the fine needle of his microscope. He could see the fine features of that fly's magnificent large brain! He examined the cross-sections of a dozen different trees and frowned at plant seeds. He repeatedly examined this bee's sting or that louse's leg. He left his specimens stuck on the tip of his odd microscope for months in order to examine other things. He created hundreds of microscopes. He then returned to those initial specimens to fix his initial errors. Until he discovered that, in certain situations, he would consistently see the same thing, he never drew anything. When someone looks under a microscope for the first time, they say, "Now I see this, then I see that—and even a skilled observer can be fooled," he added.

He claimed that although I have spent more time on these observations than most people realize, I have done it joyfully and have ignored some who have questioned why the trouble is necessary or what the point is—but I only write for the philosophical, not for such individuals! Without an audience, he worked in that manner for twenty years. The first audience Antony Leeuwenhoek had was at the Royal Society of England.

Many of the protozoan forms he described are now easily recognized due to his remarkably accurate descriptions. He was the first to accurately describe and illustrate his observations. Then, from his descriptions of them, specific species may be identified with such precision. Because he was the first to genuinely cultivate, observe, and characterize a wide variety of microbiological life, Leeuwenhoek is known as "The first microbiologist." In fact, he took measurements of the bugs' growth. The fact that he published his findings is even more astounding.

The British amateur scientist Robert Hooke (1635–1702) had a significant impact on Leeuwenhoek, particularly through his well-known work Micrographia, which was released in 1665. A comparable book for the general public, *Arcana Naturae Detecta*—1695 (in Latin), was published by Antonie van Leeuvenhoek thirty years later. Its purpose was to inform the public about his microscopic observations, which he sent to the Royal Society in London (UK) on a regular basis in the form of letters. Within this extensive book (600 pages),The evolution of a "flea," from the egg through the larval stages to an adult specimen, was described and illustrated in extraordinary detail by van Leeuwenhoek under the well-known title "Nature's Mysteries Disclosed." Hooke did not identify the microbes, even though he was the first to notice their existence. Among the greatest explorers and naturalists is Leeuwenhoek.

Leeuwenhoek was a mulish, exacting man. He repeatedly viewed the world via such lenses. Because of his intense passion for lenses, his neighbors made fun of him.

However, his work gained widespread recognition during his lifetime, and his significance was recognized right away. The Royal Society for the Communication and Publication of Scientific Work had been founded in England around the time Leeuwenhoek started making observations. A few years later, in 1680, Leeuwenhoek was elected a Fellow of the Society after being asked to share his observations with its members.

Leeuwenhoek for about 50 years, until his death in 1723 shared his findings with the Royal Society in a lengthy series of letters written in Dutch. After being translated and published in English in the Proceedings of the Royal Society, the majority of these letters spread swiftly and extensively.

The newly established Royal Society of London actively sought out works that "promote natural knowledge" between 1657 and 1677. Regnier de Graaf (1641-1673), a corresponding member of the Delft society, did not make fun of him. Conversely, Leeuwenhoek's ability to see through these lenses astounded him. In 1673, he was introduced to the Royal Society of London by Regnier de Graaf. Leeuwenhoek was lucky—or we are lucky—to have a friend named Hoogvliet who assisted in translating his letters into Latin. Leeuwenhoek told the Royal Society that he could see amazing things with his new lenses, and they were amazed. He produced ever-better lenses. He studied everything with intense interest.

He described the "very little animalcules," which we now know to be free-living protozoa, in one of the earliest letters, dated September 7, 1674, to Henry Oldenburg, Secretary of the Royal Society. The British experts read his impassioned messages with curiosity. In a letter, Oldenburg requested that Leeuwenhoek "acquaint us with his method of observing." Throughout his life, Leeuwenhoek refused to provide any explanation of his microscopical techniques.

Leeuwenhoek was a crazy observer; He focused his lens on pure, clean water that had just descended from the heavens. What might be in the water? Maria, his daughter, looked after her father, who was a little crazy. Through his lens, he narrows his eyes. Then Leeuwenhoek's joyful voice came! "Come on over! Act quickly! This rainwater contains tiny creatures that can swim!

They play around! They're a thousand times smaller than any organism we can see with our own eyes. Look! "Look what I discovered!" Those animals were quite little. Many questions arose in his thoughts. But where did these strange little

rainwater creatures come from? Had they descended from the sky? Had they crept stealthily up the side of the pot from the ground? Or were they formed out of thin air by a capricious God? His common sense told him that life stems from life.

He focused his lens on several types of water, including water stored in the confined air of his study, water in a jar on the high roof of his house, water from the not-so-clean canals of Delft, and water from the deep cold well in his yard. He could find those small animals everywhere. He discovered that many thousands of them were not as large as a grain of sand; he compared them to a cheese-mite, and they were as small as a bee to a horse. He never got tired of seeing them "swim about among one another gently like a swarm of mosquitoes in the air."

- **On October 9, 1676, he wrote:**

In the year 1675, I discovered living creatures in rain water which had stood but a few days in a new earthen pot, glazed blue within. This invited me to view this water with great attention, especially those little animals appearing to me ten thousand times less than those . . . which may be perceived in the water with the naked eye.

He described his little animals in great detail, leaving little doubt that he saw bacteria, fungi, and many forms of protozoa. For example, he reported that on June 16, 1675, while examining well water into which he had put a whole pepper the day before:

I discovered, in a tiny drop of water, incredibly many very little animalcules, and these of divers sorts and sizes. They moved with bendings, as an eel always swims with its head in front, and never tail first, yet these animalcules swam as well backwards as forwards, though their motion was very slow.

In the first letter, he reported how microorganisms proliferated in crushed pepper in water, resulting in 2,700,000 germs per drop of water. In his letter of June 12, 1716, van Leeuwenhoek stated that "my work, which I've done for a long time, was not pursued in order to gain the praise I now enjoy, but chiefly from a craving for knowledge, which I notice resides in me more than most other men." Leeuwenhoek was highly aware of contamination; he supplemented evaporating water with snow water, the purest available at the time, and made every effort not to introduce small creatures from other sources. He collected water from a variety of sources, including his well, the sea, rainwater, drain pipes, and lakes, always being sure to clean his receptacles. In a later letter, he mentions having tested distilled or boiling water. In each example, he depicts changing populations of animalcules throughout time.

Leeuwenhoek also describes tests in which peppercorns were added to water, both crushed and uncrushed. Leeuwenhoek noted an astounding multiplication of minute organisms in these infusions, calling them "incredibly small."

Leeuwenhoek observed, characterized, and micrographed the primary types of bacteria and protozoa. In his letters from 1683, Leeuwenhoek recounted scraping rods, cocci, and spirochetes off his teeth. He claimed that there were more animalcules living in the filth on a man's teeth than there were men in the entire kingdom, particularly those who did not clean their teeth. Throughout his life, Leeuwenhoek wrote 375 letters in Dutch to the Royal Society, many of which were lengthy. The Leeuwenhoek letters were translated into English by huge groups of Dutch scientists.

Not all Royal Society members snorted, but the majority did. In order to validate Leeuwenhoek's account, Robert Hooke

(1635–1703) and Nehemiah Grew (1641–1712) were tasked with building superior microscopes (the compound microscope in England would not reveal the bacteria that Leeuwenhoek could see with a single lens!). Disturbed by the sceptics of the Royal Society, Leeuwenhoek submitted them his calculations in painstaking mathematics along with statements from notable Delft residents. Robert Hooke brought his new microscope and the animalcules from the ground pepper that Leeuwenhoek had described to a Society meeting on November 15, 1677. Everyone gathered around the microscope to look at it. The initial letter written by Leeuwenhoek and subsequent correspondence were published in Philosophical Transactions. Leeuwenhoek was correct in his observations, and the Royal Society praised him for it. That was a proud moment for Leeuwenhoek. A little later, the Royal Society appointed him a Fellow, sending him a beautiful diploma of membership in a silver case with the society's coat of arms on the cover. He wrote, "I will serve you faithfully for the rest of my life." And he kept his word, mailing them those conversational blends of gossip and science until his death at the age of ninety.

The Royal Society even dispatched Doctor Molyneux to write a report on this janitor-discoverer of the invisible. Molyneux offered Leeuwenhoek a reasonable price for one of his microscopes—surely he could spare one, given the hundreds of them in cabinets that lined his study. But, no! Is there anything the guy from the Royal Society would like to see? The Dutchman held up his lenses for the Englishman to look through, keeping a close eye on things to make sure the most honest visitor didn't touch or contaminate anything. Here were some very curious little unborn oysters in a bottle, and here were divers who were very nimble little animals. "However, your instruments are amazing!" exclaimed Molyneux. "A thousand

times clearer they depict objects with a thousand times greater clarity than any lens available in England! "I wish I could show you my best lens, my unique way of observing," Leeuwenhoek stated. "But I keep that to myself and don't show it to anyone, not even my own family."

Everyone he could get his hands on, including himself, served as an experimental animal for that inquisitive man. He spent many hours looking through his hundreds of microscopes, making a hundred incredible discoveries.In the tail of a little fish placed head first into a glass tube, he noticed for the first time the capillary blood vessels that transport blood from the arteries to the veins, completing the Englishman Harvey's discovery of blood circulation.

The human sperm was discovered by Leeuwenhoek. As the years passed, everyone in Europe became aware of him. The Queen of England travelled to Delft just to gaze at the wonders that might be seen through his microscopes, while Peter the Great of Russia came to offer his respects.

Unlike Leeuwenhoek, Hooke provided comprehensive information of his microscopical processes and displayed them to the assembled colleagues. He later published his methodology and findings in ***Microscopium*** (1678). He even taught himself Dutch so he could read the letters of 'ingenious Mr. Leeuwenhoek'. Instead, Leeuwenhoek was made a Fellow in 1680, thanks to Hooke's outstanding demonstrations and the direct assistance of the Royal Society's sponsor, King Charles II. Leeuwenhoek had strongly opposed teaching his methods.

Leeuwenhoek promised to serve society for the remainder of his life, and he kept it. The best of his microscopes, despite being simple lenses, outperformed the compound microscopes in common usage at the time. They possessed a resolution of

approximately one millionth of a meter. Leeuwenhoek had exceptional vision.

Antony van Leeuwenhoek was an unusual scientist. He came from a tradesman family, had little fortune, no further education or university degrees, and spoke only Dutch. This would have been enough to disqualify him entirely from his time's scientific society. Nonetheless, Leeuwenhoek made some of the most important discoveries in the history of biology thanks to his skill, diligence, insatiable curiosity, and an open mind free of his time's scientific dogma.

Antony van Leeuwenhoek believed that the experimental method, backed by the evidence of the senses, was the most effective way to investigate what is true in natural philosophy. For this reason, he worked diligently and tirelessly to create some very good lenses with his own hands, which helped him uncover many secrets of nature that are now well-known throughout the philosophical world.

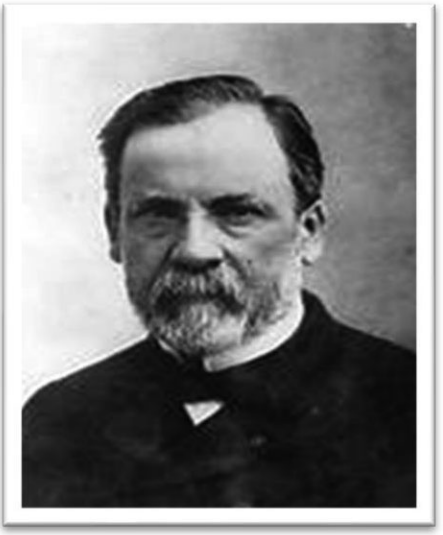
In 1680, Leeuwenhoek was chosen to join the French Academy of Science. He submitted 27 letters for publication to the French Academy throughout his lifetime. The Queen of England travelled to Holland just to view Leeuwenhoek's microscopes, and he became extremely famous in his day. He was also called upon by Peter the Great of Russia. For his well-known discovery in Natural Philosophy, the University of Louvain in Belgium awarded him a silver medal in 1716 that was engraved with his likeness. Van Leeuwenhoek created 26 lenses set on sliver plates before to his passing. After his death, he left these to his daughter to donate to the Society. Unfortunately, all of van Leeuwenhoek's microscopes have since been lost, even if she did send them.

In 1723, when he was ninety-one years old and dying, he sent for his buddy Hoogvliet. He was unable to lift his hand. His once-glowing eyes were rheumy, and their lids were beginning to adhere to the cement of death. He whispered, "Hoogvliet, my friend, please get those two letters on the table translated into Latin. Send them to the Royal Society in London. So he maintained his promise from fifty years ago, and Hoogvliet wrote, along with those last letters: "I send you, learnt sirs, this last present of my dying friend, hoping that his final word may be pleasing to you.

➢ Our Thoughts:

Even Leeuwenhoek had no higher education or university degrees and spoke no languages other than his native Dutch. This would have been enough to disqualify him entirely from his time's scientific society. He was the first to see microorganisms using his own deceptively basic, single-lensed microscopes; he did not simply observe, but also conducted inventive experiments with a keen interest. He learnt how to grind and create top quality lenses. He dedicated himself to describe the microbial world which helped for the advancement of the microbiology.

He became one of the most prolific early microscopists. Grinding lenses and building basic microscopes became his hobby. He has gained exceptional preparation and observation skills. He spent a lot of time studying a variety of specimens under his microscopes. He completed his work with great joy. He completed his effort to get knowledge that will benefit society. He published his findings. He made better and better lenses. He looked at everything with keen curiosity.



Louis Pasteur

(27 December 1822-28 September 1895)

"Chance favours invention only for minds prepared for discoveries by patience study and preserving efforts".

➢ The Father of Modern Microbiology:

Louis Pasteur, one of the greatest scientists of the nineteenth century, believed that "science knows no country, because knowledge belongs to humanity and is a torch that illuminates the world." Louis Pasteur was born on December 27, 1822 in Dole, France, and passed away on September 28, 1895 in Saint-Cloud.

Louis Pasteur is well-known for his discoveries about vaccine, microbial fermentation, and pasteurization, all of which have

had an impact on medicine, agriculture, and industry. Pasteur's first notable scientific success was his investigation into molecular dissymmetry, which he discovered while working with tartaric acid. This paper marks the beginning of the development of the field of stereochemistry. Pasteur was appointed dean of the University of Lille's new faculty of sciences in 1854, and he began his fermentation research there. His research demonstrated that fermentation was caused by the proliferation of microbes, so disproving the hypothesis of spontaneous generation. This cleared the way for pasteurization, which is the process of boiling liquids to kill bacteria that are harmful to human consumption in food and beverages.

In addition to pasteurization, Pasteur made significant contributions to the scientific development of immunology. He developed vaccinations for numerous diseases, including chicken cholera, anthrax, and rabies. These vaccines have proven effective in avoiding the spread and occurrence of dangerous diseases, saving millions of lives. His technique to weakening viruses in order to generate vaccines was unique, and it served as the foundation for modern immunology. Pasteur's discovery on the germ theory of disease had an impact on medicine and surgery, particularly the adoption of antiseptic procedures. One of the pioneers of the germ theory of disease is also thought to have been Pasteur. Many people consider Louis Pasteur (1822–1895) to be one of the greatest scientists in history. His numerous research shown that eradicating or halting microorganisms could avert diseases. His work resulted in significant advances in our knowledge of disease causes and prevention, laying the groundwork for public health, cleanliness, and a large portion of modern medicine while also significantly lowering the death rate from infectious diseases.

He has been recognized as the "father of bacteriology" and is considered to be one of the pioneers of contemporary bacteriology. It was Pasteur who proved the theory of spontaneous generation incorrect.

Despite his reputation as a renowned scientist, Pasteur's career was fraught with controversy. Some of the difficulties surrounding his life include his competition with other scientists, such as Robert Koch, as well as ethical issues in his research, particularly those involving the rabies vaccine. Although his contributions to science and medicine have helped save many lives.

His contributions to microbial fermentation are regarded as the foundation of microbiology, and they influenced sectors such as brewing, winemaking, and dairy. The method of pasteurization, named after him, is still frequently used to ensure the safety of food and beverage goods. Pasteurization, a method of heating liquids to kill harmful germs, has saved millions of people from food poisoning while simultaneously increasing the shelf life of numerous items. Pasteur's methodology and findings are still significant in the management of public health and food preservation.

He has inspired generations of scientists and researchers to seek information and generate new ideas. Pasteur's life did not end with his death, since his discoveries and innovations continue to have an impact in the modern world, particularly in microbiology, immunology, and public health.

In 1887, Pasteur founded the Pasteur Institute in Paris, which is now one of the most well-known research centre’s for infectious diseases. His work is still important today, and scientists and researchers frequently refer to it. Louis Pasteur was responsible for some of the most significant scientific

revolutions of the nineteenth century, including those in biology, agriculture, medicine, and hygiene. Louis Pasteur's life was filled with innovative discoveries, as well as a series of incidents that most likely drove his ambition to comprehend the diseases of the period. He was a hard-working and determined scientist who went extensively throughout France to demonstrate his theories and cure agricultural and industrial difficulties caused by infectious diseases.

Louis Pasteur died in 1895. There are numerous institutions, honors, and locations named after Louis Pasteur to this day. The Pasteur Institute, numerous universities, and streets named after him are examples of his contributions to science and society. His life and accomplishments are remembered and celebrated for the great impact he had on the globe and people's lives.

Louis Pasteur in his last famous speech, he says: You young men—doctors and scientists of the future—do not let yourselves be tainted by apparent skepticism; nor discouraged by the sadness of certain hours that creep over nations. Do not become angry at your opponents, for no scientific theory has ever been accepted without opposition. Live in the serene peace of libraries and laboratories. Say to yourselves, first, “What have I done for my instruction?” And as you gradually advance, “What am I accomplishing?” Until the time comes when you may have the immense happiness of thinking that you have contributed in some way to the welfare and progress of mankind.

This brilliant scientist conducted experiments based on his extensive experience and scientific guidelines. Pasteur discovered the problem and proposed a solution. It is quite astounding that Pasteur was able to solve all of the mysteries he encountered, whether it was rabies or sour wine. Pasteur's

pioneering work is widely recognized as the foundation of modern aseptic surgery.

➢ Early Life and Education:

Louis Pasteur was born on December 27, 1822, in Dole, Jura, France, into a Catholic family of poor tanners. His parents were Jean Joseph Pasteur and Jeanne Etiennette Roqui. He was Jean-Joseph Pasteur's third child with Jeanne-Etiennette Roqui. The family relocated to Marnoz in 1826, then to Arbois in 1827. They grew raised in Arbois. Pasteur began primary school in 1831. The name Pasteur translates to "Shepherd". During the Napoleonic Wars, Pasteur's father, Jean-Joseph Pasteur, worked as a tanner and sergeant major, earning the Legion of Honor. This fact most likely imprinted in the youthful Pasteur the intense patriotism that would later define his personality. He had a brother, Jean Denis Pasteur, and three sisters, Virginie, Josephine, and Emilie.

As a child, Louis adored the outdoors and lengthy excursions in the forests. He enjoyed fishing and was particularly fond of animals. Louis Pasteur was a mediocre student in his early years, but he excelled at drawing and painting. His portraits of his parents and friends, created when he was 15, are now housed in the Pasteur Institute museum in Paris, although he abandoned his art career at the age of 19 to devote more time to science. Pasteur went to high education at the Collège d'Arbois. Pasteur's family was destitute. His family made significant sacrifices to provide for his education. His sisters also obtained education (rare in those days), and Louis assisted and supported them.

In October 1838, 15-year-old Louis left his home to attend school in Paris. His dream was to be a teacher. He aspired to attend the École Normale Supérieure, which Napoleon built in

1808 to train professors for France's colleges and universities. However, young Louis became quite homesick and returned home after approximately a month.

In 1839, he enrolled in the Collège Royal de Besançon to study philosophy, and he received his Bachelor of Letters degree in 1840. He was appointed tutor at Besançon College while pursuing a degree in science with a focus on mathematics. In 1842, he received a general science degree from Dijon, although his chemistry grade was unsatisfactory.

Later, in 1842, Pasteur took the Ecole Normale Superieure admission exam. Pasteur passed the first series of tests, but due to his poor ranking, he chose not to continue and would try again next year. He returned to the Pension Barbet to prepare for the test. He also attended seminars at the Lycee Saint-Louis and lectures by Jean-Baptiste Dumas at the Sorbonne.

He enrolled in the Collège Royal in Besançon in 1839 to study philosophy, and in 1840 he graduated with a Bachelor of Letters. While pursuing a degree program in science with a focus on mathematics, he was hired as a tutor at the college in Besançon. In 1841, he failed his first test. Pasteur took the École Normale Supérieure admission exam later in 1842. Pasteur chose to attempt again the next year after failing the first round of examinations due to his poor rating.

He returned to the Pension Barbet to prepare for the test. He also attended seminars at the Lycée Saint-Louis and lectures by Jean-Baptiste Dumas at the Sorbonne. In 1843, he passed the test with outstanding marks and was admitted to the École Normale Supérieure. In 1845, he earned the licencié ès sciences (Master of Science) degree. In 1846, he was appointed professor of physics at the Collège de Tournon (now known as Lycée Gabriel-Faure) in Ardèche, but chemist Antoine Jérôme Balard

urged him to return to the École Normale Supérieure as a graduate laboratory assistant. He joined Balard and began his crystallographic study at the same time, submitting two theses in 1847, one in chemistry and the other in physics.

After serving temporarily as professor of physics at the Dijon Lycée in 1848, he became professor of chemistry at the University of Strasbourg, where he met and married Marie Pasteur (née Laurent) in 1849. She served as Pasteur's scientific assistant and was the daughter of the University of Strasbourg's rector. Three of their five children passed away while still young. Their oldest daughter, Jeanne, was born in 1850. She died of typhoid disease at the age of nine in 1859, while attending the Arbois boarding school. Camille died of a liver tumor at the age of two in 1865. They soon decided to send Cécile home from boarding school, but she died of typhoid disease on May 23, 1866, at the age of 12. Only Jean Baptiste and Marie Louise survived into maturity.

- **Career:**

Pasteur's early career was marked by scientific breakthroughs. In 1848, Pasteur was appointed professor of chemistry at the University of Strasbourg, and he was promoted to chair of chemistry in 1852. In 1854, he was appointed dean of the new faculty of sciences at the University of Lille, where he began research into fermentation. It was on this time that Pasteur made his well-known remark: "*Chance favors invention only for minds prepared for discoveries by patient study and preserving efforts*".

He travelled to Paris in 1857 to become the director of scientific studies at the École Normale Supérieure, where he took over from 1858 to 1867 and implemented a number of reforms to increase the quality of scientific work. The assessments got more stringent, resulting in higher outcomes,

increased competitiveness, and greater prestige. Many of his orders, however, were strict and authoritarian.

He began teaching geology, physics, and chemistry at the École nationale supérieure des Beaux-Arts in 1863 and remained there until 1867, when he resigned. He was appointed chair of the Sorbonne's organic chemistry department in 1867, but he resigned the post due to ill health. Pasteur requested the establishment of the École Normale's physiological chemistry laboratory in 1867, and from 1867 until 1888, he served as its director. He founded the Pasteur Institute in Paris in 1887 and served as its director for the remainder of his life.

➢ Research:

Molecular asymmetry

The German chemist Eilhardt Mitscherlich's discovery that tartrates and paratartrates behaved differently towards polarized light—tartrates rotated the plane of polarized light, while paratartrates did not—confounded Pasteur shortly after he graduated from the École Normale Supérieure. Given that the compounds had the same chemical characteristics, this was uncommon. Pasteur observed that the asymmetric shapes of the tartrate crystals matched their optical asymmetry. He discovered that crystalline paratartrate was a combination of crystals in a right-handed arrangement. However, when these crystals were physically separated, he discovered that they had right and left asymmetry. In other words, a balanced combination of right and left crystals was optically inactive. Pasteur thus uncovered the existence of molecular asymmetry, which is the foundation of stereochemistry, as indicated by optical activity. Over the next ten years; Pasteur studied the ability of organic molecules to spin the plane of polarized light. He also investigated the relationship between crystal structure

and molecular configuration. His research convinced him that asymmetry was one of the most fundamental properties of living stuff.

Spontaneous Generation

People have long believed in spontaneous generation, or the ability of living entities to emerge from nonliving elements. The discovery of microbes prompted the intriguing question, "Where did these microscopic forms originate?" For hundreds of years, the concept of spontaneous generation held that organisms, such as small worms, might emerge spontaneously from non-living material. The concept of spontaneous generation has existed since biblical times, and its fundamental principles are simple to understand. Food and other perishable materials putrefy when left to stand for an extended period of time. When inspected under the microscope, the putrefied material is swarming with bacteria. Even Aristotle (384-322 BCE) believed that some of the simplest invertebrates may emerge by spontaneous generation. This viewpoint was eventually challenged by the Italian physician Francesco Redi (1626-1697), who conducted a series of studies on decomposing meat and its propensity to produce maggots spontaneously. Francesco Redi's work caused the concept of spontaneous generation to fall out of favour. Redi placed the meat in three containers. One was left uncovered, another was wrapped in paper, and the third was coated in thin gauze to keep flies out. Flies lay their eggs on the open flesh, and maggots grew. The remaining two pieces of flesh did not naturally create maggots. However, flies were drawn to the gauze-covered container and placed their eggs on the gauze, which created maggots. Thus, the presence of fly eggs caused maggots to be produced by decomposing meat, and flesh did not generate maggots on its own, as previously thought.

Similar investigations by others served to disprove the theory for larger creatures.

Redi's convincing results did not completely undermine the theory of spontaneous generation, and it took another 200 years or so to do so. One explanation for this was that Redi's gauze was unable to stop the growth of bacteria and mould on the meat's surface, which gave Pasteur's opponents consolation. The unscientific nature of spontaneous generation has to be exposed by new experiments.

A soup of organic material was vigorously boiled in a vessel to sterilize it as part of the traditional experiment to see if microorganisms might grow and survive from nonliving stuff. After that, the vessel was promptly sealed to keep out any outside air. The notion of spontaneous creation would be supported if the solution becomes hazy after a few days, indicating that bacteria had to have developed from the organic material in the jar. Unfortunately, this experiment overlooked a number of other potential causes of the hazy condition, such as the flask's faulty sealing, the presence of airborne microbes, or the possibility that boiling did not completely destroy all life forms (i.e., spores). It was therefore not surprising that different researchers got diverse outcomes from this experiment. To address and explain these possibilities, a novel and sensible experiment was required.

Some hypothesized that microbes arose by spontaneous creation while larger species did not. They noted that cooked extracts of hay or meat produced microorganisms after sitting for a while. In 1748, the English priest John Needham (1713-1781) published the findings of his research on spontaneous generation. Needham boiled mutton broth in flasks that he then carefully sealed. Many of the fluids eventually became

murky and included bacteria. He believed that organic stuff possessed a vital force capable of conferring life-like traits on nonliving matter. Needham's experimental design was modified a few years later by the Italian biologist and clergyman Lazzaro Spallanzani (1729–1799), who was the first to seal glass flasks containing seeds and water. As long as the flasks were sealed, no growth occurred when they were submerged in boiling water for three-quarters of an hour. Although he suggested that air brought germs to the culture medium, he also made the observation that animals already in the medium might need the outside air to flourish. According to proponents of spontaneous generation, heating the air in sealed flasks eliminated the air's capacity to sustain life.

A number of investigators tried to refute these claims. Theodore Schwann (1810–1882) let air flow through a red-hot tube and then into a flask filled with a sterile nutritional solution. The flask remained sterile. Theodor von Dusch (1824–1890) and Georg Friedrich Schroder (1810–1885) later let air to enter a flask of heat-sterilized media after it had passed through sterile cotton wool. The air had not been heated, but there was no growth in the medium. In 1859, the French naturalist Felix Pouchet (1800–1872) asserted that he had conducted tests that definitively demonstrated that microbial growth was possible even in the absence of air contamination. This allegation prompted Louis Pasteur (1822-1895) to resolve the issue. Who was correct? To resolve this debate, keen understanding was required, and this was precisely the type of subject that drew Louis Pasteur's interest. Pasteur became a strong opponent of spontaneous generation.

Pasteur's rebuttal of spontaneous generation, published in 1861, was a masterwork of logic and experimental research. He started by proving that germs are present in the air. To do this,

air was filtered through a cotton plug, which trapped germs and allowed them to be examined under a microscope. Many of the creatures that were captured had the exact same appearance as those that had been previously seen by others in other infusions. Infusions are nutrient-rich solutions that allow microorganisms to grow. Pasteur demonstrated that the organisms rapidly proliferated, causing the cotton plug to become hazy when dropped into a sterilized infusion.

Pasteur hypothesized that bacteria in putrefying materials were descendants of cells that had come from the air or had been present on the decaying materials from the beginning. Pasteur also reasoned that if food were treated to remove all living organisms present—that is, if it was declared sterile—and then safeguarded from additional contamination, it would not putrefy. Pasteur employed heat to destroy harmful bacteria, and he discovered that thoroughly heating a nutrient solution followed by sealing prevented it from spoiling. Proponents of spontaneous generation criticized the trials, claiming that "fresh air" was required for the phenomena to occur. Pasteur cleverly and simply addressed this criticism in 1864 by creating the swan-necked flask, which is now known as a Pasteur flask. Nutrient solutions could be boiled and sterilized in such a flask. Although air could return once the flask cooled, the bend in the neck stopped particles, especially bacteria, from getting into the nutritional solution and starting the putrefaction process. In such flasks, nutrient solutions maintained their sterility permanently.

The debate regarding spontaneous generation was permanently resolved when particulate debris from the flask's neck was let to enter the liquid within the flask before the microbial growth was noticed. The claims that unheated air or the infusions themselves contained a "vital force" required for

spontaneous creation were ultimately disproved by these straightforward and tasteful trials. Effective sterilization techniques were developed as a result of Pasteur's work on spontaneous generation; these techniques were later standardized and applied to clinical medicine as well as basic and applied microbiological research. Pasteur's invention of swan neck flasks marked the beginning of microbiology's golden age. Pasteur's work also helped the food sector because his ideas were swiftly modified to preserve milk and a variety of other foods through heat treatment, or pasteurization.

Louis Pasteur has long been known to be against the theory of spontaneous generation and to have provided strong scientific evidence to support his position. He felt that the concept of spontaneous genesis was incompatible with the premise that God is the source of all life. For this reason, the issue of spontaneous generation is so significant and captivating. It is the fundamental issue with life and its genesis. To produce a germ would be to induce spontaneous generation. It would be to solve the issue of its origin; it would be to create life.

➢ Studies on Fermentation:

While employed at Lille, Pasteur was inspired to study fermentation. In 1856, M. Bigot, a local winemaker whose son had studied under Pasteur, asked him for guidance on the issues of souring and beetroot alcohol production. Pasteur started his investigation into the subject by replicating and validating the findings of Theodor Schwann, who had shown ten years earlier that yeast were living things.

Pasteur sent a paper on lactic acid fermentation to the Société des Sciences de Lille in August 1857, but it wasn't seen until three months later, according to his son-in-law, René

Vallery-Radot. A memoire was later released on November 30, 1857. He elaborated on his thoughts in the memoir, saying: I intend to establish that, just as there is an alcoholic ferment, the yeast of beer, which is found everywhere that sugar is decomposed into alcohol and carbonic acid, so also there is a particular ferment, a lactic yeast, always present when sugar becomes lactic acid.

This memoir about alcoholic fermentation was published in its entirety in 1858. Jöns Jacob Berzelius and Justus von Liebig proposed the hypothesis that fermentation is generated by decomposition. Pasteur established that this notion was inaccurate, and that yeast was responsible for the fermentation of sugar into alcohol. He also demonstrated that when a different bacterium invaded the wine, it created lactic acid, turning it sour. Pasteur discovered in 1861 that when yeast was exposed to air, less sugar fermented per unit of yeast. The Pasteur effect refers to the reduced aerobic fermentation rate.

Pasteur's studies also demonstrated that the development of microorganisms was the cause of milk, wine, and beer deteriorating. After establishing this, he developed a method for heating liquids, such milk, to a temperature of 60 to 100 °C. This eliminated the majority of the germs and fungus that were already inside of them. In order to combat the "diseases" of wine, Pasteur patented the method in 1865. Pasteurization is the name given to the process. This technique's development completely changed how breweries store their beer and wine. In fact, it was so effective that it was used on other liquids, such as milk, and stopped the spread of illness from tainted food and drink. The most significant of Pasteur's contributions to society is the heat treatment of food and drink, which lowers spoiling and gets rid of harmful bacteria for customers. Pasteurization is the term given to this procedure. Pasteur came to the

conclusion that sickness is caused by microorganisms that infect both humans and animals as a result of beverage contamination.

Although people had been unintentionally exploiting bacteria for thousands of years, industrial microbiology owes much of its development to the work of Louis Pasteur and others on the alcoholic fermentations that produced wine and other beverages. When Theodore Schwann and others hypothesized in 1837 that yeast cells were responsible for the conversion of carbohydrates to alcohol, the top chemists of the time believed microbes had no role. They were believed that fermentation was caused by a chemical instability that degraded carbohydrates into alcohol. Pasteur disagreed; he felt that fermentation was carried out by living organisms. In 1856, M. Bigo, an entrepreneur in Lille, France, where Pasteur worked, approached him for aid. His company generated ethanol from beetroot sugar fermentation, and the alcohol yields had recently fallen, resulting in a sour product. Pasteur noticed that the fermentation was failing because the yeast responsible for alcohol creation had been replaced by bacteria that made acid instead of ethanol. Pasteur solved this practical difficulty by demonstrating that all fermentations were caused by unique yeasts and bacteria, and he published multiple fermentation-related publications between 1857 and 1860. His achievement prompted the investigation of wine diseases and the creation of pasteurization to preserve wine during storage. Pasteur's research on fermentation lasted nearly 20 years. One of his most important discoveries was that some fermentative microbes were anaerobic and could only exist in the absence of oxygen, whilst others could survive both aerobically and anaerobically.

➢ Pasteur and the Germ Theory of Disease:

The germ theory of disease is the currently accepted scientific explanation for many diseases. It claims that microorganisms known as pathogens or "germs" can cause illness. These tiny creatures, which cannot be seen without magnification, infiltrate animals, plants, and even microbes. Their growth and reproduction within their hosts can result in disease. The term "germ" refers to any form of microorganism, including protists and fungi, as well as other pathogens such as parasites, viruses, prions, or viroids. Infectious diseases are illnesses brought on by pathogens. In many domains of life, pathogens are agents that cause disease and can spread from person to person. The germ theory of disease has its roots in biology. Louis Pasteur proposes that disease is caused by microorganisms. Pasteur is credited for developing his theories on fermentation and his tests on how bacteria cause milk and wine to deteriorate. The basis for sanitation and hygiene in public and international health was established by his germ theory of illness. The germ theory of illness is a fundamental biological concept. Louis Pasteur suggests that microbes cause sickness. Pasteur was responsible for developing fermentation theories and conducting studies on milk and wine rotting, which indicated sickness caused by microbes. His germ theory of illness established the foundations for hygiene and sanitation in public and global health. By the early nineteenth century, the first vaccine, smallpox inoculation, was widely used in Europe, but doctors had no idea how it worked or how to apply the principle to other diseases. Louis Pasteur's work in the late 1850s marked the start of a transitional age. Pasteur improved scientific communication and reasoning, leaving a legacy that has fuelled advancements in human health for the past 150

years. However, millions of needless deaths are being caused by infectious diseases.

Most people assumed that disease was caused by supernatural powers, poisonous vapours called miasmas, and imbalances among the four humours believed to be present in the body, even though Fracastoro and a few others had proposed that invisible organisms produced disease. Since the Greek physician Galen (129–199), the four humors—blood, phlegm, yellow bile [choler], and black bile [melancholy]—have been widely acknowledged to play a part in illness. Early in the nineteenth century, evidence from a variety of disciplines started to mount in favor of the germ theory of disease, which holds that microbes are the cause of illness. In 1835, Agostino Bassi (1773–1856) proved that a fungal infection was the cause of a silkworm disease, demonstrating for the first time that microorganisms could cause disease. He also proposed that microbial infections were the cause of many diseases. Agostino Bassi had demonstrated that a fungus that infected silkworms was the cause of muscardine. In southern France, two diseases known as flacherie and pébrine had been afflicting large numbers of silkworms since 1853, and by 1865, they were costing farmers enormous sums of money. M. J. Berkeley (1803–1889) demonstrated in 1865 that a water mould was the source of Ireland's devastating potato blight, and Heinrich de Bary (1831–1888) demonstrated in 1853 that rust and smut fungus were the cause of cereal crop diseases.

The French government invited Pasteur to look into the pèbrine sickness of silkworms that was causing problems for the silk industry after he had achieved success with his research on fermentation. The chemist, senator, and former minister of agriculture and commerce Jean-Baptiste Dumas asked Pasteur to investigate a new disease called pébrine, which was

destroying silkworm farms in southern France and Europe. The disease was characterized by black spots on a macroscopic level and "Cornalia corpuscles" on a microscopic level. Between June 7, 1865, and June 5, 1869, Pasteur accepted and spent five extended stays in Alès. After several years of effort, he discovered that the condition was caused by a protozoan parasite. Silkworms treated with pébrine were coated in corpuscles. For the first three years, Pasteur believed the corpuscles were a symptom of the sickness. In 1870, he concluded that the corpuscles were the cause of pébrine (now recognized to be a microsporidian). Pasteur also shown that the condition is inherited. Pasteur devised a method to avoid pébrine: once the female moths laid their eggs, they were ground into a pulp. The pulp was examined under a microscope, and if corpuscles were found, the eggs were killed. Pasteur came to the conclusion that flacherie was caused by bacteria. Viruses are presently believed to be the main cause. Flacherie may spread by accident or inheritance. Accidental flacherie could be avoided with good hygiene. Hereditary flacherie was prevented by utilizing moths whose digestive chambers lacked the microbes that cause flacherie to lay their eggs.

French microbiologist Louis Pasteur demonstrated in the middle of the 19th century that boric acid treatment of the female vaginal canal eliminated the bacteria that caused postpartum infections without harming mucous membranes.

Joseph Lister developed antiseptic techniques in surgery as a result of his proposal to stop microbes from entering the human body. The work of English surgeon Joseph Lister (1827–1912) on wound infection prevention provided indirect support for the germ hypothesis of illness. Lister created a system of antiseptic surgery to stop microorganisms from getting into wounds after being fascinated by Pasteur's research on the role

of bacteria in fermentation and putrefaction. Phenol was applied to surgical bandages and occasionally sprayed over the surgical site, and instruments were heat sterilized. The method revolutionized surgery and was incredibly effective. Because phenol kills germs and prevents wound infections, it also offered compelling indirect evidence for the function of microbes in disease.

➢ Immunology and Vaccination:

Chicken cholera

Vaccines have significantly altered the practice of contemporary medicine, eliminating or reducing the prevalence of some of the most deadly human diseases. Humanity has benefited from vaccines for over two centuries, but the path to developing effective vaccines was lengthy and tough. Several daring research pioneers and clinicians were needed for the job.

Pasteur was already well-known and respected in France by the early 1870s, and he was elected as an associate member of the Académie de Médecine in 1873. Nonetheless, the medical community was hesitant to accept his germ hypothesis of disease, owing to the fact that it was developed by a chemist. However, over the next decade, Pasteur created the general idea of vaccination and contributed to the establishment of immunology. Pasteur's initial efforts to produce a vaccine were for chicken cholera. Pasteur began studying illnesses. One of these was the infectious respiratory illness known as fowl cholera, avian cholera, or just chicken cholera, which affects birds.

After examining the disease, Pasteur isolated the bacterium that caused it, which he named *Pasteurella multocida*. Pasteur was unable to conduct the experiments personally due to a stroke in

1868, thus he depended primarily on his subordinates Emile Roux and Charles Chamberland. Pasteur conducted studies on hens, collecting samples, or cultures, of the disease-causing microbes. The experiment with chicken cholera began in 1877, and by the following year, Roux had established a stable culture using broths. Due to his daughter's wedding and poor health, Pasteur was unable to return to the laboratory until October 1879. As he later recorded in his notebook in March 1880, he gave Roux instructions to start a new chicken cholera culture using bacteria from a culture that had been left for a month, which is typically thought to render them useless.

However, he inoculated these old cultures into his chickens anyway and discovered that, rather than dying from cholera, these chicks developed mild symptoms before recovering entirely. He then injected the chickens that had recently recovered from the month-old culture with a new sample of the disease. This should have killed them, but they showed no signs of infection. These experiments provided vital insights into how bacteria could be artificially attenuated in the laboratory.

Pasteur submitted his findings to the French Academy of Sciences in February 1880, titled "On virulent diseases, and in particular on the disease commonly known as chicken cholera," and they were published in the academy's journal. He claimed that the bacteria were weakened by exposure to oxygen. He emphasized that bacteria stored in sealed containers never lost their virulence, and that only those exposed to air in culture media could be utilized as vaccines. Pasteur had accidently identified the optimal amount of time to expose the culture to oxygen in order to immunize hens against cholera. He'd discovered a successful remedy. Pasteur and Roux observed that culturing the cultures for long periods of time between transfers reduced the bacteria's potential to cause disease. When the hens

were injected with these attenuated cultures, they stayed healthy and developed the ability to resist sickness when exposed to more virulent cultures. Pasteur named the attenuated culture a vaccine (Latin vacca, cow) after Edward Jenner (1749-1823), who utilized material from cowpox lesions to protect people from smallpox many years before. Shortly after, Pasteur and Chamberland created an attenuated anthrax vaccine.

His research on chicken cholera had a significant impact on the early stages of inoculation development and would later help create more effective vaccines.

In his presentation to the Academy, Pasteur used the term "attenuation" to describe this reduction in virulence, stating:

We can diminish the microbe's virulence by changing the mode of culturing. This is the crucial point of my subject. I ask the Academy not to criticize, for the time being, the confidence of my proceedings that permit me to determine the microbe's attenuation, in order to save the independence of my studies and to better assure their progress... [In conclusion] I would like to point out to the Academy two main consequences to the facts presented: the hope to culture all microbes and to find a vaccine for all infectious diseases that have repeatedly afflicted humanity, and are a major burden on agriculture and breeding of domestic animals.

Following his work on cholera, Pasteur moved to another disease: anthrax. Anthrax was a frightening disease that killed both humans and animals and caused significant problems for agricultural productivity at the time.

Anthrax

During the 1800s, anthrax devastated livestock, particularly sheep, across Europe. Over ten percent of the sheep were dying

in certain French fields. Both Louis Pasteur and Robert Koch came to the opinion that *Bacillus anthracis* was the cause. France's economy depended heavily on sheep, and anthrax was destroying thousands of herds. Concerned stock handlers called Louis Pasteur in 1878 to discuss the possibility of creating an anthrax vaccine. It was a difficult fight; many people had doubts and skepticism about this odd science known as vaccination. Pasteur, the humanitarian, got to work, and after several weeks of vaccination, the sheep that had received the vaccine survived while those who had not received the vaccine died. Pasteur's hard efforts were rewarded yet again. His vaccination saved millions of animals and paved the way for a human vaccine.

During Pasteur's early anthrax investigation, a wager was placed at Pouilly-le-Fort on whether the vaccine would work. Most veterinarians, French scientists, and doctors had not yet accepted the germ hypothesis of illness. They felt that anthrax was produced by an imbalance in the sheep's body or a harmful chemical. The public wager was announced. But it was immediately clear that Pasteur had won another win, bolstering the germ theory.

Following the success of the chicken cholera immunization approach, Pasteur used it to make a vaccine for anthrax, which afflicted cattle. Following Robert Koch's discovery of the bacterium, Pasteur led his laboratory in 1877 to culture bacteria from afflicted animals' blood. When animals were infected with the bacteria, anthrax developed, demonstrating that the bacterium was the source of the disease. Many livestock died of anthrax in "cursed fields". Pasteur was informed that sheep that had perished from anthrax were buried in the field. Pasteur hypothesized that earthworms may have carried the bacterium to the surface. He discovered anthrax germs in earthworm dung,

proving that he was correct. He instructed the farmers not to bury deceased animals in the fields.

When Henri Bouley presented a report from veterinary surgeon Henry Toussaint, who was not a member of the French Academy of Sciences, to the academy on July 12, 1880, Pasteur's interest in developing an anthrax vaccine was substantially stoked. Toussaint created a vaccination against anthrax by heating the bacilli to 55 °C for ten minutes. Eleven sheep and eight dogs were used to test his vaccine; half of them died after receiving it. It wasn't very successful. Pasteur replied to the academy as soon as he heard the news, saying that Toussaint's claim "overturns all the ideas I had on viruses, vaccines, etc." and that he did not imagine that a dead vaccine would operate. In August 1880, Toussaint tested the vaccination on sheep after Pasteur criticised him for using carbolic acid (phenol) to kill anthrax bacilli. Since Pasteur felt that attenuated bacteria used resources that the bacteria required to develop, he reasoned that this kind of dead vaccine shouldn't operate. He believed that oxidizing bacteria in culture broth for extended periods of time reduced their virulence.

However, unlike chicken cholera bacillus, Pasteur's team discovered that anthrax bacillus could not be easily weakened by air culture because it produced spores. In early 1881, his laboratory discovered that cultivating anthrax bacilli at 42 °C prevented them from producing spores, and he revealed this procedure in a speech to the French Academy of Sciences on February 28. Despite uneven findings, he stated on March 21 that sheep immunization had been successful. On April 28, Pasteur signed a contract acknowledging the challenge. Pasteur's assistants, Roux and Chamberland, who were assigned the duty of conducting the study, were concerned about the unreliability of the attenuated vaccine, and consequently Chamberland

covertly produced an alternate vaccine utilising chemical inactivation. In May, Roux and Chamberland conducted the public experiment at Pouilly-le-Fort without telling anyone but Pasteur how they prepared the vaccine. Ten cattle, two goats, and fifty-eight sheep were employed; half received the vaccination on May 5 and May 17, while the other half received no treatment.

Roux and Chamberland then administered the new, deadly anthrax bacillus culture to the animals on May 31. Pasteur himself was among the more than 200 people who watched and analysed the official outcome on June 2. The outcome was exactly as Pasteur had boldly predicted: "I hypothesised that the four unvaccinated cows would perish or at least become very ill, while the six vaccinated cows would not become very ill." But all of the vaccinated sheep and goats lived, whereas the unvaccinated ones had already passed away or were in the process of doing so. The following is the conclusion of his June 13 report to the French Academy of Sciences:

By looking at everything from the scientific point of view, the development of a vaccination against anthrax constitutes significant progress beyond the first vaccine developed by Jenner, since the latter had never been obtained experimentally.

The idea that a weak form of a disease could make a person immune to the virulent variant was not new; smallpox had long been known to do this. When compared to the naturally acquired sickness, smallpox vaccination (variolation) was known to produce a far less severe illness and a significantly lower death rate. In the late 1790s, Edward Jenner also conducted research on vaccination using cowpox (vaccinia) to provide smallpox with cross-immunity. By the early 1800s, vaccination had reached much of Europe. Smallpox vaccine differed from

anthrax or chicken cholera immunisation in that the later two disease organisms had been artificially weakened, negating the necessity to find a naturally weak variant of the disease organism. Pasteur's creation of pathogens that were intentionally attenuated transformed research on infectious diseases, and he named these diseases "vaccines" in homage of Jenner's discoveries.

In 1876, Robert Koch demonstrated that *Bacillus anthracis* produced anthrax. Between 1878 and 1880, Pasteur only referenced Koch's work in a footnote. Koch met Pasteur during the Seventh International Medical Congress in 1881. A few months later, Koch claimed that Pasteur used contaminated cultures and made mistakes. In 1882, Pasteur delivered a lecture in response to Koch's hostile response. Koch said that Pasteur tested his vaccine on inappropriate animals and that his research was not sufficiently scientific. Koch's 1882 work "On the Anthrax Inoculation" criticised Pasteur for being imprecise, rushing to conclusions, and concealing his techniques, and he disputed numerous of his findings regarding anthrax. Pasteur said in 1883 that Koch misread statistics and disregarded Pasteur's work on silkworms, and that he employed cultures made similarly to his successful fermentation trials.

➢ Rabies: An Event in Pasteur’s life:

On an October day in 1831, a nine-year-old boy fled from the edge of a mob that had gathered around the blacksmith shop door in a village in eastern France's highlands. Above the awed excited whispers of the people at the entrance, this boy heard the cracking "s-s-s-s-z" of a white hot iron on human flesh, which was followed by a groan of pain. Nicole, the farmer, was the victim. He had just been mauled by a crazy wolf who

charged through the village streets, howling and spitting poison froth. The boy who fled was Louis Pasteur.

"What makes a wolf or a dog mad, father—why do people die when mad dogs bite them?" Louis said. His father, the tanner, was an elderly sergeant in Napoleon's army. He had witnessed ten thousand men die from gunfire, but he had no idea why people died from sickness. "Perhaps a devil got into the wolf, and if God wills you to die, you will die; there is no help for it," the religious tanner replied. That was as good an answer as any given by the world's wisest scientist or most costly doctor. In 1831, no one knew what caused humans to die from crazy dog bites; the etiology of all sickness was unknown and enigmatic.

Pasteur once said, “I have always been haunted by the cries of those victims of the mad wolf that came down the street of Arbois when I was a little boy”.

Pasteur focused on human diseases after his success with anthrax. Although the sickness was actually quite uncommon in humans, it had long been feared due to its effects on animals. Laws were created in France to prevent the shooting of persons who were thought to be dying of rabies because of the country's extreme fear of the disease. Prior to Pasteur's studies, cauterization—which involves using a hot iron—was the method used to cure an animal bite caused by an infection. This was quite painful and, in most cases, did not eradicate the condition.

Pasteur set out to investigate the cause of hydrophobia, or rabies. Saliva samples from the lips of sick and dangerous dogs whose sudden lunge and bite could have resulted in a terrible death were collected by him personally. He also collected human victim samples. It was a risky task for the researchers to trap and confine rabid dogs and let them attack healthy dogs.

Laboratory animals were also inoculated with the saliva of the insane dogs. The outcomes were peculiar: While some animals died of rabies right away, others took weeks or months to do so. Moreover, in contrast to what had been noted in other illnesses. Pasteur was unable to identify any bacteria that would grow in or on any of his media, nor was he able to isolate a bacterium that was obviously responsible for rabies. Nonetheless, the rabies victims' unavoidable convulsions suggested that the bacterium was most likely found in the central nervous system. Though he was concerned that the injected virus "would get lost in the body before it could travel to the brain," he considered cultivating the organism in animal brain. Roux proposed trephining as a simple and painless method of directly injecting rabies fluid into a dog's brain, but Pasteur banned the practice, claiming it would do harm to the animal. However, Roux quickly performed the operation without Pasteur's presence and informed him the following day. Roux then showed Pasteur the rambunctious puppy, which calmed his concerns. The sad dog died shortly after exhibiting signs of rabies two weeks later, but scientists now have a 100% accurate method for transmitting and cultivating the elusive organism.

After hundreds of deadly trials on dogs and other animals, Pasteur understood how the rabies bacterium attacked the nervous system and eventually reached the brain. He and his colleagues discovered a method to attenuate the virus for use as a vaccine by drying an infected rabbit's spinal cord in a sterile bottle. He discovered that 14 shots of rabies vaccine would protect every rabid dog inoculated.

Pasteur created the first rabies vaccine by cultivating the virus in rabbits and then weakening it by drying the infected nerve tissue. Emile Roux, a French doctor and Pasteur collaborator, developed the rabies vaccine after successfully

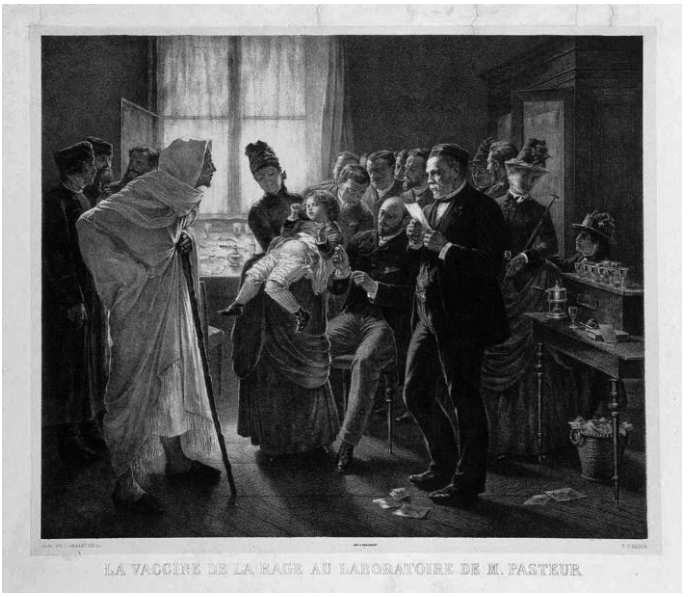
producing a lethal vaccination using this method. Prior to its initial human trial, the vaccine had been tested on hundreds of dogs. Letters from all over the world, including the leader of Brazil, rushed in, pleading for the vaccine for humans facing death from rabies, but Pasteur withheld his ultimate test. The vaccination must function the same way in humans, but it may not. He even pondered starting with himself.

He wrote to a friend that he would infect himself, and then take the vaccine. On July 6, 1885, a woman from Alsace brought her 9-year-old son, Joseph Meister, to Pasteur's laboratory. The kid had been bitten in 14 places by a crazy dog the day before, and his mother implored Pasteur to save him. When Joseph arrived, it was evident that he would die if no action was taken. At the time, rabies was a lethal disease with no cure. Pasteur consented to try immunization because the boy would die if no treatment was provided. Edward Jenner had foreshadowed the present era of vaccination almost a century before, and this marked the start of it. However, because the rabies vaccine had only been successfully tested on dogs and rabbits, Louis Pasteur's associates, including Émile Roux, did not want to administer it. Louis Pasteur was persuaded to try the unthinkable by a physician named Jacques Joseph Grancher, who allowed him to cure the Alsacian boy. Pasteur took considerable personal risks in doing this because he was not a qualified doctor and might have been prosecuted for treating the youngster. He made the decision to proceed with the treatment after speaking with doctors. Meister was given 13 inoculations over the course of 11 days, each utilizing viruses that had been weakened for a brief amount of time. He checked on Meister three months later and discovered that he was doing well. Pasteur received hero status. Soon later, the small Paris laboratory was overrun by people from outside of France.

Nineteen days previously, 19 peasants from Russia were bitten by a rabid wolf, and some of them were so mutilated they could not walk, capturing the attention of all of France when they came at the laboratory despite knowing only one word of French "Pasteur". Because it had been so long since the peasants had been bitten, Pasteur was concerned that few, if any, could be rescued, so he gave them two injections every day to make up for lost time. Surprisingly, all the Russians survived. The Russians returned to a country that greeted them with the reverence one would have for a person raised from the dead. The Tsar of Russia granted Pasteur the Diamond Cross of St. Anne, as well as a hundred thousand Francs to create a research facility, which served as the foundation for the Pasteur Institute.

In 1885, a 15-year-old shepherd named Jean-Baptiste Jupille arrived at the Ulm Street Laboratory. He was brutally bitten by a rabid dog that had previously attacked six other shepherds. On October 20, 1885, Pasteur began treating Jean-Baptiste Jupille, and the treatment was once again successful. Later in 1885, people, including four youngsters from the United States, visited Pasteur's laboratory to be infected. In 1886, he treated 350 patients, of whom just one contracted rabies. The breakthrough had far-reaching consequences. The treatment's effectiveness paved the way for the production of numerous additional vaccines. Patients with rabies travelled from all over the world to get the vaccine. The enormous volume of patients inspired Dr Grancher to establish a dedicated vaccination centre in an annexe of the École Normale Supérieure, not far from Louis Pasteur's laboratory. Grancher contributed significantly to the establishment of the Pasteur Institute. On November 14, 1888, the Institute Pasteur was officially opened. People from all over the world helped build the Pasteur Institute in Paris,

France, as homage to Pasteur's vaccine research. One of the institute's initial duties was vaccine production. Pasteur's reputation for rabies research was legendary, prompting the French government to create the Pasteur Institute in Paris in 1888. The Pasteur Institute was founded as a clinical centre for the treatment of rabies and other dangerous diseases, but it is now a significant biomedical research centre specializing in antiserum and vaccine development and production.



Rabies vaccination in Pasteur's laboratory in Paris

- **Controversies:**

In 1878, Pasteur, a 55-year-old French national hero, discreetly instructed his family not to share his lab notebooks with anybody. His family complied, and all of his records were kept and passed on in secret. The documents were eventually given to the French national library (Bibliothèque nationale de France) in 1964 by Pasteur Vallery-Radot, Pasteur's grandson

and last living male descendent. Nevertheless, until Vallery-Radot's passing in 1971, the papers were only available for historical research. Only in 1985 were the documents assigned a catalogue number.

In his 1995 book The Private Science of Louis Pasteur, which marked the centenary of the scientist's death, Gerald L. Geison analyzed Pasteur's personal notebooks and concluded that Pasteur had provided multiple false accounts and fabricated his most significant discoveries. Following additional inspections of Pasteur's documents, French immunologist Patrice Debré concluded in his book Louis Pasteur (1998) that, despite his genius, Pasteur had faults. According to one book review, Debré "sometimes finds him unfair, combative, arrogant, unattractive in attitude, inflexible, and even dogmatic."

- **Awards and Honours:**

The Pharmaceutical Society awarded Pasteur 1,500 francs in 1853 for his work on racemic acid production. In 1856, the Royal Society of London awarded him the Rumford Medal for his discovery of the nature of racemic acid and its relationship to polarized light, and the Copley Medal in 1874 for his work on fermentation. In 1869, he was chosen as a Foreign Member of the Royal Society.

For his experimental debunking of spontaneous generation, Pasteur received the 1859 Montyon Prize for experimental physiology from the French Academy of Sciences in 1860, the Jecker Prize in 1861, and the Alhumbert Prize in 1862. He won the 1862 election to join the mineralogy division of the French Academy of Sciences, despite losing the 1857 and 1861 elections. In 1887, he was chosen to serve as the academy's permanent secretary for the physical science division, a post he kept until 1889.

Pasteur was appointed commander of the Brazilian Order of the Rose and elected to the Académie Nationale de Médecine in 1873. He was chosen to fill Émile Littré's vacancy of the Académie française in 1881. In 1882, Pasteur was awarded the Albert Medal by the Royal Society of Arts. He joined the Royal Netherlands Academy of Arts and Sciences as a foreign member in 1883. He was chosen to join the American Philosophical Society in 1885. Pasteur received 10,000 Ottoman liras and the Order of the Medjidie (I Class) from Ottoman Sultan Abdul Hamid II on June 8, 1886.

In 1889, he received the University of Edinburgh's Cameron Prize for Therapeutics. In 1895, Pasteur received the Royal Netherlands Academy of Arts and Sciences' Leeuwenhoek Medal in recognition of his contributions to microbiology.

The Legion of Honor awarded Pasteur a Chevalier in 1853, followed by promotions to Officer in 1863, Commander in 1868, Grand Officer in 1878, and Grand Cross in 1881.

- **Legacy:**

Many streets around the world are named in his honor. Both the Institute Pasteur and the Université Louis Pasteur are named after Pasteur. Lycée Pasteur in Neuilly-sur-Seine, France, and Lycée Louis Pasteur in Calgary, Alberta, Canada, are both named after him. In South Africa, the Louis Pasteur Private Hospital in Pretoria and Life Louis Pasteur Private Hospital in Bloemfontein are named after him. The Louis Pasteur University Hospital in Košice, Slovakia, is likewise named after Pasteur.

A statue of Pasteur has been constructed at San Rafael High School in San Rafael, California. A bronze bust of him is on the French Campus of Kaiser Permanente's San Francisco Medical

Centre in San Francisco. Harriet G. Moore designed the sculpture, which was cast in 1984 by Artworks Foundry.

The UNESCO/Institute Pasteur Medal was established on the centenary of Pasteur's death and is awarded every two years in his honor, "in recognition of outstanding research contributing to a beneficial impact on human health".

The French Academician Henri Mondor stated: "*Louis Pasteur was neither a physician nor a surgeon, but no one has done as much for medicine and surgery as he has*.

- **Pasteur Institute:**

The Institute Pasteur is named after its distinguished founder and owes much to his scientific genius. Its tale is intertwined with the lives and discoveries of numerous other scientists, all of whom were inspired by Louis Pasteur's humanist principles, whose scientific triumphs have improved people's health around the world.

Pasteur suggested an institute for the vaccination after creating the rabies vaccine. The Pasteur Institute started soliciting money in 1887, and donations came from all across the world. The institute's goals were listed as "the treatment of rabies according to the method developed by Pasteur" and "the study of virulent and contagious diseases" in the formal statute that was registered in 1887. The institute opened its doors on November 14, 1888.

He brought together scientists with diverse specialties. The first five departments were led by two École Normale Supérieure graduates, Émile Duclaux (general microbiology research) and Charles Chamberland (microbe research applied to hygiene), as well as a biologist, Élie Metchnikoff (morphological microbe research), and two physicians, Jacques-

Joseph Grancher (rabies) and Émile Roux (technical microbe research). One year after the institute's inception, Roux established the first microbiology course ever taught in the world, titled 'Course of microbe research methodologies'. Since 1891, the Pasteur Institute has expanded to include 32 institutes in 29 countries throughout the world.

- **Louis Pasteur in his last famous speech, he says:**

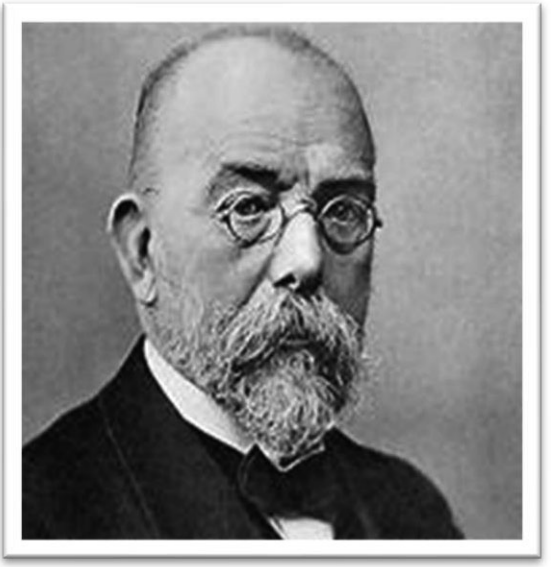
You young men—doctors and scientists of the future—do not let yourselves be tainted by apparent skepticism; nor discouraged by the sadness of certain hours that creep over nations. Do not become angry at your opponents, for no scientific theory has ever been accepted without opposition. Live in the serene peace of libraries and laboratories. Say to yourselves, first, “What have I done for my instruction?” And as you gradually advance, “What am I accomplishing?” Until the time comes when you may have the immense happiness of thinking that you have contributed in some way to the welfare and progress of mankind.

This brilliant scientist conducted experiments based on his extensive experience and scientific guidelines. Pasteur discovered the problem and proposed a solution. It is quite astounding that Pasteur was able to solve all of the mysteries he encountered, whether it was rabies or sour wine. Pasteur's pioneering work is widely recognized as the foundation of modern aseptic surgery.

Pasteur's significant contributions to science, microbiology, and medicine are acknowledged by nearly all historians. He practiced operational science on a daily basis and was an experimentalist. Pasteur is a shining example of the idea that good science may be done without being an evolutionist. His creationist and Christian beliefs, however, have come under

scrutiny in recent years. His tests that refute spontaneous generation provide the strongest evidence for his unique creation theory. Over the course of roughly five years, these experiments were conducted. Pasteur "converted" from a chemist to a microbiologist during this period.

Pasteur experimenting in his laboratory



Robert Koch

(11 December 1843 - 27 May 1910)

"If the importance of a disease for mankind is measured by the number of fatalities it causes, then tuberculosis must be considered much more important than those most feared infectious diseases"

➢ Robert Koch:

Heinrich Hermann Robert Koch was a pioneering German physician and microbiologist who made substantial contributions to bacteriology and advanced the germ theory of disease. His revolutionary work in identifying the causative agents of anthrax, TB, and cholera transformed medical science and public health. He is regarded as one of the main founders of

modern bacteriology. As a result, he is commonly referred to as the "**father of medical bacteriology.**" His discovery of the anthrax bacterium (*Bacillus anthracis*) in 1876 is regarded as the origin of modern bacteriology. Koch's discoveries demonstrated that germs "could cause a specific disease" and directly gave confirmation for the germ theory of diseases, so forming the scientific basis of public health and saving millions of lives.

His development of Koch's postulates created a systematic framework that is still used today to connect particular pathogens to diseases. Koch received many distinguished awards for his outstanding work, including the Nobel Prize in Physiology or Medicine in 1905. Organizations such as the Robert Koch Institute continue to carry on his legacy.

In recognition of his efforts, he was appointed as a government advisor at the Imperial Health Office in 1880, promoted to a senior executive position in 1882, Director of the Hygienic Institute and Chair (Professor of hygiene) of the Faculty of Medicine at Berlin University in 1885, and the Royal Prussian Institute for Infectious Diseases (later renamed the Robert Koch Institute after his death) in 1891.

Following his discovery of tuberculin as a treatment for tuberculosis, which was later found to be unsuccessful, a significant dispute ensued. However, the drug was later developed for the diagnosis of tuberculosis. He was awarded the Nobel Prize in Physiology or Medicine in 1905 for his work on TB. The World Health Organization has designated March 24, 1882, the day he announced the discovery of the tuberculosis bacterium, as "World Tuberculosis Day" since 1982.

Other scientists were inspired by Koch's study. As a result of their efforts, other germs that cause diseases like meningitis, pneumonia, and diphtheria were found. Because doctors now

knew that bacteria were the source of sickness symptoms and that they needed to be eliminated, Koch's work significantly benefited British medicine.

➢ Early life and Education:

Koch was born in Clausthal, Germany, on December 11, 1843, to Hermann Koch and Mathilde Julie Henriette. His father was a mine engineer. He was the third of thirteen siblings. He excelled academically from a young age. At the age of five, he shocked his parents by informing them that he had taught himself to read using newspapers. He completed his secondary studies in 1862, excelling in science and maths. He attended the local high school (Gymnasium), where he shown an interest in biology and, like his father, a strong desire to travel.

In 1862, Koch enrolled in the University of Göttingen to study natural science at the age of 19. He studied botany, physics, and mathematics. He was hired as a Pathological Museum assistant at the university. After three semesters, he changed his major to medicine since he wanted to become a doctor. He was influenced by the belief of Jacob Henle, an anatomist who published a theory of contagion in 1840, that infectious diseases were caused by living, parasitic organisms while he was a medical student. He was invited to join Jacob Henle's study on the anatomy of the uterine nerve. This research earned him a university research prize and allowed him to briefly study under Rudolf Virchow, who was then regarded as "Germany's most renowned physician". After receiving his M.D. in 1866, Koch travelled to Berlin for six months of chemical study, where he was influenced by Virchow. Koch began his research at the Physiological Institute in his sixth

semester, where he investigated the secretion of succinic acid, a signalling chemical involved in mitochondrial metabolism.

In January 1866, he graduated from medical school with the highest distinction. After working as an Assistant in the General Hospital in Hamburg, he went into general practice in 1867, first in Langenhagen and then, in 1869, in Rackwitz, Posen. Here, he passed his District Medical Officer Examination. He enlisted for service in the Franco-Prussian War in 1870, and he served as Wollstein's District Medical Officer from 1872 to 1880. It was here that he conducted groundbreaking research, propelling him to the forefront of scientific workers.

In 1875, he visited many of Germany's leading scientific research institutions, exposing him to the nascent field of microbial science. Louis Pasteur had discovered that bacteria cause putrefaction; Joseph Lister had developed techniques of antiseptic surgery; and Jacob Henle, Koch's anatomy teacher in Göttingen, was defending the idea of contagium animatum, which held that disease could be caused by living transferable entities. The 'germ theory' was widely contested, and the role of bacteria in communicable disease remained obscure.

- **Anthrax:**

Robert Koch is well known for discovering the *Bacillus anthracis* as the cause of anthrax, a fatal disease that affects both people and animals. In the Wollstein district at the time, anthrax disease was common among farm animals and was frequently killing people and livestock with no known cause. Koch started researching this disease despite lacking any scientific tools and being completely shut off from libraries and other scientific professionals. His four-room flat served as his laboratory, along with his tools—aside from the microscope his wife had given him. His ground-breaking research, carried out in

a lab with very little equipment, confirmed the germ theory of disease and showed that a particular microbe was the cause of the illness. Following his official appointment as a district physician in 1872 in Wollstein (now Wolsztyn), Poland, Robert started researching the illness known as anthrax. Koch eventually made the amazing discovery that anthrax was caused by a single pathogen in 1876. Koch was able to solve the mystery of the anthrax disease by discovering the dormant stage, the anthrax spores. He was able to clarify the bacterium's exceptional resistance to environmental factors by learning more about this pathogen. Koch's discovery that a microscopic creature was responsible for the transmission of a disease was a significant accomplishment. His findings were especially surprising since they were conducted in a poorly equipped laboratory in Wollstein.

He published his discovery in a booklet titled "*The Aetiology of Anthrax Disease*, Based *on the Developmental History of Bacillus Anthracis*." In 1877, he published his findings on the structure of the anthrax bacterium, which was the first time a bacteria was photographed. He discovered that anthrax bacteria produce spores, which can remain dormant under certain conditions. However, under ideal conditions, the spores were activated, causing disease. To determine the causal agent, he dry-fixed bacterial cultures on glass slides, stained them with dyes, and examined them under a microscope. His study on anthrax is important because he was the first to link a specific microbe with a specific disease, so establishing the germ theory of disease.

➢ Koch's Postulates:

The methods Koch used in bacteriology led to the development of a medical concept known as Koch's postulates,

which are four generalized medical concepts used to determine the association between pathogens and specific diseases. The concept is still in use in most situations. The German physician Robert Koch's investigation of anthrax provided the first direct demonstration of bacteria's role in diseases. Koch used the criteria set by his former master Jacob Henle to establish the link between *Bacillus anthracis* and anthrax; his findings were published in 1876.

Koch injected healthy mice with diseased animal tissue, and the mice became ill. After transferring anthrax by inoculation through a series of 20 mice, he incubated a piece of spleen with the anthrax bacillus in beef serum. The bacilli multiplied and formed endospores. When the isolated bacilli or spores were introduced into healthy mice, anthrax emerged. His criteria for proving the causal relationship between a microorganism and a specific disease are known as **Koch's postulates**. Koch's evidence that anthrax was caused by B. anthracis was independently verified by Pasteur and his colleagues. They found that when dead animals were buried, anthrax spores persisted and were carried to the surface by earthworms. The spores were subsequently consumed by healthy animals, who then fell ill. Following his research on anthrax, Koch thoroughly described his hypotheses in his paper on the etiology of tuberculosis. In 1884, he discovered that this disease was caused by the rod-shaped bacteria *Mycobacterium tuberculosis*, and his study earned him the Nobel Prize in Physiology or Medicine in 1905. Koch's postulates were immediately accepted by others, who utilized them to link various ailments to the causative agent. However, their utilization is not always possible. For example, the causal agent of leprosy, *Mycobacterium leprae*, cannot be isolated in pure culture.

While working as a government advisor, Robert Koch discussed his discovery of the tuberculosis bacterium and its role in the disease. He emphasised the significance of isolating pathogens using pure cultures, as described in Koch's postulates. These postulates, developed from his work on anthrax, created a fundamental approach for identifying the causal agents of infectious diseases and became a standard in the area. Although Koch created the concepts, his subordinate Friedrich Loeffler formalised them as postulates in 1883. The fourth postulate was added by Erwin Frink Smith in 1905.

1. The organism must always be present in every case of the disease, but not in healthy individuals.

2. The organism must be isolated from a diseased individual and grown in pure culture.

3. The pure culture must cause the same disease when inoculated into a healthy, susceptible individual.

4. The microorganism must be re-isolated from the inoculated, diseased experimental host and identified as being identical to the original specific causative agent.

- **Development of Techniques for Studying Microbial Pathogens:**

However, Koch continued to lack proper workspace and conditions for his work until 1880, when he was hired by the Imperial Health Bureau in Berlin. It was then that he was given a small, subpar room and a better laboratory, where he could work with assistants like Loeffler and Gaffky. In this instance, Koch kept improving the bacteriological techniques he had applied in Wollstein.

Koch developed numerous breakthrough microbiological procedures while working as a physician. He was the first to employ an oil immersion lens, a condenser, and microphotography in microscopy to improve the visibility of smaller microbes. His development of the bacterial culture method, which used agar and glass plates, making him the first to cultivate bacteria in the lab.

He also devised new methods of staining germs, making them more visible and easier to identify. All of this effort resulted in the development of ways for obtaining harmful bacteria in pure culture devoid of other species, as well as detecting and identifying them.

During Koch's research on bacterial infections, it became important to isolate suspected bacterial pathogens in pure culture, which contains just one type of microorganism. Initially, Koch cultivated bacteria on the sterile surfaces of cut, boiled potatoes, but the germs did not always thrive. Eventually, he created culture media from meat extracts and protein digests, thinking that these were analogous to bodily fluids. Initially, he attempted to harden the media by adding gelatin. Separate bacterial colonies formed after a bacterial sample was streaked across the surface of the solidified medium.The sample can alternatively be combined with liquefied gelatin medium. When the gelatin media hardened, the bacteria formed distinct colonies. Despite its benefits, gelatin was not the best solidifying agent because it is digestible by many microorganisms and dissolves at temperatures above 28°C. Fanny Eilshemius Hesse, the wife of Walther Hesse, one of Koch's helpers, suggested a superior choice. She proposed using agar as a hardening ingredient, which she had used to produce jellies. Most germs did not attack agar. Additionally, handling boiling liquid was not necessary because it did not

melt until it reached a temperature of 100°C and, once melted, did not harden until it reached a temperature of 50°C. Some of the media that Koch and his colleagues created, like nutritional agar and nutrient broth, are still in use today. Richard Petri (1852–1921) invented the petri dish (plate), a container for storing solidified medium, which was another crucial instrument created in Koch's lab.

➢ Development of Petri dish:

The 1881 booklet "Methods for the Study of Pathogenic Organisms" by Koch has been referred to as the "Bible of Bacteriology." In it, he explained a brand-new technique for cultivating bacteria on glass slides with agar. A thin layer of gelatin was applied to the glass slide after a liquid agar had been poured across it. The culture media solidified due to the gelatin, allowing for the homogeneous distribution of bacterial samples.The entire bacterial culture was then placed on a glass plate, along with a little piece of damp paper. Koch dubbed this container the wet chamber. The standard chamber was a circular glass dish of 20 cm in diameter and 5 cm in height, with a lid to avoid contamination. The glass plate and transparent culture material allowed for easy viewing of bacterial growth.

In August 1881, Koch gave a public demonstration of his plating technique at the Seventh International Medical Congress in London. Louis Pasteur cried out, "What a great progress, Sir!" there. His students found novel microorganisms utilising Koch's microscope and agar-plate culture approach. Georg Theodor August Gaffky identified the typhoid bacterium (*Salmonella enterica*) in 1884, while Friedrich Loeffler identified the glanders (*Burkholderia mallei*) and diphtheria (*Corynebacterium diphtheriae*) bacteria in 1882 and 1884, respectively.

Julius Richard Petri, Koch's assistant, modified the procedure and published it in 1887 under the title "A minor modification of the plating technique of Koch". The culture plate was given the name, Petri dish. It is often said that Petri invented a novel culture plate, although this is not true. He just dumped the glass plate and utilized the circular glass dish immediately. This significantly minimized the possibility of contamination.

- **Cholera:**

In August 1883, the German government sent a medical team led by Koch to Alexandria, Egypt, to investigate a cholera outbreak. Koch discovered that the intestinal mucosa of patients who died from cholera was always infected with bacteria, but he could not determine whether the bacteria were the causative pathogens. As the outbreak in Egypt subsided, he was sent to Calcutta (now Kolkata), India, where there was a more serious outbreak. He immediately discovered that the Ganges River was the source of cholera. He did autopsy on nearly 100 bodies and discovered bacterial infections in each one. He detected the same bacteria in water tanks, indicating the source of the sickness. He isolated the bacteria in pure culture on January 7, 1884. He then established that the bacterium was a new species, describing it as "a little bent, like a comma." His investigation with fresh blood samples revealed that the bacterium could damage red blood cells, and he proposed that the organism employed some form of chemical to create the sickness.

In 1959, Indian scientist Sambhu Nath De developed the cholera toxin. Koch reported his discovery to the German Secretary of State for the Interior on February 2nd and published it in the "German Medical Weekly the following

month". When Koch and his colleagues returned to Berlin in May 1884, they were welcomed as heroes.

Despite his conviction that the bacteria was the cholera pathogen, Koch was unable to provide conclusive proof that the bacterium caused the symptoms in healthy individuals (as per Koch's postulates). His pure bacterial culture experiment on animals did not result in illness, and it accurately demonstrated that animals are resistant to human pathogens. In the past, the bacterium was referred to as "the comma bacillus" and, in science, as *Bacillus comma*. An Italian scientist named Filippo Pacini (1812–83) first described the comma-shaped bacteria, which he named Vibrio, thirty years ago in 1854. The scientific community mainly disregarded Pacini's work. The cholera organism was separately found by Robert Koch, who was also ignorant of Pacini's work at the University of Florence. The organism was not properly renamed as Vibrio cholerae Pacini 1854 until 1965, 82 years after Pacini's passing. Koch received a prize of 100,000 German Marks for his realisation that cholera spread by tainted water, even though he cannot be credited with being the first to find the bacteria.

His research resulted in the implementation of public health initiatives and sanitary measures, such as the provision of clean drinking water, which assisted in containing cholera outbreaks in Hamburg, Germany. Koch was named both the director of the newly created Institute of Hygiene at the University of Berlin and a professor of hygiene there in 1885.

Photograph of Koch (third from the right) and other members of the German Cholera Commission in Egypt, 1884

- **Tuberculosis:**

At Berlin, he began to focus on tuberculosis, which was a major health threat in Europe at the end of the nineteenth century. During his time as a government advisor for the Imperial Health Agency in Berlin in the 1880s, Robert Koch had a strong interest in tuberculous research. At the time, tuberculosis was largely assumed to be hereditary, but Koch was confident it was caused by a bacterium. In 1882, he identified Mycobacterium tuberculosis as the disease's causal agent and reported his results in "The Aetiology of Tuberculosis". Koch announced his discovery to the German Physiological Society on March 24, 1882, stating that staining procedures revealed rod-shaped bacteria in tubercular tissue.

He improved the staining procedure for visualizing the tuberculosis bacillus in experimentally afflicted animals and correctly determined that the bacillus had "a special wall of

unusual properties". He noted that bacteria were typically packed in bundles, and that portions carrying TB and leprosy bacilli were identical. He called them tubercle bacillus.

He began isolating the bacterium in pure form from afflicted tissues. Initially, he was frustrated since the culture procedures that worked for anthrax did not work for tuberculosis (TB). After more than ten days, he was able to successfully culture the organism using solidified blood serum.

Koch's work on tuberculosis persisted throughout his career. In the mid-1880s, he concentrated on developing effective disinfection treatments for tuberculosis sputum, experimenting with arsenic and creosote, but both proved ineffectual. He also attempted to create a tuberculosis vaccine, but his initial efforts were unsuccessful. By 1888, Koch had turned his attention to synthetic dyes for antibacterial tests. Koch made a revolutionary discovery in 1890: a glycerine-based extract from tuberculosis cultures could eliminate diseased tissue in guinea pigs, halting the disease's growth. He made an initial announcement at the Tenth International Medical Congress in Berlin and later demonstrated the extract's efficacy in treating humans using the Bacillus Calmette-Guerin (BCG) procedure.

Despite initial excitement, Koch's vaccination elicited severe reactions in some test animals, which became known as the Koch phenomenon. This reaction, characterised by an intense immunological response at the vaccine site, demonstrated the complexities of tuberculosis treatment. Koch initially described the substance as a brownish-transparent fluid. Josephs Pohl-Pincus first used the term "tuberculin" in 1844 to describe to tuberculosis culture media, and Koch eventually embraced this nomenclature and referred to his extract as "tuberculin." Koch's work, published in early 1891, was first hailed as a

breakthrough, but it is now widely viewed as a serious failure in medicinal applications. While this endeavour severely tarnished his image, he spent the rest of his life tirelessly working to develop tuberculin into a marketable drug. Despite this setback, Koch's discovery was not entirely unsuccessful; the chemical is presently used to measure tuberculosis-related hypersensitivity in patients.

- **Tuberculin:**

At the 10th International Congress of Medicine in Berlin in August 1890, he stated that tuberculin generated from the TB bacillus could be used to cure tuberculosis in guinea pigs and kill them. The declaration was met with enormous enthusiasm by both the administration and the general people. When Koch discovered tuberculin in 1890 as a tuberculosis treatment, he kept the discovery a secret and did not reveal the source. After a year of public pressure, he finally publicised the experiment and its source. A clinical investigation with tuberculin was promptly conducted on 1769 patients, and the results were released in February 1891. Tuberculin did not have a protective effect; just 1% was cured, 34% showed some improvement, 55% showed no change and 4% had died. Clinical experiments with tuberculin were terrible and completely failed. Rudolf Virchow's autopsy report of 21 tuberculin-treated victims to the Berlin Medical Society on January 7, 1891 revealed that the subjects died as a result of the treatment rather than being healed of tuberculosis. In late 1891, a German official assessment concluded that tuberculin did not treat tuberculosis. Koch's reputation deteriorated after this point.

His desire for financial gain from the novel medication and the subsequent creation of his own research institute were the causes of his early concealment. He had attempted to leave

government service and start his own autonomous state-run institute since 1885. After the setback, he was dismissed from the University of Berlin and compelled to serve as the Director of the recently founded Royal Prussian Institute for Infectious Diseases in 1891.

- **Acquired Immunity:**

Koch's observations contributed to our understanding of acquired immunity. Subsequently, on December 26, 1900, he set off on an expedition to German New Guinea. There, he investigated the blood samples of indigenous Papuans and discovered the existence of Plasmodium parasites, which cause malaria. Despite this, Papuans endured only minor or even undetected malaria cases. In contrast, newly arrived German settlers and Chinese labourers were more likely to contract malaria. However, these visitors gradually gained resistance to the disease.

- **Awards and Honours:**

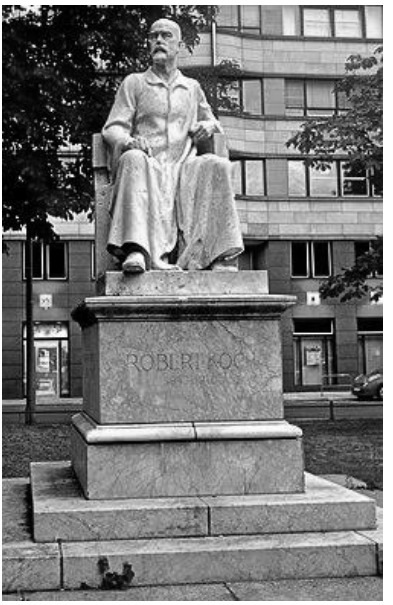
Koch was appointed a Knight Grand Cross in the Prussian Order of the Red Eagle on November 19, 1890, and became a Foreign Member of the Royal Society (ForMemRS) in 1897. He received the Nobel Prize in Physiology and Medicine "for his investigations and discoveries in relation to tuberculosis" in 1905. In 1906, his research on tuberculosis and tropical diseases earned him the Order Pour le Merite, and in 1908, he received the Robert Koch Medal, which was established to honour the greatest living physicians. Emperor Wilhelm I bestowed upon him the Order of the Crown, 100,000 marks, and appointment as Privy Imperial Councillor, Surgeon-General of the Health Service, and Fellow of the Science Senate of the Kaiser Wilhelm Society.

Koch founded the Royal Prussian Institute for Infectious Diseases in Berlin in 1891. Following his death, it was renamed the Robert Koch Institute in his honour.

Since 1982, the World Health Organisation has commemorated "World Tuberculosis Day" on March 24 to commemorate Koch's discovery of the tuberculosis bacterium. Koch's name is one of 23 from the fields of hygiene and tropical medicine to appear on the frieze of the London School of Hygiene & Tropical Medicine building on Keppel Street in Bloomsbury.

Following his death, the Royal Prussian Institute for Infectious Diseases, which Koch established and administered, was renamed the Robert Koch Institute. A massive marble statue of Koch is in Berlin's Robert Koch Platz (fourth image), and it was constructed in 1916. In 1960, on the 50th anniversary of his death, a commemorative postage stamp was issued in his honour.
His life was the subject of a 1939 German film starring Oscar-winning actor Emil Jannings in the lead role.

In 1938 the National Tuberculosis Association paid tribute to Koch and issued a U.S. ***Christmas Seal.***



Statue of Koch at Robert-Koch-Platz (Robert Koch square) in Berlin

➢ Controversies:

Koch and Pasteur were cordial when they first met in August 1881 at the Seventh International Medical Congress in London. However, they had scientific disagreements for the remainder of their careers. The dispute began when Koch took his 1876 discovery of the anthrax bacillus as proof that the germ was the cause of anthrax infections. He did not prove that the bacterium was the cause of the illness; rather, it was an inference, even though his postulates had not yet been developed. Thus, Pasteur contended that Koch's discovery did not provide complete evidence of causality. "Anthrax never occurs without viable anthrax bacilli or spores," Koch wrote in his 1881 conclusion.

In my judgement, no more compelling evidence can be provided that anthrax bacilli are the genuine and only cause of anthrax, and that vaccination, as indicated by Pasteur, is impossible. Pasteur sent his aide Louis Thuillier to Germany to demonstrate his vaccine, which proved Koch's theory incorrect. In a heated public argument at the International Congress for Hygiene in Geneva in 1882, Koch denounced Pasteur's methods as "unreliable," claiming they "are false and inevitably lead to false conclusions." Koch later continued to attack Pasteur, claiming, "Pasteur is not a physician, and one cannot expect him to make sound judgements about pathological processes and disease symptoms."

Alexander Fleming

(6th August 1881– 11th March 1955)

One sometimes finds what one is not looking for. When I woke up just after dawn on September 28, 1928, I certainly didn't plan to revolutionize all medicine by discovering the world's first antibiotic, or bacteria killer. But I suppose that was exactly what I did.

"I did not invent penicillin. Nature did that.
I only discovered it by accident."

"One sometimes finds what one is not looking for".

➢ Sir Alexander:

Scottish physician and scientist Sir Alexander Fleming (6 August 1881 – 11 March 1955) is renowned for having discovered penicillin, the first widely used antibiotic. The "single greatest victory ever achieved over disease" was the term used to characterise his 1928 discovery of what was eventually known as benzylpenicillin (or penicillin G) from the mould *Penicillium rubens*. Millions of lives have been saved by the straightforward discovery and application of the antibiotic agent. He and Howard Florey and Ernst Chain, who developed techniques for the mass isolation and synthesis of penicillin, shared the 1945 Nobel Prize in Physiology or Medicine for this discovery.

In 1922, he also identified a bacteria he called *Micrococcus lysodeikticus*, which he later renamed *Micrococcus luteus*, and the enzyme lysozyme from his nasal discharge. In 1944, Fleming received a knighthood for his contributions to science. He was listed as one of the 100 Most Important People of the 20th Century by Time magazine in 1999. He was selected as one of the 100 Greatest Britons in the BBC's 2002 television poll, and he was ranked third among the "greatest Scots" in a 2009 STV opinion poll, trailing only William Wallace and Robert Burns.

➢ Early life and Education:

Alexander Fleming was the third of four children born to farmer Hugh Fleming and Grace Stirling Morton, the daughter of a local farmer, on August 6, 1881, at Lochfield farm near Darvel, in Ayrshire, Scotland. Hugh Fleming's first marriage produced four surviving children. He passed away when Alexander was seven years old, and he was fifty-nine when he married Grace for the second time.

Before moving to London and enrolling at the Royal Polytechnic Institution, Fleming attended Loudoun Moor School, Darvel School, and Kilmarnock Academy on a two-year scholarship. Twenty-year-old Alexander Fleming received some money from his uncle, John Fleming, after four years of employment at a shipping agency. The younger Alexander enrolled in St Mary's Hospital Medical School in Paddington (now a part of Imperial College London) in 1903 after his older brother, Tom, who was already a doctor, advised him to pursue a similar career. In 1906, he graduated with honors, earning an MBBS degree from the institution.

Fleming had been a member of the medical school rifle club and served as a private in the London Scottish Regiment of the Volunteer Force from 1900 to 1914. Research was not Fleming's intended career path. He gained recognition as a marksman while he was a soldier in the Territorial Army's London Scottish Regiment. The captain of the rifle club persuaded Fleming to choose a career in research over surgery in order to retain him in St. Mary's. Sir Almroth Wright, a pioneer in immunology and vaccine research and an enthusiastic club member, agreed to mentor Fleming after the captain introduced him to him.

Alexander Fleming joined the research department of St. Mary's Hospital after completing his medical studies, where he was supervised by Sir Almroth Wright. Wright was a pioneer in vaccine therapy and immunology, renowned for his creative methods of treating and preventing bacterial illnesses. Fleming became very interested in bacteriology under Wright's guidance, and he studied the body's immunological reactions to bacterial infections in great detail. This early stage of his profession expanded his knowledge of bacterial infections and influenced

his scientific methodology. Fleming spent the entirety of his career with this research team.

In 1915, Fleming married Sarah Marion McElroy, an Irish-born nurse known by the nickname Sareen. After nine years of marriage, they had a son, Robert Fleming, who later became a general practitioner. After 34 years of marriage, Sareen died, which had a great impact on Fleming. He then immersed himself in his job, working longer hours in his lab behind closed doors.

- **Antiseptics:**

Fleming was a member of the Royal Army Medical Corps during World War I, having been commissioned as a lieutenant in 1914 and elevated to captain in 1917. He saw personally the terrible effects of infected wounds on soldiers while working in battlefield hospitals on the Western Front in France, along with many of his colleagues. Many of his fellow troops died during this time, not often from combat injuries but rather from the uncontrollable infection that followed. These events had a significant impact on his subsequent study. The horrible trench conditions and the prevalence of infected wounds among injured soldiers left an indelible effect on Fleming. Antiseptics were the principal means of infection control, and they usually caused more harm than benefit. He discovered that antiseptics employed at the time were sometimes ineffective against deep-seated infections, might increase tissue damage, and frequently worsened injuries. . In an article published in the medical magazine The Lancet in 1917, he reported an intriguing experiment that explained why antiseptics killed more soldiers than infection during the war. Antiseptics were effective on the surface, but deep wounds tended to protect anaerobic bacteria from the antiseptic agent. Fleming noted the existence of

anaerobic bacteria in deep wounds that persisted despite antiseptic treatment. Despite Wright's strong support for Fleming's findings, the majority of army doctors continued to use antiseptics throughout the war, even when doing so made patients' conditions worse. These findings strengthened Fleming's resolve to find a cure and highlighted the pressing need for more potent antibacterial therapies. This time in his life had a significant impact on his subsequent studies, which finally resulted in the revolutionary discovery of penicillin.

➢ Discovery of Lysozyme:

Fleming carried out more research on the growth of bacteria and antibiotic agents at St. Mary's Hospital. Fleming discovered that one of the agar plates he was keeping for bacteria in late 1921 was tainted with airborne bacteria. He added nasal mucus while he was sick with a cold and discovered that it prevented the growth of bacteria. A transparent, clear circle, one centimeter from the mucus, surrounded the mucus area, signifying the bacterial killing zone. He utilized bacteria kept in saline that produced a yellow suspension in the following test. Within two minutes of adding fresh mucus, the yellow saline became totally clear. He expanded his testing with tears donated by his coworkers. Allison reminisced, "For the next five or six weeks, our tears provided the supply for this extraordinary phenomenon." Following the failure of onions, we employed many lemons to induce a flood of tears. We had such a high demand for tears that laboratory attendants were forced into action, earning threepence each contribution. After more research, Fleming identified a material in the mucus that prevented the growth of bacteria, which he called lysozyme. He also tested sputum, cartilage, blood, semen, ovarian cyst fluid, pus, and egg white, and all of these contained the bactericidal

ingredient. In December, he presented his findings to the Royal Society and the Medical Research Club.

In his report "On a remarkable bacteriolytic element found in tissues and secretions" published in the Proceedings of the Royal Society B: Biological Sciences on May 1, 1922, Fleming wrote:

In this letter, I'd like to bring attention to a chemical found in the body's tissues and secretions that can quickly dissolve specific germs. Because this chemical has qualities similar to ferments, I've referred to it as a "Lysozyme" and will continue to do so throughout this conversation. The lysozyme was discovered during studies into a patient with acute coryza. This was the first known finding of lysozyme. He collaborated with Allison to publish additional research on lysozyme in the October issue of the British Journal of Experimental Pathology that same year. Even though he was able to extract more lysozyme from egg whites, the enzyme had little therapeutic potential because it was only efficient against small number of harmless bacteria. This highlights a key distinction between harmful and benign microorganisms. The person who was described as "a patient suffering from acute coryza" in the original paper turned out to be Fleming. Additionally, he named the species Micrococcus Lysodeikticus, which means "lysis indicator" due to its vulnerability to lysozymal activity, after identifying the bacterium found in the nasal mucus. In 1972, the species was renamed *Micrococcus luteus*.

➢ Discovery of Penicillin:

The discovery of penicillin in the 1940s, which marked the beginning of the antibiotic era, is regarded as one of the most significant advancements in therapeutic medicine. The discovery of penicillin and the early identification of its

therapeutic potential happened in the United Kingdom, but due to World War II, the United States took the lead in developing large-scale manufacture of the drug.

The era of antibiotics began with the discovery of penicillin. Prior to its debut, there was no reliable remedy for rheumatic fever, pneumonia, or gonorrhoea. Blood poisoning from cuts or scratches was common in hospitals, and the only treatment available to doctors was to wait and hope. Bacteria and fungi create substances called antibiotics that have the power to either kill or suppress other microbial species that compete with them. It is possible that this long-known phenomenon explains why the ancient Egyptians applied a plaster of mouldy bread to wounds that were infected.

One of the most fortunate discoveries in medical history was made by Alexander Fleming in September 1928. After a two-week holiday, Fleming returned to his laboratory at St. Mary's Hospital on September 3, 1928, and saw something strange on an uncovered Petri dish. He put staphylococci on culture plates and placed them on a bench in a corner of his lab before departing for his vacation. A mould that was later determined to be *Penicillium notatum* had contaminated the plate that held colonies of Staphylococcus germs. Fleming saw that the mould had formed a clean zone around itself in which bacteria could not grow. Fleming was intrigued by this phenomenon and began research to further understand the mold's antimicrobial characteristics. He discovered that the mould produced a chemical that killed a wide range of hazardous bacteria, including those that cause pneumonia, meningitis, and diphtheria. After months of referring to it as "mould juice" or "the inhibitor," he named the antibiotic ingredient found in the mould penicillin on March 7, 1929. His initial observations and

studies revealed penicillin's promise as a formidable antibacterial drug, ushering in a new era in medical science.

The Alexander Fleming Laboratory Museum, located at St. Mary's Hospital in Paddington, is where Fleming discovered and tested penicillin. The fungal contaminant was identified in 1966 as originating from La Touche's chamber, which was just below Fleming's.

He then sent to his assistants, Stuart Craddock and Frederick Ridley, the laborious task of isolating pure penicillin from mould juice. It proved to be extremely unstable, and they could only create primitive material solutions to deal with. Fleming reported his findings in the British Journal of Experimental Pathology in June 1929, but the study received little attention. His challenge was the difficulty of generating penicillin in big quantities. Even with the assistance of Harold Raistrick, Professor of Biochemistry at the London School of Hygiene and Tropical Medicine, attempts to purify penicillin failed. As a result, penicillin was mostly forgotten during the 1930s.

Despite the encouraging results, Fleming encountered substantial difficulties in isolating and manufacturing penicillin in sufficient quantities for practical application. Penicillin extraction and purification were complex and time-consuming, with low initial yields. Fleming's laboratory lacks the necessary resources and skills to overcome these technological challenges. Furthermore, the scientific community and pharmaceutical business had little interest in Fleming's finding. Many researchers questioned the viability of large-scale penicillin production, while others questioned its practical applicability.

The development of penicillin was hampered by this lack of funds and support, and Fleming's revolutionary discovery was

largely ignored for a number of years. In spite of these initial difficulties, Fleming's persistence and the work of other scientists later resulted in the widespread use of penicillin, turning it into a life-saving medication.

Nobody took Fleming seriously when he spoke about its medical significance at the Second International Congress of Microbiology in London. According to Allison, his partner at the International Congress and Medical Research Club meetings, on both occasions:

At the Medical Research Club conference, Fleming hypothesised that penicillin could be useful in the treatment of infections in humans. Again, there was no interest or discussion. Fleming was quite disappointed. He presented a paper on his penicillin research at the International Congress of Microbiology, which was attended by leading bacteriologists from around the world. There was no backing for his views on its potential future utility in the prevention and treatment of human infections, and discussion was limited. Fleming suffered these disappointments stoically, but they did not change his mind or prevent him from continuing his research into penicillin.

➢ Penicillin Research at Oxford University:

Fleming wasn't the only one who helped turn penicillin into a commonly used antibiotic. A group of scientists from the University of Oxford, including Norman Heatley, Ernst Boris Chain, and Howard Florey, took on the task of expanding on Fleming's finding in the late 1930s and early 1940s. With Heatley's biochemistry knowledge, Florey and Chain started a mission to isolate, purify, and manufacture penicillin in greater numbers after realizing its potential. The Oxford Group significantly improved penicillin production and purification.

They greatly increased yields by creating new techniques for removing and concentrating penicillin from mould cultures. Important research that showed penicillin's efficacy in treating bacterial infections in both humans and animals were part of their work.

At Oxford University's Sir William Dunn School of Pathology, Howard Florey, Ernst Chain, and their associates transformed penicillin from a lab experiment into a medication that might save lives. Just as wartime conditions were starting to make research very challenging, they started working seriously on the chemistry and purification of penicillin in 1939. The team had to process up to 500 liters of mould filtrate per week in order to conduct a program of clinical trials and animal tests. They started cultivating it in an odd variety of culture containers, including food tins; milk churns, bedpans, and baths. Later, a specially made fermentation jar was created to make it simple to remove and to replenish the broth underneath the mold's surface while also saving space. The Oxford lab was essentially being transformed into a penicillin factory. Fleming called Chain's head of department, Howard Florey, shortly after the team's initial results were released in 1940, to inform him that he would be stopping by in the coming days. Chain said, "Good God!" upon learning that Fleming was approaching. I believed him to be deceased.

In the meantime, biochemist Norman Heatley used a countercurrent technique to extract penicillin from massive amounts of filtrate that were flowing off the production line by first extracting it into amyl acetate and then back into water. Prior to clinical trials, the biochemist Edward Abraham, who was hired to assist in increasing production, used the recently developed method of alumina column chromatography to eliminate contaminants from the penicillin.

Fleming was humble about his role in the invention of penicillin, referring to his fame as the "Fleming Myth," and he complimented Florey and Chain for turning a laboratory curiosity into a useful medication. Fleming stored, grew, and circulated the original mould for twelve years, and he tried until 1940 to seek help from any chemist with the necessary skills to manufacture penicillin. In 1998, Sir Henry Harris summarized the process as follows: "Without Fleming, no Chain; without Chain, no Florey; without Florey, no Heatley; and without Heatley, no penicillin."

The Oxford team consisted of many more individuals, and at one stage the entire Sir William Dunn School of Pathology contributed to its creation. A number of clinical trials followed the team's 1940 approach of refining penicillin to an effective initial stable form, and their remarkable success motivated them to devise techniques for large manufacture and distribution in 1945.

Florey conducted vital research in 1940 that demonstrated penicillin's ability to protect mice from lethal Streptococci infections. Then, on February 12, 1941, a 43-year-old police officer named Albert Alexander became the first to receive the Oxford penicillin. He had scraped the side of his lips while cutting roses, resulting in a life-threatening infection with large abscesses in his eyes, face, and lungs. He recovered quickly after receiving penicillin. However, supplies of the medicine ran out, and he died a few days later. Wartime conditions made industrial penicillin manufacture challenging. A number of British companies, including Glaxo (now GlaxoSmithKline) and Kemball Bishop, a London corporation later acquired by Pfizer, accepted the challenge.

➢ Medical use and Mass production:

In 1928, Fleming sent some of his original penicillin samples to Arthur Dickson Wright, a fellow surgeon, for clinical testing. According to reports, it "seemed to work satisfactorily" for Wright. The first person to effectively employ penicillin for medical therapy was Cecil George Paine, a pathologist at the Royal Infirmary in Sheffield and a former pupil of Fleming. On November 25, 1930, he treated three infants of neonatal conjunctivitis and one adult of conjunctivitis.

Fleming successfully treated severe conjunctivitis in 1932. Keith Bernard Rogers, a medical student at St Mary's since 1929, was captain of the London University rifle team and was preparing to compete in an inter-hospital rifle shooting competition when he contracted conjunctivitis. Fleming used his penicillin to cure Rogers before the competition. It is claimed that "penicillin worked and the match was won."

Howard Florey and Ernst Chain of the Radcliffe Infirmary in Oxford took on the research to mass-produce it. By mid-1942, the Oxford team had manufactured pure penicillin as a yellow powder. Harry Lambert (an acquaintance of Fleming's brother Robert) was taken to St Mary's Hospital in August 1942 with a potentially fatal nervous system infection (Streptococcal meningitis). Fleming administered sulphonamides, but Lambert's condition deteriorated. He examined the antibiotic susceptibility and discovered that penicillin might kill the bacteria. He asked Florey for the isolated sample. Florey provided an incompletely purified sample, which Fleming immediately injected into Lambert's spinal canal. Lambert showed signs of progress the next day and was fully recovered within a week. Fleming reported the clinical case in The Lancet in 1943.

Following this medical breakthrough, Allison informed the British Ministry of Health about the importance of penicillin and the necessity for large manufacture. The War Cabinet was convinced of its utility, and Sir Cecil Weir, Director General of Equipment, convened a discussion on the mode of action on September 28, 1942. The Penicillin Committee was formed on April 5, 1943. Weir chaired the committee, which also included Fleming, Florey, Sir Percival Hartley, Allison, and pharmaceutical company representatives. The primary goals were to rapidly develop penicillin in huge quantities with the help of American firms, and to supply the medication solely to Allied armed forces. By D-Day in 1944, enough penicillin had been produced to treat all of the injured Allied forces.

- **Mass production of Penicillin in the United States during World War II**

World War II provided the push for the discovery and production of penicillin. The high rate of infected wounds and infections among soldiers highlighted the critical need for better antibacterial therapies. The success of penicillin in early clinical trials piqued the interest of the US and British governments, who recognized its potential to save many lives. With government assistance, efforts to mass-produce penicillin increased considerably. In the United States, pharmaceutical corporations such as Pfizer, Merck, and Squibb developed novel fermentation techniques to make penicillin on a large scale. By the end of the war, penicillin had been mass-produced, making it widely available for military and civilian use. Penicillin's impact on medicine was significant and far-reaching. It significantly reduced the death rate from bacterial illnesses such pneumonia, rheumatic fever, and syphilis. Its success paved the path for the discovery and development of further antibiotics,

revolutionizing the treatment of bacterial illnesses and considerably improved public health outcomes. The antibiotic age had begun, revolutionizing medical procedures and saving millions of lives around the world.

Penicillin's success revealed the effectiveness of natural substances in combating bacterial infections, prompting the discovery and development of numerous other antibiotics, including streptomycin, tetracycline, and erythromycin. The introduction of penicillin resulted in considerable modifications in medical procedures. It transformed the treatment of bacterial infections, making previously life-threatening illnesses easily manageable. Penicillin and other antibiotics significantly reduced the need for invasive surgical operations to treat infections and allowed for more effective management of infectious disorders. By reducing postoperative infections, the broad availability of antibiotics significantly enhanced surgical outcomes and advanced a number of medical specialities. It was essential in containing epidemics and slowing the spread of infectious diseases, which raised life expectancy and enhanced living standards everywhere. Fleming's discovery signalled the start of the antibiotic era, which drastically changed medicine and left a legacy that still shapes medical practice and research today.

- **Antibiotic resistance:**

Fleming also made the early discovery that bacteria were resistant to antibiotics when penicillin was used insufficiently or for an extended length of time. Antibiotic resistance was predicted by Almroth Wright before it was discovered in experiments. In his numerous addresses around the world, Fleming warned against the use of penicillin. He warned that "a host of penicillin-fast organisms is bred out and the microbes

are educated to resist penicillin" on June 26, 1945. In these situations, the careless individual who plays with penicillin bears moral responsibility for the man's demise as he eventually becomes infected with the bacterium that is resistant to the antibiotic.

"I hope this evil can be avoided." He advised against using penicillin unless there was a well identified reason for doing so, and that if it was used, it should never be taken in excess or for an insufficient period of time, as these are the conditions under which bacterial resistance to antibiotics develops. *S. aureus* could develop penicillin resistance when exposed to it for an extended period of time, as demonstrated in 1942. Fleming elaborated on the prospect of penicillin resistance in clinical situations in his Nobel Lecture.

Penicillin may soon be available in stores for purchase by anyone. Then there is the risk that the uneducated individual will underdose himself, exposing his microorganisms to non-lethal amounts of the medicine and making them resistant.

➢ Recognition and Legacy:

In 1945, Alexander Fleming, Howard Florey, and Ernst Boris Chain received the Nobel Prize in Physiology or Medicine. This distinguished prize recognized their achievements to the discovery and development of penicillin, which transformed the treatment of bacterial infections and saved countless lives during and after World War II. In addition to the Nobel Prize, Fleming got numerous additional awards and recognition for his innovative work. In 1944, King George VI knighted him and gave him the title Sir Alexander Fleming. His accomplishments were recognized worldwide, and he obtained honorary degrees, membership in important scientific groups, and several honors

from various countries and institutions, cementing his legacy as a pioneering scientist.

On November 19, 1999, the American Chemical Society and the Royal Society of Chemistry declared the discovery and development of penicillin as an International Historic Chemical Landmark at the Alexander Fleming Laboratory Museum in London, UK. The plaque honouring the event reads:

In 1928, at St. Mary's Hospital, London, Alexander Fleming discovered penicillin. This discovery led to the introduction of antibiotics that greatly reduced the number of deaths from infection. Howard W. Florey, at the University of Oxford working with Ernst B. Chain, Norman G. Heatley and Edward P. Abraham, successfully took penicillin from the laboratory to the clinic as a medical treatment in 1941. The large-scale development of penicillin was undertaken in the United States of America during the 1939-1945 World War, led by scientists and engineers at the Northern Regional Research Laboratory of the US Department of Agriculture, Abbott Laboratories, Lederle Laboratories, Merck & Co., Inc., Chas. Pfizer & Co. Inc., and E.R. Squibb & Sons. The discovery and development of penicillin was a milestone in twentieth century pharmaceutical chemistry.

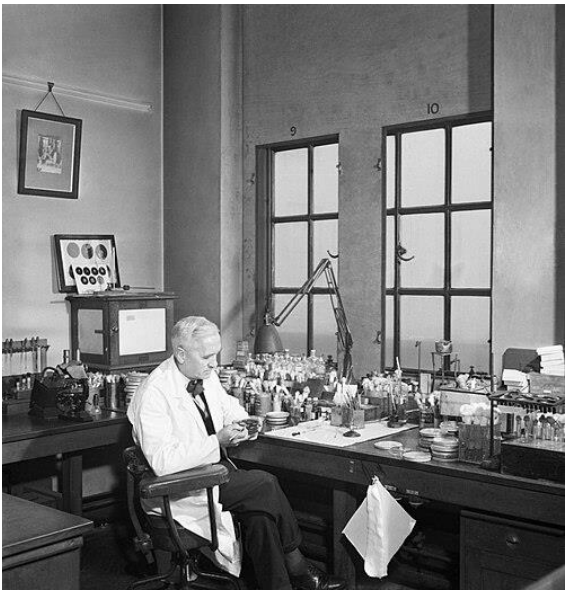
The Fleming Museum, located in the laboratory of St Mary's Hospital where Fleming developed penicillin, is a renowned London attraction. His alma mater, St Mary's Hospital Medical School, merged with Imperial College London in 1988. The Sir Alexander Fleming Building on the South Kensington campus first opened in 1998.

➢ Later years and Death:

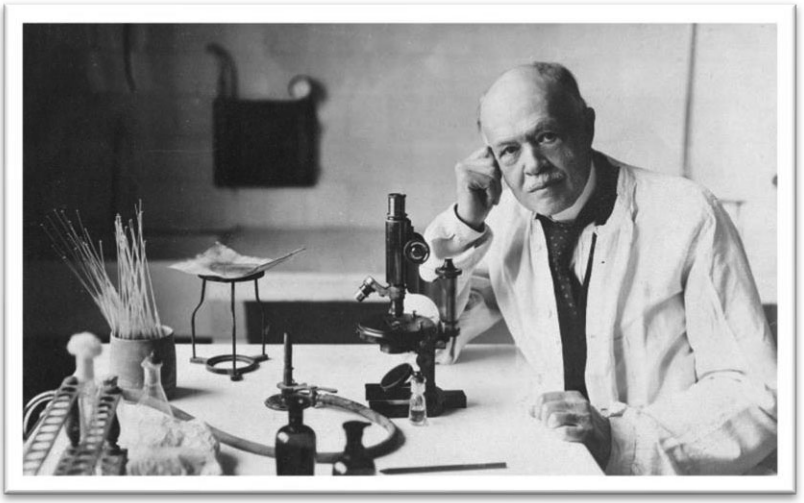
Alexander Fleming continued to investigate and teach at St. Mary's Hospital Medical School in his older years. He remained involved in the scientific community, imparting his expertise

and experiences to the next generation of scientists and medical professionals. His dedication to study and instruction maintained, resulting in advances in bacteriology and antibacterial therapy. Alexander Fleming died on March 11, 1955, following a heart attack.

He was buried in St. Paul's Cathedral in London, an honor appropriate for his tremendous contributions to science and medicine. Fleming's legacy was commemorated posthumously with several honors and commemorations. His work remains a cornerstone of contemporary medicine, and he is regarded as one of the finest scientists of the twentieth century. His name appears on monuments, memorials, and institutions around the world, ensuring that his medical achievements are recognized and respected for future generations.



Pic. Fleming working in his lab



Charles Jules Henri Nicolle

(21 September 1866 – 28 February 1936)

"And this is the ultimate lesson that our knowledge of the mode of transmission of typhus has taught us: Man carries on his skin a parasite, the louse. Civilization rids him of it. Should man regress, should he allow himself to resemble a primitive beast, the louse begins to multiply again and treats man as he deserves, as a brute beast"

➢ The Birth & Early life of Charles Jules Henry Nicolle:

Charles Jules Henry Nicolle was born on September 21, 1866, in Rouen, the historic capital of Normandy, France. He devoted his entire life to serving society as a doctor, microbiologist, novelist, philosopher, and historian. In addition to receiving a classical education, he developed lifelong passions

for literature, history, and the arts. His mother, Aline Louvrier (1839–1925), came from an artisanal family and was instrumental in fostering an intellectually stimulating and educated home. Charles and his siblings were greatly impacted by this setting. Eugène Nicolle, his father, practiced medicine at a nearby Rouen hospital. Charles's father provided him and his brothers with early biology instruction. While his younger brother, Marcel Nicolle, chose to become an art critic, his older brother, Maurice Nicolle, became a medical microbiologist and professor at the Pasteur Institute in Paris.

- **Academic Journey:**

He studied for three years at the nearby medical school after graduating from the Lycée Corneille de Rouen, and then he followed in his older brother Maurice's footsteps by working in Parisian hospitals. Following his father's wishes, Nicolle shifted to Paris & pursued a medical degree from Pasteur Institute in 1893. In the meantime, Charles completed a thesis titled "Recherche's sur la chancre mou" (Researches on the soft chancre) under the guidance of A. Gombault at the Faculty of Medicine and Roux at the Pasteur Institute, where he also served as a demonstrator in the microbiology course. This work earned him an M.D. in 1893. When Nicolle was 27, he went back to his hometown to work at L'École préparatoire de médecine et pharmacie de Rouen as the Director of the Bacteriological Laboratory and a member of the medical faculty. His eight years in Rouen were challenging because he had an untenured position, his colleagues didn't want to embrace his new perspectives on bacteriology, and he had a hearing loss that made it hard for him to use a stethoscope effectively. When the position of director of the Pasteur Institute in Tunis opened up, these difficulties might have spurred him to take a risk that he

might not have otherwise. His brother, Maurice (1862–1932), a renowned experimental scientist, was the first to be offered it, but he declined. After that, Charles applied and was hired.

- **Discoverer of the Invisible Carrier (Inapparent Infections):**

Nicolle worked on cancer early in his career and studied the production of diphtheria antiserum at Rouen. In 1902, at the age of 36, Nicolle travelled to Tunis, the expansive capital of Tunisia, a country in North Africa. Infectious diseases such as brucellosis, diphtheria, leishmaniasis, leprosy, malaria, measles, Mediterranean spotted fever, relapsing fever, scarlet fever, tuberculosis, and typhus were all well-studied in North Africa. However, Nicolle claimed that epidemic typhus was "the most important and the least explored" of all the issues he encountered in Tunisia. Under his leadership, the Institute in Tunis swiftly rose to prominence in North Africa as a hub for bacteriological research and the development of vaccines and serums to treat the majority of infectious diseases.

In 1903, Nicolle distinguished between the classical louse-bound (Pediculus humanus corporis, a hematophagic ectoparasite louse that infests humans) epidemic typhus and murine typhus, which is spread to humans by the rat flea (Parasite of rodents), a phenomenon of inapparent infection. For seven years, Charles Nicolle meticulously studied typhus—a disease long synonymous with poverty, war, and overcrowding. He was deeply familiar with its classical clinical presentation: high fever, a blotchy rash, and progressive stupor—symptoms that had claimed millions of lives throughout history. In early 20th-century Tunis, it struck cyclically during winter, devastating prisons, asylums, and hospitals, claiming lives indiscriminately, including those of medical staff. The disease,

often fatal and highly communicable, had been historically confused with typhoid and was known by names like "war typhus" and "jail fever." Nicolle himself narrowly escaped the disease in 1903. He had planned to investigate a prison outbreak of typhus but cancelled his visit at the last moment. His two colleagues proceeded without him, spent a night in the affected prison, and tragically both died from typhus shortly afterward. This near-death experience intensified Nicolle's resolve. What followed was a meticulous and courageous investigation that would eventually reveal the true vector of typhus: the human body louse.

- **The Nobel Prize Winner:**

Charles Nicolle's landmark discovery of typhus transmission emerged from careful observation at Sadiki Hospital in Tunis, where he noted that patients ceased to be infectious once they were bathed and dressed in hospital clothing. The fact that secondary cases frequently occurred among those handling patients' garments led Nicolle to suspect lice as vectors. To test this, in 1909 he conducted a series of experiments—first infecting a chimpanzee with typhus-infected blood, then transferring the infection to a macaque. By feeding lice on the ill macaque (Old world Monkey) and then transferring them to healthy ones, he successfully reproduced the disease. These findings, presented to the French Académie des sciences in September 1909, conclusively demonstrated that lice were the carriers of typhus. Subsequent studies confirmed that transmission occurred primarily through infected louse excreta entering broken skin or mucous membranes. Nicolle's work not only solved a longstanding medical enigma but also saved countless lives, particularly in war-torn or impoverished regions. His discovery came not just from laboratory work, but from

careful clinical observation, epidemiological reasoning, and immense personal risk—hallmarks of a truly extraordinary scientist. Nicolle also tried to make a simple vaccine for typhus. He crushed the lice and mixed it with blood serum, collected from recovered patients. He successfully tried it first on himself and then on a few children. However, the practical vaccine was later invented by Polish biologist Rudolf Stefan Weigl. Unlike most prominent scientists of his era, Nicolle made his discoveries outside the scientific capitals of Europe, at the Pasteur Institute in Tunis. Working in resource-limited conditions, he made world-changing discoveries—like identifying lice as the vector of typhus. His dedication to improving public health in North Africa and understanding local diseases was far ahead of Western-centric scientific priorities of the time. Long before the concept of "One Health" (connecting human, animal, and environmental health), Nicolle believed that diseases were deeply connected to human behaviour, social systems, and environmental change. His work anticipated how urbanization, hygiene, and vector control influence epidemic patterns. This year is the centenary of his discovery about typhus transmission, made in the summer of 1909, for which he was awarded the 1928 Nobel Prize in Physiology or Medicine. Despite winning the 1928 Nobel Prize in Medicine, Nicolle remained modest. He saw the award not as a personal triumph but as a recognition of dedicated, collective effort in science for public good.

- **Other glories & Discoveries:**

In addition, he made significant contributions to our current understanding of rinderpest, measles, influenza, tuberculosis, and trachoma; Malta fever, where he developed a preventive vaccination; tick fever, where he identified the mode of

transmission; scarlet fever, by using streptococci for experimental reproduction; and tuberculosis and trachoma. He was responsible for the introduction of many new techniques and innovations in bacteriology. Nicolle was one of the first to recognize the protective properties of the convalescence serum against typhus and measles; and succeeded in cultivating *Leishmania donovani* and *Leishmania tropica* on artificial culture media. His discovery of the mechanism of the transmission of typhus fever has created the basis for the preventive precautions against this disease, during the 1914-1918 and 1939-1945 Wars.

Although Nicolle is not credited with discovering the cause of human influenza, he carried the experiment to possibly the first isolation of human influenza virus after experimental transmission. Nicolle made many other fundamental contributions to knowledge of infectious diseases. In 1903, guided by Émile Roux, Charles Nicolle became familiar with "filter-passing" agents—then-hypothetical sub-bacterial pathogens—through the pioneering work of his brother Maurice, who had isolated the rinderpest agent. This background uniquely positioned Nicolle to investigate the 1918 influenza pandemic. Suspecting a viral cause, he injected filtered and unfiltered patient sputum into volunteers and monkeys, inducing influenza-like symptoms in some. Though large-scale studies were hindered by the pandemic's pace, Nicolle's experiments marked the first experimental isolation of the influenza agent, a fact recognized only years later after the virus was formally identified—confirming his foundational role in viral pathogenesis. Charles Nicolle's discovery of the louse as the vector of typhus marked both a culmination and a turning point in medical science. It concluded a remarkable era in which arthropods were identified as vectors of numerous major

diseases—malaria, dengue, yellow fever, and more—and ushered in a new phase in infectious disease control. Nicolle's breakthrough laid the foundation for the eventual suppression of typhus epidemics; a goal realized decades later with Paul Müller's discovery of DDT in the 1930s. The strategic use of DDT during World War II, notably in Naples, halted deadly outbreaks. Once a scourge of war and poverty, epidemic typhus is now rare. Together, the achievements of Nicolle and Müller exemplify how persistent scientific inquiry can transform global health and alter the course of human history.

- **Nicolle: The friend:**

Hans Zinsser (1878–1940), an American microbiologist and historian, dedicated his classical work, Rats, Lice and History, to Charles Nicolle "with affectionate friendship." In his autobiography, Zinsser speaks of Nicolle's qualities as a scientist: *"Nicolle was one of those men who achieve their success by long preliminary thought, before an experiment is formulated, rather than by the frantic and often ill-conceived experimental activities that keep lesser men in ant-like agitation."* Nicolle's findings were soon validated by contemporaries like Howard Ricketts and Russell Wilder, while the causative agent, *Rickettsia prowazekii*, was later named in honor of researchers who died studying the disease. Nicolle's legacy exemplifies the power of insight and precision in scientific discovery. Émile Roux, one of the foremost figures at the Institute Pasteur and mentor to Charles Nicolle, held him in exceptionally high regard. Roux supported Nicolle's appointment as the director of the Pasteur Institute in Tunis in 1903, a major endorsement considering the prestige and responsibility of the position. He recognized Nicolle's intellectual rigor, calm demeanour, and ability to draw deep insights from limited but well-designed experiments—traits that

aligned with the Pasteurian ideal of meticulous, hypothesis-driven research. Moreover, when Nicolle made his groundbreaking discovery about the transmission of typhus via lice in 1909, Roux was among the first to recognize its significance. As director of the Paris Institute Pasteur, Roux ensured Nicolle's work was communicated swiftly to the Académie des Sciences, where it gained international attention.

➢ Charles Jules Henry Nicolle: The Writer:

Charles Nicolle also enjoyed considerable reputation as a philosopher and as a writer of fanciful stories, such as *Le Pâtissier de Bellone* (The Pastry Chef of Bellona), *Les deux Larrons* (The Two Thieves), and *Les Contes de Marmouse* (The Tales of Marmouse). He was said by Jean Rostand to be "a poet and realist, a man of dreams and a man of truth". Nicolle wrote several important books including *Le Destin des Maladies infectieuses* (The Destiny of Infectious Diseases); *La Nature, conception et morale biologiques* (Nature: Biological Conception and Morality); *Responsabilités de la Médecine* (Responsibilities of Medicine) and *La Destinée humaine* (The Human Destiny).

➢ A Philosopher in a Lab Coat:

The idea of "destiny" in disease patterns: how societal, environmental, and biological factors affect disease evolution. His book *Le Destin des Maladies infectieuses* is a broader and more personal reflection on human life, destiny, suffering, and death, written near the end of his life. It is deeply philosophical, combining his scientific knowledge with spiritual and existential questions. Nicolle's writing was known for its clarity, elegance, and philosophical depth. He wrote not just as a scientist but as a humanist, blending empirical observation with moral reflection. His works were widely read in both scientific and

literary circles in France and remain influential in discussions about medical ethics, epidemiology, and public health philosophy.

➢ Personal Life & Legacy:

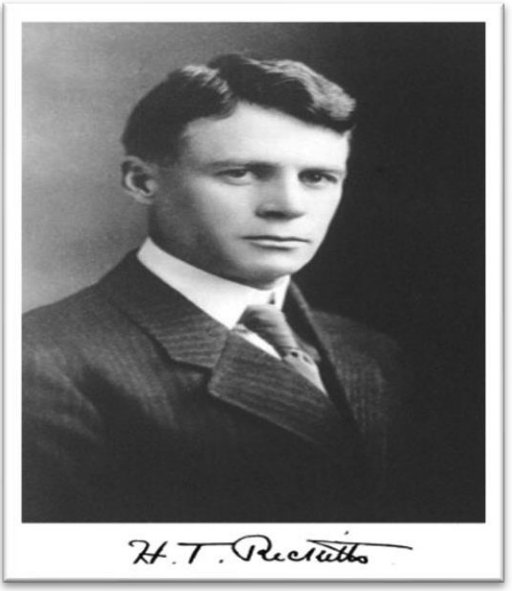
In 1928, Nicolle received the Nobel Prize in Medicine or Physiology for his work on typhus. A year before that he had also received Osiris prize for the same work. In 1929, he was named non-resident member of the French Academy of Medicine. In 1895, Nicole married Alice Avice. The couple had two children, a daughter named Marcelle born in 1896 and a son named Pierre born on 1898. Marcelle later grew up to be a doctor in Tunisia.

➢ The last Message:

Charles Nicolle was well ahead of his time when he introduced the concept of *"inapparent infections"*—the idea that individuals could carry and transmit disease without exhibiting symptoms. This revolutionary insight reshaped epidemiology and anticipated the modern understanding of asymptomatic carriers, pivotal in managing diseases such as typhoid, tuberculosis, and COVID-19. Unlike many contemporaries focused narrowly on data, Nicolle also reflected deeply on the philosophical dimensions of disease, destiny, and morality. At the Pasteur Institute in Tunis, which he led, Nicolle cultivated an atmosphere akin to a monastic haven for scientific inquiry—marked by intellectual rigor, calm discipline, and humility. He was admired for his serene dedication, even in the face of deadly pathogens. His landmark identification of the typhus transmission cycle was achieved without the aid of DNA sequencing, PCR, or electron microscopy. Instead, he relied on sharp clinical observation, logical reasoning, and simple yet

effective animal models such as chimpanzees and guinea pigs. His empirical brilliance was evident in the elegant deduction that typhus became non-contagious after patients changed clothing—an insight that ultimately led him to identify lice as the disease vector. Nicolle remained active until his death in 1936, still serving as director of the Pasteur Institute, writing, teaching, and mentoring.

Born to a well-educated family, Nicolle followed the footsteps of his father & brother Maurice. Nicolle dedicated his whole life for the public good. Nicolle viewed microorganisms not as enemies but as co-inhabitants of the world, with their own roles in the web of life. Beyond scientific discoveries, he left behind a moral and intellectual legacy—a model of how science should be pursued with empathy, integrity, and a profound sense of humanistic purpose.



Howard Taylor Rickettes

(February 9, 1871 – May 3, 1910)

"I seem to have been only like a boy playing on the seashore, … finding a smoother pebble or a prettier shell … whilst the great ocean of truth lay all undiscovered before me."

➢ The Birth & Early life of Howard Taylor Ricketts:

Howard Taylor Ricketts, regarded as one of the most well-known microbiologists in medical history, was born in Findlay, Ohio, on February 9, 1871, and spent his childhood in Nebraska. Born on a farm, Ricketts is the son of Jeremiah and Nancy Jane Ricketts. Jeremiah Ricketts, his father, was a farmer and a veteran of the Civil War. Mary Ricketts, his mother, was

well-known for being a devout Christian who was instrumental in giving her kids discipline and a strong moral compass. Growing up in a modest, hardworking Midwestern family, Ricketts was influenced by the values of the countryside, such as tenacity and an interest in the natural world. He was a young man with a strong Methodist faith who was husky and active. After graduating from preparatory school, he enrolled at Northwestern University in 1890. He moved to the University of Nebraska two years later. Ricketts worked his way through school after his family's fortune was destroyed by the panic of 1893 (the well-known financial crisis and economic depression in the USA). He enrolled at Northwestern Medical School in 1894. W. H. Allport, his patron, assisted him in getting a job at the medical museum.

- **Academic Journey:**

Ricketts interned at Cook County Hospital until 1899 after graduating from Northwestern Medical School in 1897. He then accepted a dermatology pathology fellowship at Rush Medical College to research blastomycosis, also referred to as Gilchrist's disease, which is a fungal infection of the lungs brought on by *Blastomyces dermatitidis*.

He also worked in the dermatological clinic for a portion of this period. He met Myra Tubbs while attending Northwestern Medical School, and the two were married in 1900. Myra gave him devoted support, intense interest, and consistent encouragement in his work. Both then travelled to Europe in the first year of their marriage, where Ricketts attended The Pasteur Institute in Paris then went to Vienna, Berlin to finish his studies. Ricketts is the father of two children; his daughter Elizabeth was born in Chicago, and his son Henry was born in Berlin. After spending a year in laboratories in Europe, he

returned to the University of Chicago in 1902 to teach in the newly established Department of Pathology and Bacteriology. He later rose to the rank of assistant professor, and in early 1910 he accepted the position of pathology chair at the University of Pennsylvania, a position he fully anticipated taking on in the fall. He made the conscious decision to focus on pathology research and teaching rather than the temptations of active medical practice. He had high aspirations and a genuine desire to find the truth in his field from an early age. These attributes stuck with him, provided him with a high-minded outlook on all of his obligations and connections, and imbued his work with a distinctive mark. In the end, the University openly and creatively supported the work that would yield such noteworthy outcomes. He never let his research instinct rest idle; instead, it carried him farther and farther as it became stronger. In the few years that he was given, he advanced the torch farther than we may now realize because he paved the way for subsequent advancements. The torch was placed in capable hands.

➢ The Father of Rickettsia:

One of the oldest pestilential diseases in human history is epidemic typhus, which is brought on by *Rickettsia prowazekii*. Body louses are the disease's vector of transmission to humans. Despite the effectiveness of antibiotics, public health authorities continue to view *Pediculus humanus corporis* as a serious threat because unsanitary conditions encourage the growth of louses. In addition to accompanying human-impacting disasters, epidemic typhus has arguably influenced the outcome of more wars than soldiers and generals. Millions of people died from epidemic typhus outbreaks in Europe, Mexico, South America, and Central America in earlier centuries, despite the fact that

the disease is now thought to be rare. These outbreaks were common among impoverished individuals, homeless and displaced people, prisoners, and military personnel. “Epidemic typhus has accompanied disasters that impact humanity and has arguably determined the outcome of more wars than soldiers and generals,” say infectious disease researchers Emmanouil Angelakis, Yassina Bechah, and Didier Raoult. There are now fresh worries about potential epidemic typhus outbreaks in conflict-torn regions, like some regions of Ukraine. The brilliant work on Rocky Mountain fever, however, is where Dr. Ricketts fully reveals himself as an investigator of the first rank. He took up the study of this fever in the spring of 1906 as a sort of pastime during an enforced holiday on account of overwork. The disease is a remarkable one; it occurs in well-defined areas in the Mountains, is sharply limited to the spring months, varies greatly in severity, the mortality in one place being about 5, in another between 80 and 90, per cent. For some time, it had been regarded as caused in some way by the bite of a tick. Dr. Ricketts promptly found that the disease is communicable to lower animals and that a certain tick, which occurs naturally on a large number of animals in those regions, by its bite can transmit the disease from the sick to the healthy animal.

Ricketts's earlier research on blastomycosis and immunological issues is characterized by thoroughness, directness, and clear and forceful reasoning. Naturally, Dr. Ricketts and his volunteer assistant, Mr. Russell M. Wilder, started working after becoming well-versed in all the disease's features. Results of significant importance were obtained before many weeks had gone by; it was discovered that, despite their many similarities, typhus and Rocky Mountain fever are not the

same; Mexican typhus is contagious to monkeys; and it may be spread by insects (Pediculus vestamenti).

- **The last breath:**

Mexico City became the site of political, artistic, and urban planning experiments around 1910. Since colonial times, typhus fever, also referred to locally as tabardillo, has been endemic in the Mexican capital. It frequently escalated to epidemic proportions, spreading devastatingly in hospitals, impoverished neighbourhoods, and prisons. The Porfirio Diaz government declared in 1909 that the discovery of the cause and treatment of typhus would earn a prize of 50,000 pesos. The call was answered by foreign scientists, including Howard Taylor Ricketts, a pathologist from the University of Chicago who had found that ticks carried and spread Rocky Mountain spotted fever. According to reports, 550 of the 1,230 doctors who worked for Irish institutions over a 25-year period died of typhus.

Russell Wilder, AS 1905, SB 1907, PhD 1912, a recent College graduate and his medical student, accompanied him. Early in 1910, they established themselves at the city's Instituto de Bacteriología, keen to collect, analyze, and publish data as soon as possible. The two went to the infamous Belém prison in Mexico City, where typhus and lice were common. In April, Ricketts wrote to a colleague, "I am a lucky fellow," despite the fact that an Ohio State researcher had already died of the illness. The Mexican scientists who inquired about his research, however, were accused of "spying" in his letters. Tenorio writes, "Even when they went for lunch, Ricketts and Wilder did not leave their notes on the laboratory desks."

He believed that Mexicans were watching their monkeys and stealing their lice. Ricketts published four articles on his

findings, primarily in the Journal of the American Medical Association, as the rivalry between the teams intensified. Ricketts and Wilder were able to identify the typhus-causing germ, demonstrate that the body louse was the means of transmission, and investigate the distinctions between the European strain of the disease and tabardillo. Devoted to his studies, Ricketts repeatedly injected himself with pathogens to examine their effects. On May 3, 1910, he passed away in Mexico City from typhus fever.

- **Honouring the Legend:**

Ricketts passed away at the age of 39. During his brief life, he discovered how ticks transmitted Rocky Mountain spotted fever from animals to humans. After that, he focused on studying typhus, and as a result of his exposure to the illness while conducting his research, he contracted it himself and died. His observations created a new field, and from that point on, he dedicated himself fully to the study of the numerous issues that emerged as the work progressed, both in the field and in this laboratory.

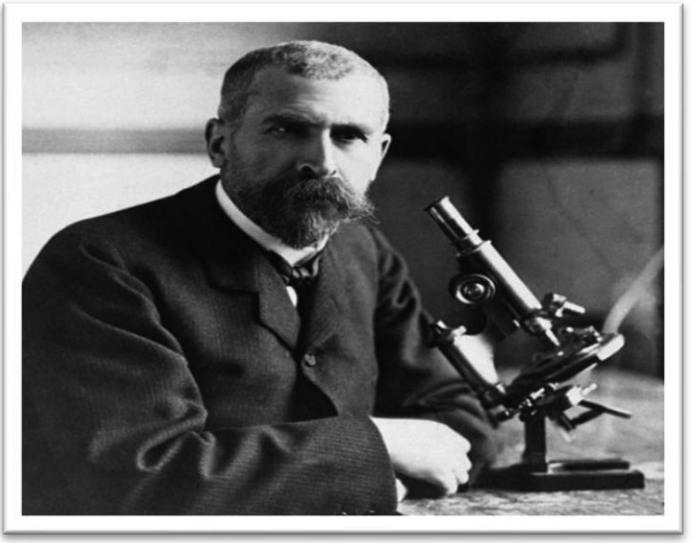
Following the different phases of this extremely active work, it is evident that Dr. Ricketts not only had the creative ability to see and trace the different paths that a problem might take to find a solution, but he also fully possessed the ability to do the meticulous, accurate, and patient work required for the more challenging task of identifying the one, true solution. He was a successful investigator because of his ability to speculate as well as his capacity for consistent labour and even drudgery, frequently under extremely trying circumstances.

Experiments on the hereditary transmission of the spotted fever virus in ticks, the prevalence of infected ticks in nature, and the role played by small wild animals like squirrels as virus

sources are among the most inventive and thorough of the experiments designed to reveal the secrets of the various orders of living things involved in spotted fever.

This Memorial Address, which Ludvig Hektoen later expanded and reprinted to open a collection of his research papers, was written in remembrance of his career. Together, these pieces of work by Ricketts amounted to a 497-page book that was written during his tragically brief career. Funded by friends and admirers in different locations and labs across the globe, the book was published as a memorial. Dr. Ricketts was a modest, unassuming man of the highest character, fiercely determined, loyal, giving, sincere, and earnest in everything he did. He had a unique and endearing personality. His colleagues from the hospital and fellowship days, who were familiar with him, his aptitude, his enthusiasm, and his unique enthusiasm for the work of the day, all looked up to him for the extraordinary accomplishment. Myra Tubbs Ricketts, Ricketts's wife, and their kids survived him. In 1912, his family founded the Howard Taylor Ricketts Prize, an annual student research award at the University of Chicago.

Howard Taylor Ricketts' life journey reflects a personality marked by extraordinary determination and perseverance. His dedicated work in Mexico on typhus fever, even at the cost of his own life, stands as a testament to his courage and scientific devotion. We believe that for a scientist, to depart this world in the midst of meaningful research is, in a way, a noble fate. Such individuals immerse themselves completely in the world of microbiology, often setting aside concerns for their own lives or families. It is through this selfless commitment that we witness the birth of groundbreaking discoveries. Ricketts remains a timeless inspiration to us all.



Pierre Paul Émile Roux

(17 December 1853 – 3 November 1933)

"The work of Pasteur is admirable; it shows his genius, but it must have been experienced intimately to know all the goodness of his heart. He imagined further experiments, to bring light, for contradictions excited him to new investigations."

➢ The Birth & Early life of Pierre Paul Emile Roux:

Émile Roux was a French immunologist, bacteriologist, and physician. He was born in Confolens, Charente, France, and is believed to have grown up without a father. Roux began his medical studies at the University of Clermont-Ferrand. In 1878, he was admitted to Louis Pasteur's laboratory at the University of Paris, where he worked for ten years and earned his medical

degree in 1881.As a medical student, Roux was recruited by Émile Duclaux to study virulent diseases at the École Normale. During this period, he played a crucial role in advancing vaccination techniques. He helped Pasteur develop the principle of using microorganisms with reduced virulence for immunization. Notably, Roux demonstrated this concept by inoculating a hen with an old culture of the chicken cholera bacterium, helping to establish the scientific basis of vaccination. His work contributed significantly to the development of vaccines against rabies, anthrax, and poultry cholera. In 1887, Roux co-founded the Pasteur Institute, and in 1888 he joined the newly established institute. He supervised the development of the first rabies vaccine for human and veterinary use. At the Pasteur Institute, Roux, along with Alexandre Yersin, demonstrated that the diphtheria bacillus secretes a toxin responsible for the symptoms of the disease. This discovery laid the foundation for diphtheria serum therapy and vaccination. Later, Emil von Behring and Kitasato Shibasaburo showed that infection with the diphtheria bacillus leads to the production of an antitoxin (antibody). Roux also played an important role in education. He established the first lecture series at the Pasteur Institute titled the "Course on Microbial Research Techniques," popularly known as "Monsieur Roux's Course." Through this program, he trained many microbiologists who later worked around the world. In 1904, Émile Roux was appointed Director of the Pasteur Institute, a position he held until his death in 1933.

➢ The Friend of Pasteur:

Émile Roux finished his secondary schooling in Puy and Aurillac before enrolling in medical studies at Clermont-Ferrand. During this time, he met Émile Duclaux, who

introduced him to the inspiring work of Louis Pasteur and deeply influenced his scientific ambitions. Determined to pursue this path, Roux later moved to Paris to complete his medical education. In November 1878, he secured a position as a laboratory assistant in Pasteur's laboratory. This marked the beginning of his lifelong association with Pasteur's scientific mission. Roux worked alongside Chamberland and Thuillier on studies investigating the cause of anthrax and experiments on weakening pathogens. These investigations became fundamental to the development of Pasteur's vaccination strategies. By 1888, Roux joined the newly established Pasteur Institute, where he taught microbiology and became director of the Service de Microbie Technique. Around this period, he began conducting some of his most significant independent research. Expanding upon the earlier findings of Klebs and Loeffler, who had identified the diphtheria bacillus, Roux confirmed that this bacterium was directly responsible for the disease. Through controlled experiments, he demonstrated that the bacillus could induce paralysis in guinea pigs, thereby proving its toxic effects. In 1894, Roux launched an important therapeutic program to combat diphtheria. His success in this effort reassured the aging Pasteur that the Institute's future was secure under capable leadership. After Pasteur's death in 1895, Roux became assistant director of the Institute under Émile Duclaux. Continuing his dedication to science and public health, Roux established Pasteur Hospital in 1900. In 1904, he was appointed director of the Pasteur Institute, a role he maintained until his death in 1933. Roux was widely recognized for his disciplined and modest way of life. His simple appearance and intense gaze gave him a reputation for seriousness and devotion. In the final fifteen years of his life, he resided in a small room at Pasteur Hospital, dedicating himself almost entirely to research and service.

➢ Roux The Scientific Devotee:

In the mid-19th century, diphtheria, then commonly known as "croup," was one of the most feared childhood diseases in Europe. The infection caused severe inflammation of the throat, leading to the formation of a thick false membrane that blocked the airway. In France alone, nearly 30,000 people were affected each year, and tragically, one out of every two infected children died, often from suffocation. Families lived in constant fear, as medicine at the time offered little hope. A turning point came in 1888, when Émile Roux, working at the Pasteur Institute with Alexandre Yersin, made a groundbreaking discovery. They demonstrated that the bacterium responsible for diphtheria did not cause harm merely by its presence, but by releasing a powerful poisonous substance into the body. This toxin circulated throughout the body, causing systemic damage. Roux dramatically remarked that even snake venom was less deadly than the diphtheria toxin, emphasizing its destructive power. This substance — later identified as a bacterial toxin — was the first of its kind ever scientifically described. This discovery revolutionized understanding of infectious diseases, proving that microbes could cause illness through toxins. Building on this insight, Roux and his colleagues, Martin and Chaillou, took the next courageous step. They tested a new treatment: a serum containing antibodies capable of neutralizing the diphtheria toxin. In clinical trials involving dozens of children, the results were extraordinary. The mortality rate was reduced by half. For the first time, there was real hope against a disease that had claimed thousands of young lives. In 1894, Roux presented these remarkable findings at the International Congress of Hygiene in Budapest. The medical community received the news with immense admiration. His work not only transformed the treatment of diphtheria but also laid the foundation for

modern serum therapy and immunology. Beyond diphtheria, his scientific investigations extended to cholera, chicken cholera, rabies, and tuberculosis, and for these pioneering contributions, he is regarded as one of the founders of immunology and medical bacteriology. Following the successful development of vaccines against chicken cholera and anthrax, attention turned toward the prevention of rabies—a disease particularly challenging to study because its causative agent, the rabies virus, was invisible and not yet identified. Roux made significant progress by successfully producing experimental rabies in animals, especially rabbits. By selecting what was known as a *virus fixe* (a stabilized strain), he was able to create consistent experimental infections. He also discovered that the virulence of rabid nervous tissue (rabic medulla) could be reduced under controlled conditions, contributing to the refinement of rabies vaccination methods. Soon after, Emil von Behring, who further developed antitoxin therapy, received the first Nobel Prize in Physiology or Medicine in 1901 — an achievement built upon the scientific groundwork laid by Roux and his team. Because of his dedication and life-saving discoveries, Émile Roux came to be celebrated as a hero of science and was affectionately called the "Saviour of Children." Roux's story is more than a scientific achievement; it is a powerful reminder of how perseverance, curiosity, and compassion can change the course of history. At a time when diphtheria meant near-certain tragedy for families, his research transformed despair into hope — and science into salvation.

- **The Secret Marriage:**

The marriage of Rose Anna Shedlock and Pierre Paul Émile Roux in 1878 was kept largely private and remained little known for many years. Their relationship unfolded during a

period in which both were deeply engaged in medical studies and professional struggles. Rose Anna Shedlock was born around 1850 in Merton, Surrey, into a large and intellectually active family. Her father, Reverend John Shedlock, was listed in census records as an independent minister, and the family included at least eight children. Several of her siblings achieved distinction in their own fields. Her elder brother, John South Shedlock, became a respected musician, music critic, and later a noted Beethoven scholar. Her younger sister, Marie Louise Shedlock, pursued a career as a professional storyteller and lecturer, including extended tours in the United States. The family also spent part of their early years in France, as census records indicate that some of the younger children were born in Boulogne while their father worked as an engineer on railway construction. Rose Anna pursued medical studies at a time when women faced intense resistance in the profession. She studied medicine in Edinburgh alongside Sophia Jex-Blake, one of the pioneers of women's medical education in Britain. Although her name does not prominently appear in many historical accounts of that struggle, she was part of this early movement for recognition. She later continued her studies at the Paris medical school, where she likely met Émile Roux, who had previously been attached to the military medical school of the Val-de-Grâce before his dismissal in 1876. Documentation of Roux's life during the years immediately following his dismissal is incomplete and somewhat unclear. However, it is known that in August 1878, at the Register Office of the District of St Olave in Southwark, London, Rose Anna Shedlock married the young French scientist who would later become famous for his work in microbiology. Tragically, their marriage was short-lived. Rose Anna died in 1879, probably from tuberculosis. Later, a romanticized but historically inaccurate biography written by Roux's niece suggested that she

contracted the disease from Roux, whose own life was later affected by tuberculosis. However, available evidence indicates that Rose Anna had been in poor health for several years before their marriage, making it more likely that she transmitted the illness to him rather than the reverse. Interestingly, in April 1874, Rose Anna had served as a witness at the London wedding of Frances Morgan and George Hoggan — recognized as the first marriage in Britain between two qualified doctors. This detail reflects her close connection to the early generation of medical professionals, particularly women striving for equality in medicine. The brief union between Rose Anna Shedlock and Émile Roux remains a lesser-known yet poignant chapter in Roux's life. Behind the image of the devoted scientist stood a man who experienced personal loss early in adulthood — a sorrow that may have quietly shaped the intense dedication and disciplined lifestyle for which he later became known.

➢ Too Close Yet Too Far:

Although Émile Roux appeared strict and serious, he suffered from haemorrhagic tuberculosis for many years. Behind his simple and disciplined lifestyle, there was deep emotion and dedication. When he died in 1933, the announcement said:

"His life contains the history of the Pasteur Institute, just as the Pasteur Institute contained his entire life." This means that Roux devoted his whole life to the Institute, and its growth and success were closely connected to him. Today, his monument can still be seen inside the grounds of the Pasteur Institute at 25, rue du Docteur Roux, shaded by chestnut trees. The name "Roux" will always be remembered together with "Pasteur," because of their close scientific partnership and shared mission. During 1872–1873, Émile Duclaux, who was a professor of chemistry in the Faculty of Sciences, held an assistant

professorship. He later became one of Roux's close colleagues and collaborators.

In 1901, history was made when the very first Nobel Prize in Physiology or Medicine was awarded. The honour went to the German immunologist Emil von Behring for his groundbreaking work on serum therapy, particularly for its success in treating diphtheria — a disease that had once claimed countless young lives. But behind this celebrated moment lay a complex and carefully debated selection process. At the time, the Nobel Committee followed strict rules. According to the Nobel statutes and the scientific thinking of that era, the prize was to recognize a *single, most outstanding discovery* rather than a series of shared contributions. The committee sought to identify one decisive breakthrough and one principal figure to represent it. In this context, Émile Roux, who had helped isolate the diphtheria toxin in 1888 and had played a central role in advancing serum therapy, was considered. However, his work was judged to be less decisive than von Behring's direct development of antitoxin treatment. Roux's contribution was acknowledged, but it was seen as part of a broader collaborative effort rather than the defining discovery. Similarly, Shibasaburo Kitasato was viewed mainly as von Behring's collaborator, and Alexandre Yersin as Roux's colleague. The Nobel Committee's approach tended to elevate one name above others, even when science itself had been built through teamwork. In the years that followed, Roux continued to receive recognition from the scientific community. In fact, between 1901 and 1932, he was nominated for the Nobel Prize an extraordinary 120 times. Yet the prize never came. As time passed, his landmark achievement of isolating the diphtheria toxin in 1888 was increasingly considered too "old" to qualify for the award. Moreover, he did not produce another single discovery that matched the Nobel

Committee's narrow definition of a prize-winning breakthrough. And so, Émile Roux became one of what history might call the "highly qualified losers" — brilliant scientists whose contributions shaped the world but who never received the Nobel honour. His work saved lives, transformed medicine, and laid foundations for modern immunology. Yet the prize eluded him.

Still, history's judgment is often broader than that of any committee. Though he never held a Nobel medal, Roux's legacy lives on in the lives he helped save, in the Pasteur Institute he led, and in the scientific principles he helped establish. In the end, his impact on humanity was far greater than any single award.

Roux perfected large-scale production of diphtheria antitoxin using horses and successfully treated hundreds of children, reducing mortality by half. He also conducted research on tetanus, tuberculosis, syphilis, and pneumonia. A gifted teacher, he trained thousands at the Pasteur Institute, later serving as its director from 1904 until his death, dedicating his life to scientific advancement and public health.

Emil Adolf Von Behring

(15 March 1854 – 31 March 1917)

"A new therapy for infectious diseases is born; the therapy by immune serum. By serum therapy we have conquered a disease which killed thousands of children each year. In serum therapy the physician is only the instrument; it is Nature that cures."

➢ The Birth & Early life of Emil Von Behring:

The "Savior of Children," Emil Adolf von Behring, was born in Hansdorf, Kreis Rosenberg, Province of Prussia (now Lawice County, Poland) on March 15, 1854. The family had thirteen children, and his father was a schoolmaster. In 1874, Emil enrolled in the renowned Army Medical College in Berlin since his family could not afford to maintain him at a university. This

made his studies financially feasible, but it also meant that after earning his medical degree in 1878 and passing the State Examination in 1880, he would have to serve in the military for a number of years. After that, he was moved to Poland to live in Wohlau and Posen. During his early career as a military doctor, Emil von Behring conducted research on the medical use of iodoform, studying its antiseptic properties. His academic progress advanced significantly through his work on Neurotomia opticociliaris (optociliary neurotomy), which helped him qualify as a physician attached to the institute and later enabled him to pass his licensing examination in Marburg. In 1878, as part of his military duties, he was posted to Poland, where he focused on the treatment and study of septic diseases.

- **A Bridge Between the Laboratory & the Bedside:**

His growing reputation for scientific ability led to his recall to Prussia, where he was given the opportunity to study under the renowned bacteriologist Robert Koch. Behring's education was financially supported by the Prussian army, which required him to serve as a military surgeon in return. For each semester of study, he owed one year of service. As a result, from 1881 to 1883, he served with the Second Hussar Regiment. Alongside his bacteriological interests, Behring also conducted lesser-known research in ophthalmology. While working at Wicherkiewicz's hospital in Poznań (1881–1883), he published a paper describing a case of an eye tumour. Although the patient ultimately died of leukaemia, the case contributed valuable insights into eye surgery and treatment methods. During this period, he trained under leading ophthalmologists such as Carl Ernst Schweigger and Wilhelm Uhthoff, experiences that shaped his doctoral dissertation and deepened his understanding of eye diseases.

➢ Von Bohring:

After ten years in the Army Medical Corps, he joined Robert Koch as an assistant at the Institute for Hygiene in Berlin in 1889. He demonstrated there, alongside the Japanese bacteriologist Kitasato Shibasaburo, that an animal could be given passive immunity against tetanus by injecting it with the blood serum of another animal that had contracted the disease. Behring used this antitoxin method—a phrase he and Kitasato coined—to develop immunity to diphtheria. Behring called this method "**serum therapy**," describing it as a way to create lasting immunity or to stimulate the body's internal defence system. The extracted antitoxins were able not only to protect healthy animals from infection but also to cure already infected, non-immunized animals. In 1892, Behring began the first human trials of diphtheria antitoxin. These early attempts were unsuccessful. However, by 1894, after improving the production process and accurately measuring the dosage of antitoxin, the treatment became effective. In recognition of this achievement, he received the Cameron Prize for Therapeutics from the University of Edinburgh in 1894. The following year, in 1895, Behring was appointed Professor of Hygiene in the Faculty of Medicine at the University of Marburg, a position he held for the rest of his life. He worked in the same building as the pharmacologist Hans Horst Meyer and encouraged Meyer's interest in studying how tetanus toxin acts in the body. After being created with Paul Ehrlich and commercially sold in 1892, the administration of diphtheria antitoxin became a standard component of the disease's treatment. He was honoured with Prussian nobility in 1901, henceforth being known by the surname "von Behring".

Behring wed Else Spinola (1876-1936) on December 29, 1896. She was the daughter of Bernhard Spinola, the director of

Berlin's Charité hospital, and Elise Spinola, a Jewish woman who had converted to Christianity after marrying Behring. Six sons were born to them.

Behring continued to receive international recognition. In 1902, he was elected a Foreign Honorary Member of the American Academy of Arts and Sciences. In 1904, he founded Behringwerke in Marburg, a company dedicated to producing antitoxins and vaccines.

At the International Tuberculosis Congress in 1905, Behring announced that he had identified a substance derived from the tuberculosis organism, which he named “T C.” He believed this substance played a key role in the immune response produced by his “Bovi vaccine,” designed to prevent bovine tuberculosis. However, his attempts to develop a protective or therapeutic agent for humans against tuberculosis were not successful.

- **The Controversy:**

On connection with joint research on diphtheria, von Behring is suspected of defrauding Paul Ehrlich of recognition and financial gain. By repeatedly injecting a horse with the lethal poison, the two men created a diphtheria serum. In Germany, the serum proved to be useful during an outbreak. Both individuals were offered contracts by a chemical company that was planning to produce and commercialize the diphtheria serum commercially, but von Behring used cunning to keep all of the significant financial gains for himself. To make matters worse, only Behring's contributions earned him the first Nobel Prize in Medicine in 1901. Nevertheless, Ehrlich's work in immunology earned him the 1908 Nobel Prize in Medicine.

➢ Last Words:

Emil Adolf von Behring was not just a German physiologist; he was a man who gave countless children a second chance at life. At a time when diphtheria silently stole the lives of thousands of young ones, he discovered the life-saving diphtheria antitoxin—a breakthrough that earned him the very first Nobel Prize in Physiology or Medicine in 1901. People began to call him the "saviour of children," because in hospital wards where despair once echoed, hope slowly began to return. His work on diphtheria and tetanus transformed fear into faith in science and established a new era of healing through immunity. Behring passed away in Marburg on 31 March 1917, but his legacy did not fade with him. His name lives on through major biomedical institutions and the prestigious Emil von Behring Prize. His Nobel medal, displayed in Geneva, stands not merely as an award—but as a silent tribute to the lives he helped save and the dawn of modern immunology, he helped create.

Alexandre Yersin

(22 September 1963 – 01 March 1943)

"I am very happy to treat those who come to me asking for advice, but I wouldn't like to make medicine my profession… I could never ask a patient to pay me for treatment. I consider medicine a calling, like priesthood."

➢ The Birth & Early life of Alexandre Yersin:

This is the story of the right man, in the right place. Alexandre Yersin was born into a French family on September 23, 1863, in Lavaux, close to Aubonne, Switzerland. A few weeks prior to Alexandre's birth, his father, a teacher, passed away. Out of the four children, he was the youngest. Three

weeks prior to Alexandre's birth, his Swiss father, a biology teacher at a high school, passed away. He was a bold and inquisitive boy. When Yersin was eight years old, he murdered his mother's cat, dissected it, and used a microscope to study its organs. Yersin was fascinated by nature as a child and collected a variety of little creatures, such as insects, which he meticulously examined.

He was raised in Morges and attended Lausanne for his secondary schooling before enrolling in the university there. Later, in the late 1980s, he studied at the Paris Faculty of Medicine and the University of Marburg. He was employed at the Hôtel-Dieu in the laboratory of Professor André Victor Cornil. By chance, he met Pierre-Paul-Émile Roux, a fellow bacteriologist. He accidentally injured himself while doing an autopsy on a deceased rabies case. Yersin studied bacteriology under Robert Koch in Berlin and Émile Roux in Paris, as well as medicine at the universities of Marburg and Paris. After studying medicine in Lausanne, Marburg, and Paris, young Yersin joined the renowned French team of bacteriologists (including Emile Roux, Shibasaburo Kitasato) led by Doctor Louis Pasteur in 1886 because he was passionate about the expanding field of bacterial research. He soon became a part of the development alongside Roux.

- **Days at Pasteur Institute:**

Alexandre Yersin was an eminent Pasteurian. While working at Pasteur Institute, in 1888 he and Roux isolated a toxin secreted by the diphtheria bacillus (bacterium) and showed that the toxin—and not the microorganism—gives rise to the symptoms of the disease. There, after cutting himself while dissecting the cadaver of a patient who had died of rabies, he helped create a serum that prevented rabies and saved his own

life. After completing a paper on tuberculosis for his PhD in 1888, Yersin briefly studied under Koch. In 1890, at just 26 years of age, Alexandre Yersin left for French Indochina, inspired both by his Christian faith and his desire to serve through medical mission work.

He began working as a ship's physician aboard steamships sailing along the coast of French Indochina. This experience marked the start of a four-year period of exploration in the central regions of Southeast Asia.

While serving at sea, Yersin did more than treat patients. He carefully learned practical navigation skills, including how to use compass bearings and interpret maps.

These skills later proved invaluable during his inland expeditions across the Indochinese region.

What began as medical service aboard a ship gradually prepared him for a life of scientific discovery and geographic exploration in Southeast Asia, where the worlds fate was waiting for him.

➢ The Black Death:

Across human history, diseases like malaria, tuberculosis, and smallpox have claimed more lives than the plague. Yet the very word *plague* still sends a chill through the human heart. It is remembered not only for death—but for the terror, the silence of empty streets, and the collapse of entire societies. For centuries, plague arrived like a dark tide, often traveling along busy trade routes, turning prosperity into mourning. Its shadow stretches back to ancient times. The Plague of Justinian (541–740 A.D.) is believed to have wiped out nearly one-fifth of the known world. Centuries later, the Black Death swept across Europe and Asia in the 14th century, killing one in three

Europeans and reshaping history itself. Cities lost more than half their populations; economies crumbled, and the feudal system began to fall. In the 19th century, a third pandemic rose from China and India, claiming millions more lives and even reaching San Francisco in 1900. There, through the determined efforts of public health leader Dr. Rupert Blue, the disease was finally contained, preventing further catastrophe. For generations, the cause of this "Black Death" remained a mystery. Then, in the 1890s, in the humid and fearful atmosphere of Hong Kong, a young scientist named Alexandre Yersin made a breakthrough. Working with courage and urgency, he isolated the tiny bacterium responsible for centuries of devastation. Around the same time, Japanese scientist Kitasato Shibasaburō also described the organism, though history would largely remember Yersin's clearer findings. The bacterium, first called *Bacterium pestis*, was later renamed *Yersinia pestis* in his honor. What had once seemed like a curse from fate was finally revealed to be a microscopic enemy—one that science could confront. The story of plague is a reminder of humanity's vulnerability, but also of its resilience: how curiosity, courage, and scientific determination can turn fear into understanding and tragedy into progress.

➢ The Voyage to Asia:

Yersin left Europe in 1890 to serve as a physician aboard steamships operating off the coast of Indochina and soon began his four-year exploration of the central region. He discovered the sources of the Dong Nai River and explored the Lam Vien Plateau, where he recommended that a town, the future Da Lat, be built. In 1892 he joined the colonial health service and was sent to Hong Kong in 1894, where he and Kitasato Shibasaburo independently discovered the plague bacillus while studying an

outbreak of plague in China. Yersin opened a laboratory at Nha Trang the next year. He spent four years studying Annam's shore and hinterland before being assigned by the French government in 1894 to cope with the plague outbreak that was wreaking havoc in Yunnan, China. After arriving in the nation, he found Yersinia pestis, the causative agent, which he characterized as "small stocky spindles with rounded ends," in spite of the Japanese team's competition. Yersin is best remembered among the medical community today for his discovery of the bacillus responsible for the bubonic plague, which was later named in his honour: *Yersinia pestis*. That discovery, in Hong Kong in 1894, ironically came about in part because Yersin, then a relatively junior figure, did not have access to the latest scientific equipment, such as incubators, which inadvertently heated the cold-loving bacillus beyond its viability. Yersin also established that the same bacillus that infected people, *Yersinia pestis*, infected rodents, thus undeniably establishing the long-suspected means of transmission for the disease. Yersin was able to demonstrate, for the first time in history, that the same bacillus was present in both rodents and humans, thus highlighting the probable means of transmission of the disease. Then, until the end of his life, he carried out a significant deal of scientific research in a wide range of subjects. He advocated the following medical practices and was an idealist. There, he researched smallpox, cholera, tetanus, and cattle diseases while also creating serums to prevent plague in humans and cattle. He brought the rubber tree (Hevea brasiliensis) to Indochina and cultivated rice, coffee, and corn (maize) to fund the laboratory, which was named the Pasteur Institute of Nha Trang in 1903. He established a medical school in Hanoi in 1903–04, but he then went to Nha Trang, where he introduced a quinine source (Cinchona ledgeriana) in 1920–23.

He passed away in 1943 at his Nha Trang residence, which is now preserved as the Yersin Museum.

➢ The Vietnam Hero:

In May 1894, when plague struck Hong Kong again, the British authorities sought international help. The Pasteur Institute recommended Alexandre Yersin, who quickly sailed from Saigon. However, three days before his arrival, the renowned Japanese bacteriologist **Professor Kitasato Shibasaburō** and his team had already been warmly received with full media attention, hospital facilities, equipment, access to plague victims' bodies, and strong political support. In contrast, 31-year-old Yersin was dismissed as an outsider "The Frenchman." Lacking English fluency and high-society manners, he was ridiculed during a meeting with Kitasato, who refused collaboration. Denied access to corpses and suspecting bribery, Yersin, with the help of Italian priest Bernardo Vigano, bribed mortuary guards to obtain infected buboes for study. With no official support, he built a bamboo hut laboratory in 24 hours near the hospital. Meanwhile, Kitasato quickly announced he had isolated the bacillus and left Hong Kong. Later, his findings proved inaccurate and contaminated, revealing he had acted too hastily. Yersin pioneered early **One Health** approaches, studying zoonoses and coordinating multidisciplinary efforts long before they became standard practice. He established anti-plague serum centres in India and Vietnam, acclimatized quinine and rubber cultivation, and selected the site for Dalat. Later, he was appointed Honorary Director of the Pasteur Institute in Paris. The plague—later known as the Black Death—had killed an estimated 50 million people between the 14th and 17th centuries. The bacterium responsible was eventually identified and named *Yersinia pestis* in his honor.

Today, his legacy is most deeply remembered in Vietnam, through the institutions he founded and the lives he faithfully served. Yersin went back to Hanoi in 1895 and later played a key role in founding Indochina's first medical school in 1902, serving as its director during its initial two years. Today, Hanoi Medical School is the largest in Vietnam, but in its early days it struggled with a shortage of qualified teachers. To fill these gaps, Yersin taught himself subjects such as physics and zoology, taking on multiple roles to ensure students received a complete education—something reflected in the regular letters he wrote to his mother. Because he lived and worked during the colonial period, some critics label Yersin a colonial figure. However, historical records show his deep compassion for local communities, as he consistently treated the sick and cared for village children, presenting a very different image. For many young researchers, Yersin remains inspiring for his ability to work across multiple disciplines—what we now describe as a transdisciplinary approach.

- **The love for Pasteur:**

In honor of his mentor, Louis Pasteur, Yersin gave the bacillus the *name Pasteurella pestis*. It was assigned the newly established genus Yersinia in 1944. The French team that created the first anti-plague serum included Yersin. In 1895, this was refined and manufactured in Yersin's facility in Nha Trang, Vietnam, which later joined the Pasteur Institute. He was appointed honorary president of the Paris-based Pasteur Institute in 1933. He was given the honorific title of the country's Fifth Uncle by the Vietnamese government. At the age of 80, he passed away in his new nation in 1943. His house was dubbed Lau Ông Năm, or Home of the Fifth Uncle, and was turned into a shrine and museum. To

commemorate the 150th anniversary of Yersin's birth, France (Scott #4480-1) and Vietnam (Scott #3488-9) jointly released a pair of stamps in 2013. A youthful Yersin is shown on one stamp standing in front of the Pasteur Institute in Paris, where he started his career.

On the other, an older Yersin is shown with the Pasteur Institute in Nha Trang and a vista of the Đà Lạt / Lam Vien Plateau. Vietnam granted Yersin "honorary citizenship" in 2014. His research laid the foundation for later advances in antiserum therapy, antibiotics, and vaccines. His investigative approach remains influential in studying emerging infectious diseases such as SARS and Ebola.

Yersin spent much of his life in French Indochina, permanently settling there to advance medical science. **His tombstone says: "Benefactor and humanist, venerated by the Vietnamese people." The right man, in the right place, at the right time**

Kitasato Shibasaburo

(29 January 1853 – 13 June 1931)

"No matter how much academic research a scholar may conduct and make public, if the results of that research are not used in practice, they cannot have any effect on life."

➢ The Birth & Early life of Kitasato shibasaburo:

In the Aso region of Higo Province (now Kumamoto Prefecture), in the tiny village of Kitasato in Oguni, Shibasaburo Kitasato was born in 1853. Despite Kitasato's constant preference for martial arts above academics, his parents made an investment in his education when he was a child. He had a desire of joining the military because it was his passion. Although Kitasato attended the Kojo Medical School

in Kumamoto in 1871 at his father's request (later renamed Kumamoto Medical School and now the School of Medicine, Kumamoto University), his desire to be in the military did not change.

Meeting C. G. van Mansvelt, a Dutch doctor at the medical school, was a pivotal moment in his life. The young Kitasato, who could speak a fair number of Dutch, won Mansvelt over and he attempted to install in him a respect for medicine. However, Kitasato didn't fall in love with the field until he saw tissue magnified under a microscope for the first time. It was a turning point in Kitasato's life when he realized how important it was to pursue a profession in medicine. Knowing Kitasato's promise, Mansvelt emphasized to him the value of studying in Tokyo and subsequently Europe. In 1874, Kitasato left his native of Kumamoto and headed for the capital Tokyo. His subsequent medical expertise and research were made possible by this action. His education at the Tokyo Medical School played a significant role in forming his knowledge of contemporary medical procedures and research techniques. Kitasato later joined Tokyo Medical School (now the Faculty of Medicine, University of Tokyo). At that time, the school atmosphere was rough, with strong nationalist attitudes and undisciplined students. The principal, Sensai Nagayo, struggled to manage them and sought help from an old friend from his student days at Tekijuku school. That friend was Yukichi Fukuzawa, the founder of Keio. Fukuzawa sent two supervisors to maintain order in the dormitories. But it would be many years before Kitasato and Fukuzawa would cross paths.

➢ The Turning Point:

Following his graduation from Tokyo Medical School in 1883, Kitasato secured employment in the Health Department

of the Japanese Home Ministry. In 1885, Kitasato's career took a significant turn when he was sent to Germany to study under the renowned bacteriologist Robert Koch, one of the founders of modern bacteriology. There he studied with Emil von Behring and Paul Ehrlich. In 1889, Kitasato was able to obtain the first pure culture of the bacilli that cause tetanus in the globe there. He gained international prominence the following year for discovering a tetanus antitoxin, a medication composed of antibodies against the bacteria. Based on this new knowledge of antitoxins, he and German scientist Emil Adolf von Behring (1854–1917) developed a revolutionary method of treating and preventing bacterial infections in 1890 by using blood serum, known as diphtheria serotherapy. Behring himself would receive the first Nobel Prize in Physiology or Medicine in 1901 for his work in the field. If the practice of recognizing several laureates had been common, as it is now, Kitasato would have shared the coveted prize with Behring.

- **The call from the nation:**

To fight tuberculosis and other prevalent ailments of the time, the Home Ministry was moving forward with plans to construct a national institution of infectious diseases in the early 1890s. The now-famous Kitasato, who left Japan for Germany in 1885 and would return to Japan in 1892 at the age of 29, was eagerly anticipated by the ministry. However, a gathering of the Imperial Assembly shortly after his return made it apparent that it would take at least two years to get approval for the establishment of such an institution. Sensai Nagayo, Kitasato's former schoolteacher and current ministry official, once again sought advice from Fukuzawa, this time on the building of this much-needed institute rather than unruly kids. The Institute for Study of Infectious Diseases was established

that same year after Fukuzawa promised to sponsor a private institute. As a result, Kitasato became acquainted with Fukuzawa, a fifty-seven-year-old man who would serve as his mentor for the rest of his life. Following Fukuzawa's death in 1901, Kitasato wrote a eulogy in which he bemoaned, "...Oh, how sad it is! To mourn the loss of a mentor and father figure from the bottom of one's heart. ...Though not equal in ability or talent, I will carry on his good work, embody his teachings, and strive to repay my debt to him, one which can never be fully repaid." Following Fukuzawa's passing, Kitasato was asked to assist Keio University in establishing a new medical department in honor of the university's 60th anniversary. As the newly appointed dean, Kitasato once more honored his mentor during the 1917 Department of Medicine (later the School of Medicine) opening ceremony, declaring: "Though I was never a pupil of Fukuzawa, he taught me more than I ever could have hoped to learn under his tutelage." Up until 1928, Kitasato was the dean of the Keio University School of Medicine. Long after his term ended, he remained in an advising role for the rest of his life. The Kitasato Memorial Medical Library was constructed in 1937 as a tribute to his accomplishments. At Keio University's School of Medicine, a bust of Kitasato still stands at the entrance to the Kitasato Memorial Medical Library, keeping watch over the upcoming generation of medical professionals.

- **The Discoveries:**

Kitasato found antitoxins that are analogous to what we now refer to as antibodies.

Today, intractable diseases, antibiotic-resistant infections, and disorders are treated with a myriad of medications that employ antibodies. The serum therapies that form the

foundation of several of these medications were created by Kitasato. Currently referred to as antibody pharmaceuticals, they make up all but half of the newly developed medications worldwide.

When Kitasato visited Hong Kong in 1894, he independently identified the bubonic plague-causing bacteria, Yersinia pestis, nearly simultaneously with Alexandre Yersin (1863–1943) of the Pasteur Institute in France. The disease, commonly referred to as the Black Death, killed millions of people and changed the political, economic, social, and cultural landscapes of Europe in the fourteenth and eighteenth centuries. It manifested once more in northern China's Manchuria in the second part of the 1800s. The four criteria that Kitasato and others used to identify the disease are now known as Koch's Postulates.

In the years that followed, a number of other significant individuals would contribute to the field of bacteriology, such as Fritz Schaudinn (1871–1906) and Eric Hoffman (1868–1959) on syphilis and Shiga Kiyoshi (1871–1951) on dysentery. But at this point, bacteriology was starting to give way to the new discipline that is now known as microbiology, and medicine itself was changing. The discovery of viruses, which are germs smaller than bacteria, caused this shift. In the same year during an outbreak of cholera at Nagasaki, Kitasato is said to have demonstrated the presence of comma bacillus, the causative bacteria of the disease, under a microscope (When he was a child, he lost his two younger brothers and a sister to cholera at a time when medical care was still underdeveloped.) Four years later, Kitasato and his pupil Kigoshi Shiga also succeeded in identifying and characterizing the organism that caused dysentery, which is a lower intestinal tract infection that causes fever, severe diarrhoea, and pain. Many of Kitasato’s research

papers became important landmarks in bacteriology. In 1889, he described a successful method for culturing the anaerobic bacterium *Clostridium chauvoei*, which causes blackleg in cattle, by growing it in solid media under a hydrogen atmosphere.

That same year, he made a major breakthrough with *Clostridium tetani*, the bacterium responsible for tetanus. At the time, scientists believed it was impossible to obtain a pure culture because it grew mixed with other bacteria. Kitasato challenged this idea. He discovered that tetanus spores were highly heat-resistant and could survive heating at 80°C. Using this property, he heated a mixed bacterial culture to eliminate other organisms, then grew the surviving tetanus bacteria in a hydrogen environment. This method enabled him to produce the first pure culture of *Clostridium tetani*. Kitasato discovered tetanus toxin in *Clostridium tetani* culture filtrates. He determined its minimum lethal dose by injecting diluted toxin into rabbits. Nonlethal, gradually increasing doses induced immunity. Immune animals survived even high toxin doses. He also showed that serum from immune animals neutralized the toxin and provided both preventive and therapeutic protection against tetanus.

- **What if:**

The influenza epidemic, popularly referred to as the Spanish Flu, ravaged the world in 1918. The National Institute for Infectious Diseases and the Kitasato Institute for Infectious Diseases in Japan fought each other over vaccine development and therapy. The presence of viruses was yet unknown to science, and Kitasato and Richard Pfeiffer of Koch's Berlin research institution mistakenly believed that a "influenza germ" was the source of the illness. Based on this concept, both tried to create influenza vaccinations. But according to the Institute

for Infectious Diseases, the new microbe has to be a filterable pathogen—that is, a disease that is so tiny that it can get past bacterial filters. Regretfully, bacteriology was still in its infancy in 1918. Based on his theory, Kitasato worked to create a vaccine against the Spanish flu, but scientific understanding was still in its infancy and his efforts would not be fruitful. The presence of creatures much smaller than bacteria, which they called viruses, would not be confirmed by scientists until 1933, after the development of the electron microscope. Kitasato himself died two years earlier in 1931, therefore he did not survive to hear of the discovery. He had dedicated his entire life to advancing the field of bacteriology, and the new branch of virology would only emerge following Kitasato's departure.

- **Master to Many:**

Notable students of Kitasato were Sahachiro Hata, who discovered with Ehrlich the antisyphilitic effect of salvarsan, and Kiyoshi Shiga, who discovered Shigella dysenteriae, the cause of bacillary dysentery. In addition to being appointed a professor by the Prussian government, Kitasato received decorations from the governments of Norway, France, and Prussia. He was also chosen an honorary member of several nations' scientific societies and national academies. Hideyo Noguchi, whose name is on today's 1,000-yen bill, was one of the Institute's many exceptional pupils. At Kitasato's invitation, Koch travelled to Japan in 1908, and the Japanese government formally welcomed him. Following Koch's passing on May 27, 1910, Kitasato erected a tiny shrine in front of his lab in the German bacteriologist's honor. He placed a fingernail and a strand of Koch's hair—which he had surreptitiously acquired while Koch was in Japan—there. After suffering a stroke in 1931, Kitasato was buried in his revered teacher's shrine. Many

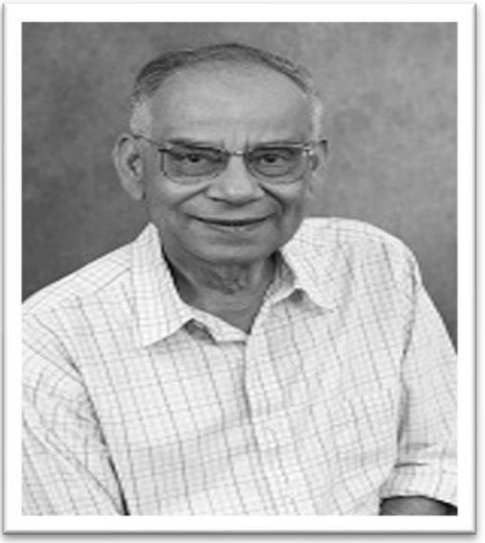
people visit the shrine every year on the anniversaries of Koch's and Kitasato's passing. In Japan, Koch and Kitasato's remarkable friendship is well recognized as an illustration of the strong attachment that can form between a teacher and student.

- **Let Down by his own:**

When Shibasaburō Kitasato identified the plague bacillus, he received international recognition. However, in Japan his achievements were not equally celebrated, and he was even criticized and labelled "ungrateful." Several scholars publicly challenged his theories. In 1901, when the first Nobel Prize in Physiology or Medicine was awarded, it went to Emil von Behring, a fellow student of Robert Koch. Although Kitasato's tetanus research was considered highly significant, strong national support from Germany helped Behring secure the prize. Rather than promoting Kitasato's accomplishments globally, influential institutions in Japan—including the University of Tokyo and the Ministry of Education—reportedly obstructed him. This opposition is often cited as a reason he did not become Japan's first Nobel laureate. Today, however, his contributions are fully acknowledged in Japan. In recognition of his dedication to infection prevention and public health, he has been honoured by being featured on the new 1,000-yen banknote. Despite possible setbacks, there is no denying that Kitasato's initial seeds, so many years ago, have produced a bountiful medicinal crop. The Kitasato Institute founded by this pioneering man of medicine continues to produce world-leading researchers and medical doctors to this day.

Along with starting his own institute, Kitasato shown unwavering leadership as an entrepreneur and in the development of new medical organizations.

He established the Japan Medical Association in 1916 and the Keiō School of Medicine in 1920.He founded the Japan Society for Tuberculosis in 1923 after founding the Terumo Corporation in 1921 to produce thermometers and other medical supplies. He would go on to establish numerous other organizations. Despite possible setbacks, there is no denying that Kitasato's initial seeds, so many years ago, have produced a bountiful medicinal crop. The Kitasato Institute founded by this pioneering man of medicine continues to produce world-leading researchers and medical doctors to this day.



Ananda Mohan Chakrabarty

(4 April 1938 – 10 July 2020)

"We all host swarms of microbes — in fact their cells outnumber our own. They help digest our food, it appears that they play vital roles in booting up immune responses, and they may even be able to attack cancers directly on our behalf. Only a handful of bacterial species are virulent, and even they have a vested interest in our health. Their fate is linked to ours. If we die, they die."

➢ The birth & early life of Anand Mohan Chakraborty:

Anand Mohan Chakrabarty was a renowned American scientist and microbiologist of Indian descent who rose to fame for his significant work in genetic engineering. Millions of

researchers have been motivated by his remarkable work to experiment with microbial genes in order to use them in a variety of sectors, adding new dimensions to the biotechnological aspects of microorganisms.

Nandipur (now Sainthia) had been a little-known place in Birbhum district, West Bengal. Before Prof. Chakrabarty was born there on April 4, 1938, to Shri Satya Dos and Smt. Sasthi Bala (Mukherjee) Chakrabarty, Nandipur (now Sainthia) was a little-known location in Birbhum district, West Bengal, India. He was the youngest of seven children born into a middle-class Bengali household. He finished his education at Ramakrishna Mission Vidyamandira and Sainthia High School. His mother, Smt. Sasthi Bala (Mukherjee) Chakrabarty, was a homemaker, while his father, Shri Satya Dos Chakraborty, was a trader. Dr. Chakraborty was inspired to seek knowledge & higher education to overcome large family & economic shortcoming.

- **Academic Journey:**

Early on, he shown a keen mind and a keen interest in science and the old Sanskrit language. Following his early schooling at Sainthia High School and Ramkrishna Belur Vidyamandir, he majored in chemistry at St. Xavier's College (now University) in Kolkata (1958). Then, under the guidance of Sailesh Chandra Roy (1965–1971), he earned his master's degree (1960) and doctorate in the "Emerging Discipline of Biochemistry" from Calcutta University. Chakrabarty's doctoral research was published in the Biochemical Journal. He was offered a postdoctoral position at the University of Illinois in Urbana-Champaign in 1965 after Irwin "Gunny" Gunsalus reviewed his papers. Numerous luminaries were trained by Gunsalus. Chakrabarty gained knowledge of the Pseudomonas bacteria's hydrocarbon degradation processes at Gunny's lab. He

was frequently heard to state, "*I only have one e-mail address, and it is pseudomo@uic.edu*," demonstrating his unwavering devotion to this genus. Dr. Chakraborty, thereafter joined the General Electric Research and Development Centre in Schenectady, USA (1971–1979). In 1979, he was named a Professor in the University of Illinois at Chicago's Department of Microbiology, where he remained until 1989 as a Distinguished Professor.

- **The SuperbugMan:**

His first job as a research scientist at General Electric's Research & Development Center, which involved employing microbes to turn cow waste into more proteinaceous animal feed, was not enjoyable. Simultaneously, significant oil spills were occurring increasingly frequently and negatively affecting the ecosystem. He started researching Pseudomonas's hydrocarbon degradation pathways on the weekends and in the nights in the hopes that someday a genetically altered strain of the bacteria will aid in oil spill cleanup.

When placed into an oil spill, the four species of oil-metabolizing bacteria that were known to exist at the time competed with one another, reducing the amount of crude oil that they could break down. Plasmids, which were transferable between species, carried the genes required to break down oil. Prof. Chakrabarty found a way to fix all four plasmid genes in place by irradiating the transformed organism with UV light after plasmid transfer. This resulted in a new, stable bacterial species (now known as pseudomonas putida) that can consume oil one or two orders of magnitude faster than the four strains of oil-eating microbes that came before it.

Chakrabarty dubbed the new bacteria "multi-plasmid hydrocarbon-degrading Pseudomonas," and it was capable of breaking down almost two-thirds of the hydrocarbons present in

an average oil spill. By introducing multiple circular DNA molecules, known as plasmids, into the bacteria, he and his colleagues developed a novel strain of Pseudomonas that was capable of decomposing crude oil on Petri dishes. Genes expressing different enzyme roles in hydrocarbon breakdown were present in each plasmid.

For Chakrabarty, this was a lightbulb moment, and he was particularly eager to share his discoveries at conferences and scientific meetings. However, his GE employers had a different plan. They encouraged Chakrabarty to submit a patent application for his microorganism because of the possibility of commercial use for his discovery. With the assistance of GE lawyer Leo MaLossi, Chakrabarty submitted a patent application in 1972, despite being well aware that no live entity had ever been granted a patent by the US Patent & Trademark Office.

- **The Trendsetter:**

While employed at the General Electric Research and Development Center, Prof. Chakrabarty gained notoriety in 1971 for creating a genetically modified Pseudomonas, commonly referred to as a "superbug" or "oil-eating bacteria." When he filed for the first U.S. patent on a genetically engineered organism, the bacteria garnered attention from all across the world. Louis Pasteur had already patented two pure bacterial cultures, among other living species, with U.S. utility patents. Before the U.S. patent was issued, Chakrabarty's modified bacterium received a patent in the United Kingdom. Because it was believed that the patent code prohibited patents on living things, the Patent Office first rejected his application.

The ruling in favour of Chakrabarty was reversed by the US Court of Customs and Patent Appeals. This discovery became a

biological remedy for removing oil pollution especially during disastrous oil spills and leakages in marine ecosystems. He finally achieved his well-earned fame in 1980 after nine years of battling for the settlement of this patent lawsuit, which was granted to him following a Supreme Court decision (US Patent No. 4259444 for "Microorganisms having multiple compatible degradative energy-generating plasmids and preparations thereof").

He earned the title of "***Father of Patent Microbiology***" for creating new avenues for the bio patenting of genetically engineered microbes and other lifeforms. Additionally, this cleared the path for bioremediation to become a recognized industry. Since then, he has participated in numerous esteemed committees and held a number of advisory positions on such legal matters.

- **The never-ending thrust:**

Professor Chakrabarty made substantial contributions to a variety of biotechnology fields. In addition to his groundbreaking discovery of the "bioengineered superbug," he has made numerous other significant contributions, such as creating anti-cancer, anti-viral, and anti-parasitic medications based on promiscuous bacterial proteins and peptides. He found that Pseudomonas aeruginosa produces a periplasmic protein called azurin, which has strong antitumor effects. In order to create vaccines, treatments, and diagnostics specifically for cancer and a number of other diseases, he co-founded two startup firms, CDG Therapeutics Inc. in Chicago and Amrita Therapeutics in India. Several US patents have been obtained based on his work at the University of Illinois, Chicago, and CDG Therapeutics Inc. is the owner of its confidential knowledge.

Several infections have cytotoxic factors with anti-cancerous capabilities that can be employed to prevent necrosis and apoptosis-related circumstances during infectious diseases like cancer, according to his patents on "cytoxic factors for modulating cell death" [US Patent 7084105, 791394, 7888468]. The materials and techniques for transporting a cargo molecule into a cancer cell using protein transduction domains generated from cupredoxins were disclosed in another patent on "cupredoxin derived transport agents and methods of use thereof" [US Patent 7691383, 8206685, 8530635. The diagnosis and treatment of cancer, specifically brain cancer, as well as other brain-related illnesses, were the focus of his invention on "transport agents for crossing the blood–brain barrier and into brain cancer cells, and methods of use thereof" [US invention 7807183, 8188251, 8545812].

The use of cupredoxins to inhibit the process of tumour-related angiogenesis in human cells and tissues is the subject of another patent on "compositions and methods to control angiogenesis with cupredoxins" [US Patent 7556810, 8,124,055, 8372962]. In addition to these, he holds numerous other patents, such as: compositions and methods for using cupredoxins to prevent cancer [US Patent 7618939, 8227402, 8158574, 8232244], compositions and methods for using cupredoxins to treat conditions related to ephrin signalling [US Patent 7381701], and compositions and methods for using cupredoxin and cytochrome "c" to treat HIV infection. compounds and techniques for using cupredoxin and cytochrome to treat malaria [US Patent 7301010, 7511117, 7795410], [US Patent 7338766, 8623816, 7740857].

➢ India's Gem:

One of the original members of the United Nations Industrial Development Organization Committee that established the International Centre for Genetic Engineering & Biotechnology (ICGEB) was Prof. Chakrabarty. He also provided support to Sweden's Stockholm Environment Institute. He served on the board of directors of the Einstein Institute for Science, Health, and the Courts (EINSHAC), which is now the National Courts and Sciences Institute (NCSI) in the United States, as well as the NATO Industrial Advisory Group in Brussels, Belgium. In 1975, he received the Industrial Research Organization of the United States' Scientist of the Year award.

In addition, he was honoured with numerous honors, such as the American Chemical Society's 1984 Public Affairs award, the Patent Lawyers' Association's 1982 Inventor of the Year award, the Environmental Protection Agency's 1985 Distinguished Scientist award, the Pasteur Award in 1991, and the American Society for Microbiology's (ASM) Procter and Gamble Environmental Biotechnology Award. The Government of India granted him the Padma Shri in 2007 in recognition of his achievements to the field of genetic engineering.

➢ The Policy maker:

From developing biological product policies to advising Supreme Court judges on legal matters, Prof. Anand Mohan Chakrabarty has always sought to support and benefit the scientific community and humanity. He worked to make biotechnological products commercially viable and to give patent-oriented research a priority. He also underlined the importance of setting up a patent cell in every research and development firm. He will always be a really kind, grounded

individual who has been a creative thinker and philosopher who is willing to take on obstacles with goal-oriented, unconventional answers.

We pray and hope that his eternal presence will continue to inspire scientists and microbiologists worldwide for ages to come! Since then, Prof. Chakrabarty's groundbreaking work has thrust him into the global limelight and opened the door for numerous patents on genetically modified microorganisms and other life forms.

- **The Awards & legacy:**

Dr. Chakrabarty has won numerous honors, including the US Environmental Protection Agency's Distinguished Scientist Award and the Industrial Research Organization of the United States' 1975 Scientist of the Year award.

Procter & Gamble Environmental Biotechnology Award from the American Society for Microbiology; U.S. Army Public Affairs Award from the American Chemical Society; and MERIT Award from the NIH Distinguished Service Award.

In 2007, the Golden Eurydice Award was given for contributions to bio philosophy.

Esther Mariam Lederberg

(18 December 1922 – 11 November 2006)

"A pure genius……. experimentally & methodologically in the lab- Stanley Falkow (Renowned Cancer Researcher) on Esther Lederberg."

➢ The Birth & Early life of Esther Mariam Zimmer/Lederberg:

Esther Miriam Zimmer was the first of two children born on December 18, 1922, in the Bronx, New York City, USA. She was the eldest child in a family of Jewish immigrants of Eastern European origin. Her parents had migrated to the United States from Bukovina, which at the time was part of the Austro-Hungarian Empire (now divided between Romania and Ukraine). Like many immigrant families of that period, they came seeking better economic opportunities and stability. Her

father, David Zimmer, worked as a printer and ran a small print shop. Her mother, Pauline Geller Zimmer, managed the household and supported the family's educational aspirations. Her younger brother, Benjamin Zimmer, was born in 1923. Esther grew up in a modest, hardworking, and intellectually encouraging household. Despite limited financial resources, her parents valued education highly — a common trait among immigrant Jewish families in New York during the early 20th century. At the age of 15, Zimmer graduated from the Bronx's Evander Childs High School in 1938. She received a scholarship to Hunter College, City University of New York, to study biochemistry when she was 16 years old. At first, Zimmer planned to study literature or French, but she changed her major to biochemistry against the advice of her lecturers, who believed that a woman would find it more challenging to pursue a career in the sciences.

➢ The start of Academic journey:

Esther Lederberg (born Esther Zimmer) began her scientific career as a research assistant to Alexander Hollaender at the Carnegie Institution of Washington (later Cold Spring Harbor Laboratory), where she conducted early work on Neurospora crassa with Bernard Ogilvie Dodge. She graduated with honors in genetics in 1942 and joined Stanford University for her master's degree under George Wells Beadle and Edward Tatum. Despite financial hardships, her analytical abilities impressed Tatum, earning her a teaching assistantship. She also trained under Cornelis Bernardus van Niel, gaining strong foundations in microbial physiology. She completed her M.Sc. in 1946 and later married Joshua Lederberg. She pursued her PhD at the University of Wisconsin under R. A. Brink, completing it in 1950 with a thesis on genetic mutability in Escherichia coli.

During the 1950s, she made groundbreaking contributions, including the discovery of lambda bacteriophage, work on lysogeny and transduction, identification of the F fertility factor with Luigi Luca Cavalli-Sforza, and development of replica plating. These achievements established her as a pioneer in bacterial genetics. In 1956, she and Joshua Lederberg were awarded the Pasteur Medal for their contributions to the field.

➢ The fruit started ripening:

Esther Lederberg was the first scientist to isolate the λ (lambda) bacteriophage, initially reporting her discovery in 1951 during her PhD research and later elaborating it in a 1953 publication in *Genetics*. While working with an ultraviolet (UV)-mutagenized strain of Escherichia coli K-12, she observed plaque formation when the mutant strain was mixed with its parental strain on agar plates. These plaques indicated the presence of bacteriophages originating from the parental strain. The UV treatment had eliminated the phage from the mutant strain, rendering it susceptible to infection by the same phage, which she named λ. Her research revealed that λ bacteriophage exhibits two distinct life cycles: a lytic cycle, where it replicates rapidly and lyses the host cell, and a lysogenic cycle, where it integrates into the host genome and remains dormant. In collaboration with Joshua Lederberg, she demonstrated that in its lysogenic state, λ integrates near the galactose metabolism (gal) genes of the bacterial chromosome. This integrated form, known as a prophage, replicates along with the host DNA. Upon induction, the prophage may excise from the chromosome; however, this process can occasionally include adjacent bacterial genes. This leads to the transfer of host genetic material to another bacterium, a mechanism termed specialized transduction. Lederberg further disseminated her

findings through international conferences, notably in 1957 in Canberra and in 1958 in Montreal, contributing significantly to the understanding of phage genetics and gene transfer mechanisms.

➢ Further Discoveries:

Esther Lederberg discovered the bacterial fertility factor (F factor) during her studies on the genetic mapping of λ prophage in Escherichia coli. While performing genetic crosses, she observed that certain strains failed to produce recombinants, leading her to propose the existence of a "fertility factor" required for genetic exchange. This F factor was later identified as a DNA element that enables bacteria to transfer genetic material through conjugation, either as an independent plasmid or integrated into the chromosome. In collaboration with Joshua Lederberg, she also developed the replica plating technique, which allowed the transfer of bacterial colonies onto multiple media while preserving their spatial arrangement. This method demonstrated that mutations, such as antibiotic resistance, arise spontaneously rather than in response to selective agents, confirming earlier findings of Salvador Luria and Max Delbrück. Later, at Stanford University School of Medicine, she directed the Plasmid Reference Center, where she catalogued plasmids and introduced systematic nomenclature for genetic elements like insertion sequences and transposons, contributing significantly to microbial genetics research.

➢ Fight with the World:

Despite her achievements, Lederberg faced significant gender bias. Many of her contributions were overshadowed, often attributed to her husband. This reflects the "Matilda Effect," where women scientists receive less recognition. She was denied

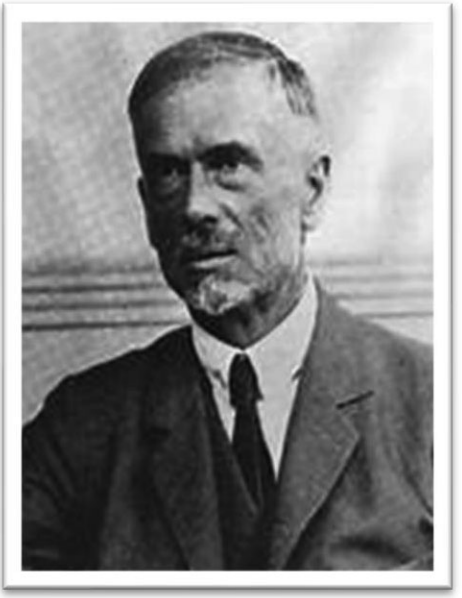
equal academic positions and often held non-tenured roles, even at Stanford, where her husband led the genetics department. Her exclusion from major scientific publications and recognition further limited her visibility.

➢ Legacy and Scientific Recognition:

Despite facing systemic discrimination, Esther Lederberg made groundbreaking contributions that shaped modern microbiology. She is recognized as a pioneer in bacterial genetics, having discovered the lambda bacteriophage, the F fertility factor, and developed the replica plating technique. These innovations laid the foundation for understanding gene transfer, mutation, and molecular biology. Although formal recognition during her lifetime was limited, her legacy has grown significantly posthumously. Today, she is celebrated for her independent scientific contributions and as a symbol of perseverance for women in science. Her work continues to influence genetics, biotechnology, and medical research, ensuring her lasting impact on the scientific community.

➢ Esther Beyond Science:

Apart from her scientific achievements, Esther had a deep passion for music and literature. She was particularly devoted to early music (medieval, Renaissance, and Baroque periods) and played instruments like the recorder. In 1962, she founded the Mid-Peninsula Recorder Orchestra, which continues to perform classical compositions. She also had a strong interest in literature and was an admirer of authors like Charles Dickens and Jane Austen, actively participating in literary societies dedicated to



Sergei Winogradsky

(01 September 1856 – 24 February 1953)

"A complete synthesis of organic material by the action of living organisms has been accomplished on our planet independent of solar energy."

➢ The Birth & Early life of Sergei Winogradsky:

Russian Microbiologist Sergey Nikolayevich Winogradsky was born in Kiev, Russian Empire, on September 1, 1856. He was related to the Skoropadsky family on his mother's side and Cossack atamans on his father's side. Winogradsky was "strictly devoted to the Orthodox faith" when he was younger, but he eventually lost his religious beliefs. His discoveries about the

physiology of soil bacteria's nitrification and nitrogen fixation processes contributed to the development of bacteriology as a significant biological field. The Ukrainian economy and way of life underwent a significant transformation in the late 1870s as a result of the sugar beet's cultivation and the country's growing beet sugar trade, particularly in Kiev. The Winogradsky family's wealth skyrocketed after his father was appointed director of a recently established bank. As a result, Sergei was raised in a wealthy and privileged environment. His father chose one of the nearby gymnasia for his early education since it offered both Latin and Greek instruction, whereas the other gymnasium only offered Latin instruction. Young Winogradsky found his classes "not only uninteresting and unpleasant but depressing, both physically and morally," despite this clear benefit. When he received a gold medal for his academic achievement, he sold it right away, demonstrating his disdain for his academic experience there. This was meant to hint at his dissatisfaction with the intellectual and scientific mediocrity he would frequently come against over his life and career.

After graduating, he enrolled in the University of Kiev to study law for two years, but as expected, he found it boring. The students were already engaged in revolutionary activities, but he was irritated and uninterested in them. In an attempt to find a way to express his undeveloped but strong creative impulses, he moved to the Division of Natural Sciences. He was disappointed once more, this time by the dull and disjointed lessons and the absence of any analytical science. At this stage, one can sense the frustration of the highly talented and creative young Sergei Winogradsky as he tried to determine the direction of his life. Setting aside his earlier intellectual inclinations, the 20-year-old turned toward music and enrolled at the St. Petersburg Academy of Music (Imperial) to study

piano. Coming from a musically supportive family and having trained since childhood, he was skilled enough to study under the renowned teacher Theodor Leschetizky. However, after just over a year, he abandoned this path as well, feeling that artistic expression alone, without intellectual engagement, was insufficient. His dilemma mirrors that of Jacques Monod, who also faced a choice between music and science. Ultimately, both chose microbiology and made significant contributions to the field.

- **The Artist turned Scientist:**

Winogradsky soon realised that St. Petersburg was not Kiev, and its university was exceptional. He enrolled in the natural sciences faculty once more, but this time he was much luckier. With notable professors like Elie Metchnikov in biology and Dmitri Mendeleev in chemistry on the faculty, Winogradsky quickly came to believe that he was at last headed in the right direction. Following three years of education, Winogradsky selected Plant Physiology as his major after discovering the lab of renowned and captivating botanist Andrei Famintsyn. Famintsyn consented to supervise Winogradsky and accept him as an undergraduate research student. Winogradsky chose to pursue a master's degree in Famintsyn's laboratory after graduating, and as they say, the rest is history.

The fact that Famintsyn had studied under renowned botanist Anton deBary in Strasburg would play a significant role in Winogradsky's postgraduate research. After returning to St. Petersburg from DeBary's lab, Famintsyn conducted research on how light affected the growth of the unicellular alga Spirogyra. He employed microscopic and microchemical monitoring of internal starch granules as a measure of algal growth. Winogradsky later used this experimental method in his

research on Beggiatoa in Strasburg, where he developed the theories of chemolithotrophy and autotrophy as a result of the formation and disappearance of intracellular sulfur granules. The emphasis of Famintsyn's research was on the relationships between an organism's nutrition and its physiological properties. And the choice of the yeast *M. vini* offered the opportunity for Famintsyn to examine an organism which bridged the gap between plants and animals. It is a happy coincidence, or perhaps fated, that the organism Winogradsky was assigned to work on for his Master's degree in Famintsyn's laboratory was *Mycoderma vini. (In addition to plaguing the sugar beet industry, Mycoderma vini was the organism that Pasteur used to conduct research that resulted in "Etudes sur la biere," which was a key component of the revolutionary paradigm shift toward the idea of a cause-and-effect relationship between germs and chemical change.)* Despite working in a plant physiology lab, Winogradsky was aware of and intrigued by the work of early German microbiologists like Ferdinand Cohn and Robert Koch, but he was particularly impressed by Louis Pasteur's work on fermentation in France. It is reasonable to argue that Pasteur set the bar for Winogradsky's whole career with his insistence on factual accuracy, his sharply logical experimental methodology, and his capacity to derive clear and convincing conclusions from his experiments.

- **Worshipping the Greats:**

From the outset, Sergei Winogradsky strongly embraced Louis Pasteur’s view that microorganisms are the cause, not the result, of chemical transformations, and he even replicated many of Pasteur’s early experiments during his training. He was deeply influenced by Ferdinand Cohn’s precise studies on bacteria and his belief in their stable and defined characteristics. The pioneering work of Robert Koch in developing pure culture

techniques proved essential to his understanding of microbial research. Additionally, Andrei Famintsyn's method of integrating microscopic observation with physiological and nutritional studies became a guiding principle in his work. Together, these influences laid the foundation for the next significant phase of his scientific career. Sergei Winogradsky successfully obtained a pure culture of *M. vini* through repeated serial dilutions until only a single cell remained. At that time, although Robert Koch had already introduced solid media techniques, this method had not yet reached St. Petersburg. Winogradsky then investigated how different organic and inorganic nutrients, along with varying oxygen levels, influenced microbial growth. For this purpose, he used a Geissler chamber, an apparatus earlier employed by Louis Pasteur, which allowed controlled environmental conditions and long-term maintenance of pure cultures while observing microbial behaviour.

His work represented one of the earliest systematic studies on how controlled environmental factors affect microorganisms. Although these findings were not formally published, he presented them in 1883 at a university botanical meeting. The work was later summarized by Alexander Borodin, who praised the exceptional purity of his cultures, highlighting the scientific rigor of Winogradsky's early research.

➢ Strassburg Awaiting:

In 1883, Sergei Winogradsky earned his Master of Science degree and was offered an opportunity by the faculty at St. Petersburg University to remain and prepare for a professorship. However, he declined, as he was never particularly drawn to academic life and had different aspirations. By this time, he had married Zinaida Alexandrovna Tikhotskaya, who remained his

devoted companion for nearly six decades. Due to the harsh climate of St. Petersburg, which adversely affected his wife's health, the couple moved to the milder region of Crimea. During this period, Russia was experiencing political repression under Tsar Alexander III following the assassination of Alexander II, creating an unfavourable environment for independent thinkers. Seeking a more progressive atmosphere, Winogradsky relocated to Western Europe in 1885 and joined the laboratory of Anton de Bary at the University of Strasbourg. During this period, microbiology was divided between two opposing views: pleomorphism and monomorphism. Many classical botanists, unfamiliar with bacterial diversity and often working with mixed cultures, believed that only a few bacterial types existed and that their varying shapes were due to environmental influences. In contrast, the monomorphists, led by Ferdinand Cohn, argued that bacteria possess stable and distinct forms, forming the basis for classification. Anton de Bary supported this view and encouraged Sergei Winogradsky to investigate it further. Winogradsky studied the filamentous bacterium Beggiatoa, known for accumulating sulfur granules in its natural habitat *(Beggiatoa, An enigmatic bacterium. Beggiatoa was perplexing since it could grow into massive colonies and create vast mats in sulfurous spring waters, yet it did not grow in the nutrient mixes often employed in laboratories.)* Winogradsky travelled to a number of different springs to personally collect samples of water, which he brought back to the laboratory.

By confirming its consistent characteristics, he provided strong support for the concept of monomorphism and helped advance bacterial taxonomy. He developed the notion of chemolithotrophy there as a result of his research on the sulfur-oxidizing bacterium Beggiatoa.

By 1887, Sergei Winogradsky demonstrated that Beggiatoa obtains energy through an unusual mechanism not previously recognized. The organism derives energy from the chemical oxidation of hydrogen sulfide (H_2S) in the presence of oxygen, producing sulfur and water. The sulfur formed is stored within the cells and can later be further oxidized to generate additional energy when required.

This was the first evidence of an organism utilizing inorganic substances as an energy source, a mode of metabolism now known as lithotrophy. Winogradsky also noted that the presence of carbon dioxide was essential for the bacterium's activity, an observation that later proved significant. Shortly after this breakthrough, he had to shift his work following the death of Anton de Bary in January 1888. For the young Winogradsky, Strasbourg must have been a revelation due to its Teutonic efficiency, DeBary's personification of scientific greatness, and its function as a global hub for international scientists. His time at Strasburg was comparable to the postdoctoral period of today, as he was not constrained by the rigid customs of Russian academics, was not obligated to his family, and did not have to worry about finding a job in Russia, at least not for the time being. After De Bary passed away in 1888, he relocated to Zurich and started researching the nitrification process. There, he discovered the genera Nitrosomonas and Nitrosococcus, which oxidize ammonium to nitrite, and Nitrobacter, which oxidize nitrite to nitrate.

➢ Peak Winogrdsky:

In order to determine which bacterial communities are present in a sample, Winogradsky created the Winogradsky Column while he was living in Strasbourg. It is made comprised of a glass cylinder filled halfway with mud from a lake or river

and then filled with water. To give bacteria supplies of nourishment, a variety of chemicals are added, including cellulose (newspaper), calcium carbonate, and sodium sulfate. Scientists can regulate how much light and nutrients are available to bacteria inside the column. In 1888, Sergei Winogradsky moved to the Swiss Federal Polytechnic Institute, where he focused on bacteria involved in nitrogen transformations. Building on earlier findings by Martinus Beijerinck, he investigated how microbes convert atmospheric nitrogen into forms usable by plants.

During his work, Winogradsky identified new groups of bacteria responsible for nitrification and demonstrated that this process occurs in two distinct steps: oxidation of ammonium to nitrite, followed by oxidation of nitrite to nitrate. He isolated the first pure cultures of the nitrifying bacteria and verified that they converted ammonia to nitrite and nitrite to nitrate in distinct processes. The idea of the sulfur and nitrogen cycles in nature resulted directly from this.

His most significant contribution was providing evidence for chemosynthesis. He showed that certain bacteria utilize energy from inorganic chemical reactions and fix carbon dioxide as their carbon source, confirming his earlier hypothesis about microbial metabolism.

Sergei Winogradsky discovered the process of chemosynthesis, showing that certain organisms can produce organic matter using energy from chemical reactions instead of light. In sulfur bacteria like Beggiatoa, this energy is derived from the oxidation of hydrogen sulfide, while in nitrogen-transforming bacteria it comes from oxidation of nitrogen compounds. This finding revealed that life can exist independently of photosynthesis, a concept later supported by

the discovery of extremophiles thriving in harsh environments. (*Planetary scientists speculate that extremophile organisms using chemosynthesis might exist on Jupiter's moons Europa and Callisto and possibly below the surface of Mars.)*

Winogradsky's name had gained recognition and respect by 1890. He had made the astounding discovery that inorganic molecules could be converted into organic molecules without the necessity for photosynthesis. Winogradsky's discovery enthralled his hero, Louis Pasteur, who asked him to relocate to Paris to take a position as Head of Microbiology at the Pasteur Institute. Winogradsky would have wanted to accept the enticing offer, but he was experiencing some homesickness. He relocated to Saint Petersburg as Head of Microbiology at the Institute of Experimental Medicine after deciding it was time to return to his native country. Winogradsky wrote, "We will call it Clostridium pasteurianum in honor of the great scientist, creator of our science," after he continued to study nitrogen-fixing bacteria there between 1892 and 1895. An important finding was Clostridium pasteurianum, a soil-dwelling microbe that fixed nitrogen from the atmosphere so that plants could use it. Even in the absence of nitrogen-fixing plants like peas, C. pasteurianum raised the amount of nitrogen in the soil. Winogradsky was appointed editor of the Archives of Biological Sciences, a Russian and French journal that grew to be one of Russia's most significant scientific publications, and director of the Institute of Experimental Medicine in 1902.

Sergei Winogradsky served as director of the Institute of Experimental Medicine until 1905 but stepped down due to his dislike for administrative responsibilities, choosing to return to active research. Owing to declining health caused by the harsh climate of St. Petersburg, he retired in 1910 and divided his time between Ukraine and Switzerland. The political upheaval

following the Russian Revolution forced him to leave his homeland permanently in 1921, after which he briefly worked in Belgrade. In 1922, he accepted an invitation to join the Pasteur Institute, where he continued his scientific career. At Brie-Comte-Robert, he focused on microbial ecology, a field he helped establish, studying the interactions between microorganisms and their natural environment. His work significantly advanced understanding of the nitrogen and sulfur cycles, and he also investigated iron bacteria, Azotobacter, and cellulose-degrading microorganisms.

- **Winogrdsky The legend:**

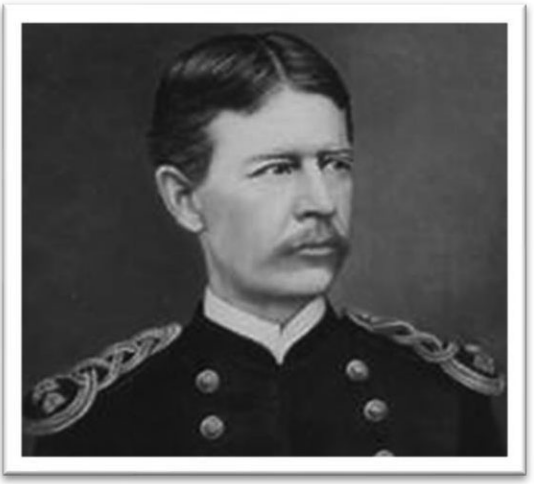
Sergei Winogradsky was not only a pioneering microbiologist but also a man of remarkable intellect, discipline, and simplicity. Though born into an aristocratic family in Kyiv, he remained democratic in spirit, deeply connected to nature, and dedicated to scientific truth rather than fame or academic prestige. He was a philosopher, an experimental scientist, and a gifted musician who continued to enjoy playing the piano throughout his life. His wife, Zinaida Alexandrovna Tikhotskaya, remained his lifelong companion until her death in 1939, and together they raised four daughters.

Even after stepping down from administrative roles, Winogradsky remained scientifically active. At the Pasteur Institute in Brie-Comte-Robert, France, he founded the field of microbial ecology, studying microorganisms in relation to their natural environment. His work on sulfur bacteria, nitrifying bacteria, nitrogen fixation, iron bacteria, and cellulose-decomposing microbes transformed our understanding of the nitrogen and sulfur cycles in nature.

His greatest contribution was the discovery of chemosynthesis (chemoautotrophy), proving that some

microorganisms obtain energy from inorganic compounds such as hydrogen sulfide and ammonia rather than sunlight. This changed the understanding of life processes and established the concepts of lithotrophy and environmental microbiology. He also developed the famous Winogradsky column, still used today to study microbial ecosystems. Winogradsky lived an unusually long and productive life. At the age of 93, he completed a 900-page work titled *Soil Microbiology: Problems and Methods*. He passed away peacefully in his sleep on 25 February 1953 at the age of 96 in Brie-Comte-Robert, France.

Those who knew him remembered him as a master—calm, brilliant, and inspiring. His life teaches that true science requires patience, observation, originality, and humility. His legacy continues to guide microbiology, ecology, and soil science across the world.



Walter Reed

(13 September 1851 – 23 November 1902)

"Instead of being simply satisfied to make friends and draw your pay, it is worth doing your duty, to the best of your ability, for duty's sake; and in doing this, while the indolent sleep, you may accomplish something that will be of real value to humanity"

➢ The Birth & Early life of Walter Reed:

Walter Reed was born on September 13, 1851, in Belroi, Gloucester County, Virginia, USA. He was the youngest of five children born to Reverend Lemuel Sutton Reed, a respected Methodist minister, and his first wife Pharaba White Reed. Growing up in a disciplined and educated family, Walter was strongly influenced by his father's values of dedication, service, and learning. His childhood was spent in a religious and

intellectually stimulating environment, where education was highly valued. Because his father frequently moved for church assignments, Walter experienced different towns and schools during his early years, which helped him develop adaptability and maturity at a young age.

From childhood, Reed showed exceptional intelligence and a deep interest in studies, especially science and literature. In 1866, his family moved to Charlottesville (When he noticed his youngest son's academic skills, he requested a transfer to a Charlotteville church so that his sons could attend the University of Virginia). Just after the move to the new church, Reed's mother died. The family was devastated.

In Virginia, where he initially planned to study classical subjects at the University of Virginia. However, his growing fascination with medicine led him to pursue medical studies instead. Remarkably, he earned his medical degree at a very young age, becoming one of the youngest graduates in the university's history. His early academic brilliance, disciplined upbringing, and strong moral values laid the foundation for his later achievements in medical science, especially his historic work on yellow fever research. Originally situated in Washington, D.C., the Walter Reed National Military Medical Center was renamed in his honor and relocated to Bethesda, Maryland, in 2011.

➢ The Youngest Doctor:

After attending the university for a while, he changed to the medical faculty, finished his medical program in nine months, and graduated as a doctor of medicine in the summer of 1869 at the age of seventeen. He enrolled as a medical student at Bellevue Medical College in New York to gain additional clinical experience, and a year later he pursued a second medical

degree, M.D. in 1870, when he was eighteen, but the degree was not awarded him officially until he was twenty-one. He was a district physician in New York and interned at multiple hospitals. However, he chose to pursue a career in the military for security rather than general practice. He was commissioned as a first lieutenant in February 1875 after passing the Army Medical Corps exam. After being sent to Fort Lowell in Arizona, Reed married Emilie Lawrence in April 1876, and she quickly joined him. Reed was on garrison duty for the next eighteen years, frequently at frontier stations, and he changed stations nearly every year. The hardships of frontier existence are vividly depicted in his letters. He was named attending surgeon and recruit examiner in Baltimore in 1889. He was permitted to work at the Johns Hopkins Hospital, where he studied bacteriology and pathology. As medical science advanced rapidly, Reed sought deeper knowledge in pathology and bacteriology. At Baltimore, Johns Hopkins University under the famous pathologist William H. Welch. There he learned modern laboratory techniques, pathology, and bacteriological research methods, which shaped his future investigations. In 1893, Reed was appointed professor of bacteriology and clinical microscopy at the newly formed Army Medical School, as well as curator of the Army Medical Museum in Washington. He was named chairman of a committee to look into the spread of typhoid illness in military camps during the Spanish-American War in 1898.

➢ The Yellow Havoc:

Yellow fever is a serious viral disease caused by the yellow fever virus, a member of the *Flavivirus* group, transmitted by infected mosquitoes, mainly *Aedes aegypti*. It is believed to have originated in Africa and later spread to South America through the transatlantic slave trade. It causes fever, jaundice, and severe bleeding in critical cases. For the most of the 19th century, it was commonly believed that fomites, or items like clothing and bedding worn by a patient with yellow fever, were the source of the disease. There were a number of ideas on the origin and spread of yellow fever by the late 1800s. In the ninth edition of Encyclopaedia Britannica (1885), Scottish medical historian Charles Creighton noted that "yellow fever, in time and place, has dogged the steps of the African slave trade." Dr. Creighton outlined the conventional wisdom that yellow fever was "a virulent filth-disease" brought to the New World on ships contaminated by the excrement of African slaves, rejecting as "altogether wide of the mark" recent claims that the disease might be spread by a microorganism: However, new theories were beginning to gain traction by the 1880s. Carlos Juan Finlay, a Cuban physician and epidemiologist, started developing a theory of insect transmission in 1881. Carlos Juan Finlay proposed in 1881 that an infectious agent spread by the mosquito now known as Aedes aegypti was the source of yellow fever. Other means of transmission had been proposed in the meanwhile. He developed and upheld the notion in the years that followed, but he was unable to prove it (later proved by reed). Giuseppe Sanarelli, an Italian bacteriologist, reported in 1896 that he had isolated a microbe he named Bacillus iceteroids from patients suffering from yellow fever.

➢ The chairman in charge:

In 1900, Reed was chosen to lead the Yellow Fever Commission in Havana, Cuba, where yellow fever was devastating both soldiers and civilians. His team included James Carroll, Jesse William Lazear, and Aristides Agramonte. Reed and his team first examined the bacterial theory proposed by Italian physician Giuseppe Sanarelli, who claimed that *Bacillus icteroides* caused yellow fever. Through laboratory investigation, Reed proved that Sanarelli's organism had no connection with yellow fever and was actually related to hog cholera. The report of the committee was not published until 1904, revealed new facts regarding this disease. On the completion of the committee's work in 1899, he returned to his duties in Washington. Almost immediately he became involved in the problem of yellow fever. The result was a brilliant investigation in epidemiology. This allowed the commission to focus fully on Finlay's mosquito theory. Building upon the earlier theory of Cuban physician Carlos Juan Finlay, Reed tested whether mosquitoes spread yellow fever. Through carefully controlled human experiments, his team demonstrated that the female *Aedes aegypti* mosquito was the true carrier. Volunteers exposed to infected mosquitoes developed yellow fever, while those exposed to contaminated clothes and bedding did not. This proved mosquitoes—not direct contact or dirty objects—were responsible. Using mosquitoes supplied by Finlay, Reed designed controlled human experiments to test mosquito transmission. Since no laboratory test existed for yellow fever, human volunteers were necessary. Some volunteers, including commission member James Carroll, allowed infected mosquitoes to bite them. Carroll developed severe yellow fever but survived. Jesse William Lazear was also bitten and tragically died from the disease. In November 1900, Reed established Camp Lazear

near Havana for controlled experiments. Volunteers were divided into groups—some were bitten by infected mosquitoes, while others were exposed to soiled clothing and bedding from yellow fever patients. Those bitten by mosquitoes developed yellow fever, while those exposed to contaminated objects did not. This proved that yellow fever spread only through the bite of infected female *Aedes aegypti* mosquitoes and not through direct contact, poor sanitation, or fomites.

- **Elimination of Yellow Fever in Havana:**

After Walter Reed and his Yellow Fever Commission scientifically proved that yellow fever was transmitted only by the bite of infected female *Aedes aegypti* mosquitoes, the focus shifted from treating patients to controlling the mosquito population. This discovery completely changed public health strategy in Cuba. The responsibility of applying Reed's findings was given to Major William C. Gorgas, the chief sanitation officer of Havana under the U.S. military government. Before this, people believed yellow fever spread through dirty clothes, bedding, bad air, or poor sanitation alone. Because of this misunderstanding, previous control measures had failed for many decades. Gorgas began a large-scale mosquito eradication campaign across Havana. First, all yellow fever patients were placed inside screened rooms so that mosquitoes could not bite them and carry the infection to others. This step was very important because mosquitoes became infected only when they fed on patients during the first few days of illness. Next, every building in Havana was inspected and fumigated to kill adult mosquitoes. Health workers searched for standing water in houses, streets, courtyards, barrels, wells, flower pots, roof gutters, and drains because these were common breeding places for *Aedes aegypti*. Water containers were emptied, covered, or

screened. Pools of stagnant water were drained, and oil was spread on the surface of water bodies to kill mosquito larvae by preventing them from breathing. Strict quarantine and sanitation rules were enforced throughout the city. Public cooperation was also encouraged so that people would remove breeding sites from their homes. This was one of the earliest examples of organized urban vector control in medical history. The results were extraordinary. Havana had suffered yearly outbreaks of yellow fever for more than 140 years, causing thousands of deaths among civilians, soldiers, and travellers. However, after the mosquito control campaign based on Reed's discoveries, the number of cases rapidly declined. Within just 90 days, yellow fever disappeared from Havana. This success became a historic victory in public health. It proved that epidemic diseases could be controlled by understanding their mode of transmission. Gorgas later used the same mosquito-control methods during the construction of the Panama Canal construction, where controlling yellow fever and malaria was essential for completing the project. Reed's scientific discovery and Gorgas's practical implementation together saved countless lives and transformed tropical medicine forever.

➢ Additional Discoveries About Yellow Fever:

After proving that yellow fever was transmitted by the bite of the female *Aedes aegypti* mosquito, Walter Reed and his team made several other discoveries that completely changed the scientific understanding of the disease. One of the most important findings was that a mosquito could become infected only if it bit a yellow fever patient during the first three days of illness. After this early stage, the patient's blood no longer carried enough infectious material to spread the disease through mosquito bites. This discovery showed that early isolation of

patients was essential in preventing outbreaks. Reed also discovered that a mosquito did not become infectious immediately after biting a patient. The mosquito required an incubation period of about 10 to 14 days before it could transmit yellow fever to another person. This explained why outbreaks often followed a delayed pattern and why mosquito control had to be continuous rather than temporary. Once infected, the mosquito could remain dangerous for several weeks, especially during warm weather, meaning even a single mosquito could infect many people if left uncontrolled. At that time, many people believed yellow fever spread through dirty clothes, bedding, touching infected patients, or through foul air and poor sanitation. Reed disproved this belief through carefully controlled experiments. Healthy volunteers were made to stay in rooms filled with contaminated clothing and blankets used by yellow fever patients, but they did not develop the disease. However, volunteers bitten by infected mosquitoes became seriously ill. This provided clear proof that mosquitoes, not fomites or direct contact, were responsible for transmission. Reed also demonstrated that blood taken from a yellow fever patient during the early stage of illness could transmit the disease if injected into a healthy person. Even more importantly, he found that the blood remained infectious after passing through a Pasteur filter, which removed bacteria. This showed that yellow fever was caused not by bacteria but by something much smaller—a virus. This became one of the earliest pieces of evidence of a human viral disease. He also observed that people who recovered from yellow fever usually did not become infected again, proving that the disease produced lasting immunity and helping future vaccine research.

➢ Global Medical Impact and Final Legacy:

The discoveries of Walter Reed had one of the greatest impacts in the history of medicine and public health. His work did not simply solve a scientific mystery; it saved countless lives across the world. Using Reed's findings, Major William C. Gorgas launched a massive mosquito-control campaign in Havana, Cuba. Yellow fever patients were isolated behind mosquito screens, standing water was drained, water containers were covered, houses were fumigated, and mosquito larvae were destroyed using oil. Within just ninety days, Havana, where yellow fever had appeared every year for more than 140 years, was freed from the disease. This was considered one of the greatest victories in public health. His discoveries also made the construction of the Panama Canal possible. Before mosquito control, thousands of workers had died from yellow fever and malaria, making the project nearly impossible. By applying the same mosquito-eradication methods in Panama, Gorgas successfully controlled yellow fever and greatly reduced malaria deaths. Without Reed's work, one of the world's most important engineering achievements may never have been completed.

Walter Reed's research also transformed the field of epidemiology. He showed that disease transmission could be understood through careful observation, scientific experiments, and evidence rather than fear or superstition. His methods became a model for studying other infectious diseases such as malaria, dengue, and plague. His work also helped establish the modern field of tropical medicine, especially in countries like Cuba, Brazil, and Panama, where mosquito-borne diseases were major threats. Although Walter Reed died in 1902 from complications of appendicitis, his legacy continued to grow.

He was honoured by the naming of Walter Reed National Military Medical Center, the creation of the Walter Reed Medal for achievements in tropical medicine, and memorials including his resting place at Arlington National Cemetery. His grave bears the famous words: “He gave to man control of that dreadful scourge, yellow fever.”

As a man, Walter Reed was remembered for humility, honesty, discipline, and courage. He never sought fame for himself and always gave credit to colleagues such as Carlos Finlay, Jesse Lazear, and James Carroll. He accepted great personal risk in dangerous experiments and remained committed to truth and public service. He is remembered not only as the scientist who solved yellow fever, but as one of the greatest medical investigators in history whose work changed global medicine forever.

Léon Charles Albert Calmette

(12 July 1863 – 29 October 1933)

"My only merit is to have avoided spreading myself too thinly over too many subjects and to have studied with perseverance those that attracted me... I think it is thanks to this continuity of thought and effort that I have been able to make myself useful. I hope that my children and grandchildren will be inspired by the same rule of conduct."

➢ The Birth & Early life of Léon Charles Albert Calmette:

Albert Calmette was a French bacteriologist who studied under Louis Pasteur and co-developed the Bacillus Calmette-Guérin (BCG) tuberculosis vaccine with Camille Guérin. He was born in Nice, France, on July 12, 1863, and passed away in

Paris on October 29, 1933. He also discussed Calmette's response, a tuberculosis diagnostic test. Calmette was raised by his stepmother, Marie Quiney, after his father, Guillaume Calmette, remarried after his mother, Adèle Reine Charpentière, passed away when he was just two years old. The family relocated to Clermont-Ferrand when Albert was 10 years old, and then to Saint-Brieuc in Brittany three years later. Calmette earned his baccalauréat at Saint Charles College in Brittany. Calmette enrolled in the Naval Medical College in Brest in 1881.

Two years later, as part of his training, he was transferred to the Far East, where the work of tropical illness pioneer Sir Patrick Manson had a big impact on him. Albert Calmette had two brothers: Émile Calmette (1851-1934), who served as the Armed Forces' medical inspector general, and Gaston Calmette (1858-1914), who directed Le Figaro from 1903 to 1914 before being killed in 1914 by Henriette Caillaux, the wife of Joseph Caillaux, the Minister of Finance. After overcoming early setbacks, Calmette went on to study medicine and finally joined the French Colonial Medical Service. When he enrolled in a microbiology course at the Pasteur Institute and started concentrating on vaccinations, his career took a significant turn. In 1881, he joined the School of Naval Physicians at Brest to pursue medical training. In 1883, he entered the Naval Medical Corps and was posted to Hong Kong. There, he worked with Patrick Manson, who was studying mosquito transmission of filarial worms causing elephantiasis. Calmette completed his medical thesis on filariasis. Later, he served in Saint-Pierre and Miquelon, West Africa, Gabon, and the French Congo, where he researched malaria, sleeping sickness, and pellagra.

➢ Academic Journey:

With this newfound understanding, Calmette went back to France in 1885 and worked on filariasis while completing the qualifications for an M.D. by 1886. Calmette researched blackwater fever and sleeping sickness in Gabon and the French Congo between 1886 and 1888. He married Émilie de la Salle upon his return to France, and the two of them had two sons. He was then assigned to the French islands of Saint Pierre and Miquelon off the coast of Newfoundland. There, he investigated the red-spotted state of salted fish, determining that it was caused by infection and showing that adding sodium sulfate to the salt might stop it. In order to pursue a career in tropical illness research, Calmette enlisted in the French Colonial Medical Service in 1890. Calmette's career took a significant turn in 1890 when he enrolled in a microbiology course taught by Pierre-Paul-Émile Roux at the Pasteur Institute in Paris. In addition to capturing his attention and curiosity, the course helped him establish himself as an exceptional student with the ability to think clearly. There he met Louis Pasteur (1822–1895) and of course Emile Roux (1853–1933), who was his professor in a course on bacteriology. In 1891, after becoming an associate, Pasteur assigned him the task of establishing and running a branch of the Pasteur Institute in Saigon (French Indochina). There, he devoted himself to the emerging science of toxicology, which had significant links to immunology. He researched curare, plant poisons, and the venom of snakes and bees. Along with conducting research on cholera and the fermentation of rice and opium, he also oversaw the manufacture of the current rabies and smallpox vaccinations.

➢ Pioneering Pasteur Institute at Saigon, Indochina:

When the undersecretary of state for the French colonies sought the help of **Louis Pasteur** to study the problems of smallpox, rabies, dysentery, and cholera in Indochina, Calmette's name was immediately suggested for this position. Albert Calmette was assigned by Louis Pasteur in 1890 to establish the first Institut Pasteur outside of mainland France in Saigon after completing Émile Roux's course at the Institut Pasteur due to his background as a sailor. On December 10, 1990 he sailed to the Indochina. Before long, rabies cases were coming from Hong Kong, Shanghai, Cochinchina, and the Malay States. Smallpox was widespread in Indochina at the time. (Many Institute Pasteur experts would later establish institutes all over the world, including in Turkey in 1893, China in 1895, India in 1896, Senegal in 1896, Brazil in 1901, Algeria in 1902, and Congo in 1906. This network, known as the Pasteur Network, now includes about thirty members). Albert Calmette coordinated the development of climate-adapted vaccinations. Under his supervision, the smallpox vaccines were mass-produced and conducted groundbreaking research on rabies and cobra venom. Soon after, 500,000 people received vaccinations against the fatal illness. Calmette was able to prove in early research that choi-ghai, a sickness that affects dogs, is actually a sign of rabies. He then successfully administered the vaccine to 47 out of 48 animal-bite victims using the spinal cords of rabid rabbits as a reservoir for the virus.

Around the same time, he became interested in the high death rate of cobra bite victims and started researching these reptiles' venoms. At the period, cobras were taking refuge in homes during floods, killing 21,000 people in India and many more in Cochinchina. He meticulously collected and categorized them, comparing them to bacterial toxins. His

research showed that a gold chloride solution might counteract the harmful effects of cobra venom on the brain. Additionally, he found that the venom could be attenuated (made less toxic) by calcium hypochlorite solution. This discovery laid the groundwork for the production of antivenom serum in animals by injecting increasing doses of the venom into the animals and then extracting the serum, which was now rich in protective antitoxin, from the animals after a few weeks. By this way he created a serotherapy remedy for stings from poisonous snakes. Later, Brazilian doctor Vital Brazil began working in this area at the Instituto Butantan in São Paulo, where he created a number of further antivenoms against spiders, snakes, and scorpions

During his time in Saigon, Albert Calmette improved the methods of alcohol and opium fermentation and also carried out important studies on Asiatic cholera. Using fresh cultures taken from patients who had died from the disease, he carefully examined the toxic effects caused by the cholera organisms. He also attempted immunization methods and suggested treatments such as peritoneal dialysis with saline solution. In 1893, after only two years in Saigon, he was called back to France, having completed an extraordinary amount of scientific work in a short time. However, the harsh conditions and repeated attacks of dysentery had severely affected his health. After returning, he joined the Pasteur Institute and continued his research on antivenom therapy. In 1894, he came back to France again and develop the first antivenoms for snake bites using immune sera from vaccinated horses (*Calmette's serum*). In recognition of his achievements in Saigon, he received the Cross of the Legion of Honor in 1893. In 1894, using his experience with snake venom research, he helped improve the anti-plague serum developed by Alexandre Yersin, which played an important role in controlling the plague outbreak in the Far

East. On his return to France, Émile Roux and Louis Pasteur tasked him with opening an Institut Pasteur in Lille. This was inaugurated in 1899 and he was to stay there for 25 years.

➢ Director of the Pasteur Institute at Lille:

Following his return to France, he established the Pasteur Institute at Lille and served as its director from 1896 until 1919. With a fatality rate of almost 300 per 100,000, TB was Lille's biggest public health concern at the time. Calmette treated the issue methodically, much as he had approached other issues he had faced in the Far East. In 1901, he started the first antituberculosis dispensary in Lille. In 1905, he established a TB sanatorium in Montigny-en-Ostrevant. He developed the conjunctival tuberculin test in 1907 to determine whether a patient had a tuberculous infection; Charles Mantoux's more practical intradermal tuberculin test quickly took its place. The creation of a vaccination against tuberculosis, which at the time was a leading cause of mortality, was Calmette's primary scientific contribution that would make him famous throughout the world and indelibly mark his name in medical history. Mycobacterium tuberculosis, the tubercle bacillus, was identified as its pathogenic agent by German microbiologist Robert Koch in 1882, and Louis Pasteur also had an interest in it. Camille Guérin, a veterinarian and immunologist at the Institute Pasteur de Lille, discovered in 1906 that live tubercle bacilli in the blood were linked to immunity against tuberculosis.

➢ The Birth of BCG:

The development of the BCG vaccine was the most important scientific achievement of Albert Calmette and became one of the greatest milestones in the history of

preventive medicine. At the beginning of the 20th century, tuberculosis was one of the deadliest infectious diseases in the world, especially among poor and working-class populations. It caused thousands of deaths every year, and there was no effective preventive vaccine available. Calmette was deeply disturbed by the suffering caused by this disease and decided to devote himself to finding a solution. Calmette was influenced by Marfan's observation, often called Marfan's law, which suggested that severe pulmonary tuberculosis was uncommon in people who had previously suffered from tuberculosis of the lymph nodes. This indicated that a mild earlier infection could provide some immunity against a more serious later infection. Inspired by this idea and by Louis Pasteur's success with the rabies vaccine, Calmette believed that tuberculosis could also be prevented by vaccination using a weakened form of the disease-causing organism. In 1906, Calmette began working closely with Camille Guérin, a skilled veterinarian and immunologist at the Pasteur Institute. Their aim was to produce a strain of tubercle bacillus that was weak enough not to cause disease but still strong enough to stimulate the immune system and provide protection.

For this purpose, they used a highly virulent strain of *Mycobacterium bovis* obtained from Edmond Nocard. This strain had originally been isolated from the udder of a cow suffering from tuberculosis. To weaken the bacteria, Calmette and Guérin repeatedly cultured the bacillus in a special medium containing potato slices, glycerin, and ox bile. They observed that growing the bacteria in bile gradually reduced its ability to cause disease. This method of attenuation was partly inspired by the ideas of Norwegian researcher Kristian Feyer Andvord. Over a period of thirteen years, from 1908 to 1921, they transferred the bacteria into fresh culture media again and again, performing more than

200 successive subcultures. With each transfer, the bacillus became less virulent.

Their work was interrupted by World War I, which delayed animal experiments and scientific progress. However, they continued the subculturing process throughout the difficult years. By 1919, they tested the weakened strain in animals and confirmed that it no longer caused tuberculosis, even though it still produced an immune response. This proved that the organism was safe enough to be used as a vaccine. This attenuated strain was named **Bacille Calmette-Guérin**, commonly known as the **BCG vaccine**, in honor of its two discoverers. In 1921, the vaccine was used for the first time on a human infant at the Hôpital de la Charité in Paris. The child was born to a mother suffering from tuberculosis and was at very high risk of infection. The vaccination was successful, and the child remained healthy. This marked the beginning of one of the most important vaccination programs in medical history.

Initially, BCG was given orally to newborns, especially infants born to tuberculous mothers. Later, after improvements by researchers such as Nègre and Bretey, the vaccine began to be administered by injection, which provided better and more reliable protection. Although local skin reactions sometimes occurred, they were minor compared to the strong protection offered by the vaccine. Between 1921 and 1928, thousands of infants received the BCG vaccine without serious side effects. Studies by Calmette and Guérin showed a major reduction in tuberculosis deaths among vaccinated children. The vaccine gained international acceptance and became a major weapon against tuberculosis across the world.

➢ The Lübeck Disaster (1930):

In 1930, a tragic event known as the Lübeck disaster created serious controversy around the BCG vaccine developed by Albert Calmette and Camille Guérin. In Lübeck, Germany, a vaccination program was started for newborn infants using the BCG vaccine to protect them from tuberculosis. However, out of 250 vaccinated babies, 73 died and many others developed tuberculosis, although most later recovered. This caused widespread fear and criticism, and many people began to question the safety of the BCG vaccine. The incident severely damaged public confidence in vaccination programs. A detailed investigation was carried out and it was later proven that the BCG vaccine itself was not responsible for the tragedy. The real cause was contamination of the vaccine in the Lübeck laboratory with a virulent strain of tubercle bacillus due to serious negligence by the local doctors and laboratory staff. The Pasteur Institute had supplied a safe and properly prepared vaccine, and the Lübeck doctors were later punished and sentenced to prison. At the International Union Against Tuberculosis meeting in Oslo, Calmette strongly defended the safety and scientific value of BCG and received support from the medical community. Although the vaccine was officially cleared of blame and mass vaccination resumed after safer production methods were introduced, the disaster deeply affected Calmette personally. It weakened his optimism and remained one of the most painful events of his life shortly before his death in 1933.

➢ A Tragedy Hit Giant:

Albert Calmette earned worldwide recognition through sheer dedication, discipline, and relentless hard work during an era dominated by giants like Louis Pasteur, Robert Koch, and Émile

Roux. Though surrounded by such legendary scientists, Calmette created his own place in medical history through his persistence and practical approach to public health. His greatest achievement was the development of the BCG (Bacille Calmette-Guérin) vaccine against tuberculosis, a disease that was devastating millions, especially among the industrial working class. Shocked by the spread of tuberculosis in northern France, he first organized anti-tuberculosis dispensaries to improve hygiene and reduce transmission. Then, with his close collaborator Camille Guérin, he focused on creating a safe preventive vaccine. Inspired by Pasteur's vaccination principles and building on Koch's discovery of Mycobacterium tuberculosis, they worked from 1908 to 1921 by repeatedly subculturing bovine tubercle bacilli (Mycobacterium bovis) in a bile-potato medium.

Over years of careful transfer, the bacteria gradually lost their virulence while retaining their immunizing power. In 1921, BCG was successfully administered to newborn infants at Hôpital de la Charité in Paris, proving to be safe and effective. From 1921 to 1928, thousands of infants were vaccinated orally with remarkable success, significantly reducing deaths from tuberculosis. However, the 1930 Lübeck disaster in Germany deeply shook Calmette, when contaminated vaccine batches caused the deaths of many vaccinated infants. Investigations proved that the tragedy resulted from laboratory contamination in Lübeck, not from the BCG vaccine itself, and the Pasteur Institute was fully cleared. Although mass vaccination resumed after safer production methods were introduced in 1932, the incident deeply affected Calmette's spirit. Despite this, BCG spread worldwide and became one of the most important vaccines in medical history.

Beyond tuberculosis, Calmette also contributed to plague serum development with Alexandre Yersin, antivenom therapy, cholera studies, hookworm control, sewage purification, and tropical medicine. He founded Pasteur Institutes in several regions and strengthened preventive medicine globally. Honors followed throughout his life: he was elected to the French Academy of Sciences, Academy of Medicine, Academy of Overseas Sciences, and was awarded the Grand Cross of the Legion of Honour. A born administrator, cheerful optimist, and brilliant scientist, he was respected for adapting laboratory science to real-world health crises. He died in Paris in 1933 and was buried at the Pasteur Institute, where he had devoted much of his life. His legacy remains immortal through BCG, which continues protecting millions worldwide, making him one of the greatest pioneers in preventive medicine and public health.

Émile Roux paid tribute to Albert Calmette in these terms: "**It was through his extraordinarily hard work, during his two and a half years in Indochina that Calmette was to show the huge service that microbiology could provide in the country. Calmette's foundation served as a model for the institutes that have since been set up in all overseas territories, under the influence of our country.**"

Barbara MaClintock

(16 June 1902 – 2 September 1992)

"If you know you are on the right track, if you have this inner knowledge, then nobody can turn you off… no matter what they say."

➢ The Birth & Early life of Barbara MaClintock:

On June 16, 1902, Barbara McClintock was born in Hartford, Connecticut, in the United States, just two years after the rediscovery of Gregor Mendel's work on inheritance. Eleanor McClintock was her birth name, but her parents quickly began referring to her as Barbara because they felt that Eleanor was too delicate and feminine a name for their daughter and that it was a wonderful fit for her direct, no-nonsense personality. Thomas Henry McClintock, her father, was a family physician whose parents immigrated to the United States

from Britain. Sara Handy, her mother, was a housewife, poet, and artist from a wealthy Boston family. Out of the couple's four children, Barbara was the third. Barbara and her mother did not get along well from the beginning. Barbara lived with her aunt and uncle in Massachusetts much of the time between the ages of three and five in order to lessen the strain on her mother. Barbara went back to Hartford to start school with her parents. The entire family relocated to Brooklyn, New York, in 1908. Barbara had a strong bond with her father, but her relationship with her mother was unstable. Barbara's parents did everything in their power to help her become the person she wanted to be, including letting her skip school if she had other commitments.

Being the person she wanted to be meant being by herself from a young age. Barbara would rather be by herself than with other people. Barbara's professors at Brooklyn's Erasmus Hall High School saw that she was incredibly intelligent and possibly headed for a career as a college professor. This made her mother very uneasy because she thought female college instructors were strange beings. Because she thought Barbara would become an oddity that no one would ever want to marry, she forbade Barbara from attending college. McClintock, whose father was a doctor, enjoyed science as a youngster and showed early signs of the independence of thought and behavior that she would display for the remainder of her life. In 1919, she graduated from high school and entered at Cornell University to major in biology. She earned a B.S. in 1923, a master's degree two years later, and a Ph.D. in 1927 after focusing on cytology, genetics, and zoology. She started the job that would take up her entire career during graduate school: the chromosomal analysis of corn (maize).

➢ Reckless to Attentive:

After her father eventually overcame her mother's objections in September 1919, 17-year-old Barbara hurried out to enroll at Cornell University in Ithaca, New York. For Barbara, leaving home was a freeing experience. She became happier, more at ease, and relished her undergraduate years. As she interacted with other students, joined a jazz band, and won the presidency of the women's freshmen class, her strong need to be alone herself also subsided. In 1921, Barbara McClintock enrolled in her first genetics course. Her teacher, Claude Hutchison, quickly saw her aptitude in this area and suggested that she enroll in the graduate-level course the following year. She was thrilled to do this and continued to be captivated by plant genetics. She chose to pursue her interest at graduate school after earning a B.S. in agriculture in 1923. McClintock received an M.S. in botany from Cornell in 1925 and a Ph.D. in the same field in 1927. She studied plant genetics for her M.S. and Ph.D. degrees. For the most of her life, this would be the subject of her research. McClintock was hired at Cornell as an instructor in the Botany Department following the completion of her Ph.D. McClintock stayed at Cornell as an instructor after earning her Ph.D. in botany in 1927, and she soon became known as an unmatched genius.

She wrote six articles—four of which were single-authored—in just two years after earning her degree, the majority of which were in prestigious journals. Cornell developed became a center for maize genetics between 1928 and 1931 because to a gifted team of young researchers funded by R.A. Emerson. McClintock produced a number of groundbreaking contributions and was a key player in this golden age of maize genetics. She created a method for seeing maize chromosomes and demonstrated the 10 chromosomes' shape for the first time. The genetic

phenomena of crossing-over—the process by which X and Y chromosomes exchange genetic information during the development of egg and sperm cells—was confirmed in a seminal publication by McClintock and coauthor Harriet Creighton in 1931.

According to Lee B. Kass, McClintock's most recent biographer, she solidified her image as "the cytology expert who could see what others could not see" during this time. Despite her renown and exceptional skills, McClintock had trouble finding long-term work that matched her ability. She continued her studies at Cornell, Caltech, and the University of Missouri in the early 1930s while surviving on fellowships due to the Great Depression's limitations on opportunities.

- **Falling in love with cytogenetics:**

Nearly the course of her career, Barbara McClintock researched the cytogenetics of maize, making results that were so revolutionary at the time that they were mostly disregarded by other scientists for nearly ten years. However, she persisted because she had faith in both the evidence and herself. Barbara McClintock came very close to not attending college. She was a gifted student, but her mother vetoed her intention to attend Cornell because she thought a college degree would hurt her prospects of getting married. Luckily, McClintock's father was able to step in after returning from the Army Medical Corps in France. McClintock enrolled in the Cornell College of Agriculture in 1919 at the age of seventeen. She succeeded in the classroom, played the banjo in a jazz band, and joined the student government while attending college. It was there that she enrolled in the genetics course that would forever alter her life. In the 1920s, Cornell provided just one undergraduate course in genetics, which was still a relatively young field.

However, McClintock embraced it right once and developed a lifetime passion for cytogenetics, the study of chromosomes and their genetic expression.

She once said “No two plants are exactly alike. They’re all different, and as a consequence, you have to know that difference. I start with the seedling and I don’t want to leave it. I don’t feel I really know the story if I don’t watch the plant all the way along. So I know every plant in the field. I know them intimately. And I find it a great pleasure to know them.” She earned her bachelor’s, master’s and doctoral degrees at Cornell and had great success in her research on the cytogenetics of maize. Even so, it wasn’t easy to find a permanent position in the midst of the Depression. Finally, McClintock was hired as an assistant professor at the University of Missouri in 1936. McClintock loved working in the lab. “I was just so interested in what I was doing I could hardly wait to get up in the morning and get at it”.

"*A Correlation of Cytological and Genetical Crossing-over in Zea mays,*" a paper she and her colleague Harriet Creighton published in 1931, proved that chromosomes were the foundation of genetics. McClintock was chosen vice president of the Genetics Society of America in 1939 and president of the Genetics Society in 1944 based on her research and publications from the 1930s. In 1933, she was awarded a Guggenheim Fellowship to study in Germany, but she departed early due to the rise of Nazism. Her alma mater, Cornell, refused to hire a female lecturer when she returned. Before she was employed by the University of Missouri (1936–41), the Rockefeller Foundation supported her study at Cornell (1934–36).

➢ Finding Home at Carnegie:

For her, teaching was a distraction. She left her university job. In December 1941, she was offered a one-year research position at the Carnegie Institution of Washington's Department of Genetics at Cold Spring Harbor on Long Island, New York. This job turned into a full-time staff position the following year. It was a perfect match: a scientist who craved independence found an institution dedicated to supporting unfettered research. McClintock started researching the mosaic color patterns of maize at the genetic level early in her time at Cold Spring Harbor. She had observed that the kernel patterns were too erratic and altered too often over a number of generations to be regarded as mutations. What caused this? The response defied accepted genetic theories. She learned that genetic information is not static in the 1940s by studying and experimenting with differences in maize kernel colors. She identified two genes that she named "controlling elements" by tracking changes in corn's color and examining the plant's big chromosomes under a microscope. The genes that actually caused pigmentation were regulated by these genes. McClintock discovered that the behaviour of nearby genes was impacted by the regulatory elements' ability to relocate along the chromosome. She proposed that new changes in pigmentation or other traits were caused by these transposable elements. By examining successive generations of maize plants, McClintock discovered that certain genes could "transpose" or move around within chromosomes, turning on or off physical traits in accordance with specific "controlling elements," rather than being fixed in place and providing instructions from generation to generation. This discovery was revolutionary. **Transposon**, class of genetic elements that can “jump” to different locations within a genome. Although these elements are frequently called

“jumping genes,” they are always maintained in an integrated site in the genome. In addition, most transposons eventually become inactive and no longer move.

- **Barbara never gives up:**

McClintock postponed publicizing her views on genetic transposition and regulating elements until other researchers had verified her findings since she was aware that her work deviated from conventional thought. Finally, in the summer of 1951, she presented her research at Cold Spring Harbor Laboratory's annual symposium. It didn't work out. The audience was either confused by her beliefs or opposed to them, as she subsequently remembered. “They thought I was crazy, absolutely mad.” Many scientists dismissed McClintock's discovery as a peculiarity exclusive to maize or found it difficult to understand its consequences. The idea of a dynamic genome might not have been accepted by the scientific community, and McClintock's focus on gene control was innovative. In the face of such resistance to her theories, McClintock stopped publishing and lecturing – she stopped trying to convince others – but she never stopped pursuing her theories.

“I just knew I was right,” she said later.

“Anybody who had had that evidence thrown at them with such abandon couldn’t help but come to the conclusions I did about it.” The National Science Foundation and the Rockefeller Foundation provided McClintock with funding in 1957 so that he could research several maize races throughout South and Central America. She went widely in the early 1960s, gathered samples of maize that showed intriguing evolutionary traits, and taught young graduate students and junior scientists about maize genetics. The Chromosomal Constitution of Races of Maize, which McClintock and her associates eventually

published in 1981, was the result of two decades of data collection on variations in South American maize. Not until the late 1960s and '70s, after biologists had determined that the genetic material was DNA, did members of the scientific community begin to verify her early findings, confirming her results and granting her the long-overdue recognition.

- **Victory At the End:**

Barbara McClintock was not just one of the greatest scientists of the 20th century—she was a mind far ahead of her time, a visionary whose discoveries were so advanced that the world needed decades to catch up with her brilliance. For years, the scientific world ignored her. But science eventually caught up with her vision.

In the 1960s and 1970s, researchers discovered transposable elements in bacteria, yeast, fruit flies, and even mammals. Suddenly, the world realized that Barbara McClintock had been right all along. Her discovery became fundamental to genetics, medicine, cancer research, immunology, evolutionary biology, and genetic engineering. Today, scientists know that nearly half of the human genome contains transposable elements. Recognition finally arrived like a flood. In 1944, she became only the third woman elected to the National Academy of Sciences. She became the first woman president of the Genetics Society of America in 1945. In 1971, Richard Nixon awarded her the National Medal of Science. She later received the MacArthur Foundation "Genius Grant," the Lasker Award, the Wolf Prize, and many other honors.

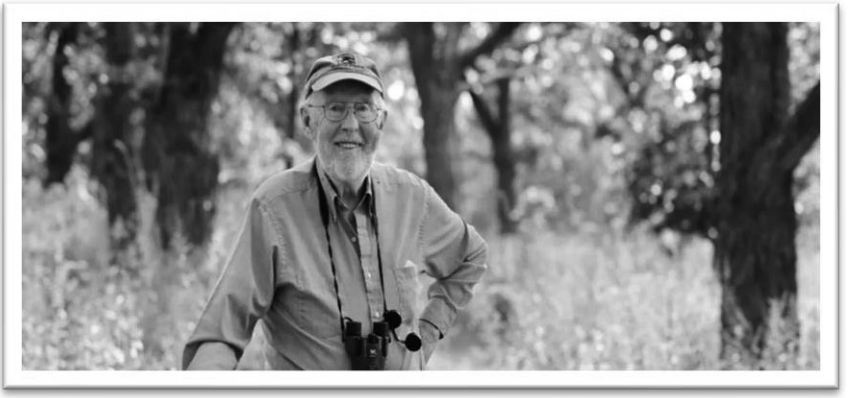
- **Then came the Greatest recognition of all:**

In 1983, at the age of 81, Barbara McClintock received the Nobel Prize in Physiology or Medicine for her discovery of

mobile genetic elements. She became the first woman to receive this prize alone in that category. More than thirty years after her original discovery, the world finally honoured the truth she had quietly defended. She humbly said, "It might seem unfair to reward a person for having so much pleasure over the years." McClintock remained at Cold Spring Harbor until her retirement in 1967 and continued there as Scientist Emerita until her death. She valued freedom above fame. She believed true science needed independence, not approval. She once reflected, "The sense of freedom to be able to pursue an extraordinary type of investigation was the most important aspect."

She never married and had no children, choosing instead a life fully devoted to discovery. She loved privacy, music, deep thinking, and the silent companionship of maize plants. She once said, "No two plants are exactly alike... I know them intimately." Her connection with nature was not mechanical—it was almost spiritual. On September 2, 1992, Barbara McClintock died peacefully at the age of 90 in Huntington, New York. Her mind remained sharp until the end. She was buried in Huntington Rural Cemetery. Her legacy is not only in Nobel medals or scientific theories, but in courage—the courage to trust your own mind when the world doubts you. She taught generations of scientists a lesson far beyond genetics: if truth lives within your work, time itself will become your witness. ***As she said, "If you know you are on the right track, if you have this inner knowledge, then nobody can turn you off… no matter what they say."***

Pic. Reporters gathering around Barbara MaClintock after Solo Nobel Prize Announcement



Thomas Dale Brock

(10 September 1926 – 04 April 2021)

"I got out of the car and, by chance, a ranger was giving a talk near a thermal pool. I saw all this colour, and he said it was blue-green algae. I got interested right away"

➢ The Birth & Early life of Thomas dale Brock:

On September 10, 1926, Thomas Dale Brock was born in Cleveland. When Tom was fifteen, his father, Thomas, an engineer who oversaw a hospital's boiler department, passed away, leaving him and his mother, Helen (Ringwald) Brock, a nurse, impoverished. Following this, he relocated to Chillicothe, Ohio, his mother's hometown, from Cleveland. Tom, the only kid, worked in shops to support her. He and a friend set up a small laboratory in the loft of a barn behind his house when he was a youngster because he was interested in chemistry. There, the two buddies experimented with poisonous gas and

explosives. He trained in cutting-edge radar and electronics technologies while serving in the U.S. Navy during World War II after graduating from high school.

He finished his service as a shore patrol on Kodiak Island, Alaska, after the war. Following his time in the Navy's electronics training program, Dr. Brock graduated from Ohio State University with a bachelor's degree in botany, a master's degree in mycology, the study of mushrooms, and a doctorate. Before being appointed as an assistant professor of biology at Western Reserve University (now Case Western Reserve University) in Cleveland, Dr. Brock worked for five years as a research microbiologist at the Upjohn Company due to a shortage of academic positions. He joined the university's medical school as a postdoctoral fellow after two years. He began teaching medical microbiology at Indiana University, Bloomington's bacteriology department in 1960.

- **The start of a Colourful era:**

In 1952, he and his first wife, Mary Louise Louden, relocated to Kalamazoo, Michigan, where he started his scientific career as a research microbiologist with The Upjohn Company. In 1960 he moved to Indiana University as an Assistant Professor of Bacteriology. He remained there until 1971. Brock was given the chance to study marine microbiology at the University of Washington's Friday Harbor Laboratories in 1963. He researched Leucothrix mucor there. His illustrations of the twisted arrangements known as "knots" created by the developing organisms were published in the New York Times and Science as a cover story. His interest in the microbial ecology of sulfur springs was also piqued by this study, and he spent the following ten years conducting research at Yellowstone National Park.

➢ A Life Channing trip to Yellowstone:

He spent the remainder of his academic career in the Department of Bacteriology at the University of Wisconsin-Madison in 1971 after serving on the faculties of Western Reserve University and Indiana University. His sixty-year list of scientific publications includes more than 20 books and more than 300 research papers in a variety of topics, including mycology, bacteriology, microbial ecology, limnology, ecological restoration, and the seminal textbook Biology of Microorganisms. He received numerous honors, such as an honorary doctorate from UW-Madison, Ohio State's Sullivant Medal for excellence in teaching and research, and the Golden Goose Award, which acknowledged the potential of fundamental scientific research motivated by pure curiosity to benefit human society in unexpected ways.

During the 1960s, while working as a professor at Indiana University, he made a journey to Yellowstone National Park that would permanently alter microbiology. At that time, most scientists believed that life could not survive in temperatures above about 160°F (around 70°C). Hot springs and boiling pools were considered too extreme for living organisms. Brock, however, noticed colorful streams flowing from Yellowstone's thermal springs and became fascinated by the possibility that microorganisms might be thriving there.

He returned with research funding, students, and an open mind. Instead of accepting the scientific assumptions of the day, he carefully collected samples from boiling pools, lowered microscope slides into hot springs, and patiently examined what grew on them. To his astonishment, life was everywhere. Microorganisms were not only surviving but actively growing and reproducing in near-boiling water. This discovery shattered

previous biological boundaries and gave birth to the field of extremophile research—the study of organisms that live under extreme conditions such as intense heat, cold, acidity, salinity, or pressure.

Brock's findings proved that life is far more adaptable than previously imagined. His work inspired scientists around the world to search for microbes in deep-sea hydrothermal vents, acidic lakes, deep underground mines, frozen glaciers, and even highly radioactive environments. Some of these organisms were later recognized as belonging to Archaea, a distinct branch of life that transformed our understanding of evolution itself. His research also strongly influenced astrobiology by expanding the possibility that life might exist on other planets with harsh conditions once thought impossible for living systems.

Beyond Yellowstone, Brock later joined the University of Wisconsin–Madison as the E. B. Fred Professor of Natural Sciences and continued groundbreaking work in microbial ecology, particularly studying nutrient cycling in Lake Mendota. He believed science should serve both discovery and responsibility. His famous textbook, Biology of Microorganisms, became a standard for generations of students worldwide. Brock did not merely discover new bacteria—he expanded the definition of life itself.

➢ Thermus aquaticus:

Among Thomas Brock's many scientific achievements, none became more famous than the discovery of Thermus aquaticus, the bacterium that transformed molecular biology. In 1966, while studying the hot springs of Yellowstone with his undergraduate student Hudson Freeze, Brock isolated a remarkable yellow-coloured microorganism from the boiling waters of Mushroom Spring. Unlike ordinary bacteria, which

die under extreme heat, this organism thrived at temperatures around 70°C (158°F) and could survive even higher conditions close to boiling point. This was revolutionary. Until then, the scientific world largely believed that bacteria could not live in such environments. Thermus aquaticus proved otherwise. Brock and Freeze published their findings in 1969, naming the bacterium after the hot water environment in which it lived. The discovery was not just another species added to a textbook—it opened an entirely new field of biology.

Scientists now realized that life could flourish in places once considered completely uninhabitable. The real importance of Thermus aquaticus emerged years later through one of its enzymes: Taq polymerase. Because this bacterium lived in extreme heat, its enzymes were specially designed to remain stable at high temperatures. One of these enzymes, responsible for copying DNA, could continue functioning during repeated heating and cooling cycles without being destroyed. This property would later become essential for one of the greatest inventions in modern biology—the Polymerase Chain Reaction (PCR). PCR requires repeated cycles of heating DNA to near-boiling temperatures so the strands separate, followed by cooling so enzymes can copy them. Before Taq polymerase, scientists had to add fresh enzymes after every cycle because ordinary enzymes were destroyed by heat. Taq polymerase solved this problem completely. It made PCR fast, efficient, inexpensive, and practical for global scientific use. Because of this, Thermus aquaticus became one of the most valuable microbes ever discovered. Its enzyme made possible DNA sequencing, forensic science, genetic engineering, disease diagnosis, paternity testing, evolutionary studies, and medical research. Even modern tests for COVID-19 rely on PCR principles rooted in Brock's discovery. What began as curiosity

about strange microbes in Yellowstone became a foundation of modern biotechnology. Few bacteria in history have changed human civilization as much as Thermus aquaticus.

➢ Meeting with Kary Mullis:

Although Thomas Brock discovered Thermus aquaticus, its greatest practical impact emerged years later through the work of Kary Mullis, the scientist who developed the Polymerase Chain Reaction (PCR). In the 1980s, Mullis was searching for a better method to amplify small amounts of DNA in the laboratory. He needed a way to repeatedly copy genetic material through cycles of extreme heating and cooling, but the major obstacle was the enzyme required for DNA replication. Normal enzymes were destroyed each time the temperature rose, making the process inefficient and expensive.

The answer was waiting in a culture collection because Brock had preserved his Yellowstone bacteria by depositing Thermus aquaticus strains in the American Type Culture Collection. Mullis and his colleague David Gelfand accessed this same bacterium and isolated its heat-stable enzyme, later known as Taq polymerase. This enzyme was exactly what PCR needed. Because it could survive repeated heating, scientists no longer had to replace the enzyme after every cycle. The process became rapid, reliable, and revolutionary.

Years later, Hudson Freeze recalled meeting Mullis at a scientific conference and telling him, “I’m the guy who found Thermus aquaticus with Tom Brock.” Mullis reportedly replied that he had used the exact same Yellowstone strain they had originally isolated. This moment perfectly connected curiosity-driven field research with one of the greatest laboratory breakthroughs in history.

PCR became a scientific supertool. It allowed billions of copies of DNA to be produced from even the tiniest sample. This transformed criminal investigations through forensic DNA evidence, helped determine paternity, enabled rapid diagnosis of infectious diseases, advanced cancer research, and opened the door to modern genomics and personalized medicine. During the COVID-19 pandemic, PCR became the gold standard for detecting viral infection worldwide, once again reminding the world of Brock's foundational contribution.

Mullis received the 1993 Nobel Prize in Chemistry for PCR, while Brock and Hudson Freeze later received the 2013 Golden Goose Award for the unexpected global impact of their Yellowstone discovery. Brock himself often emphasized that his work began simply as basic research—pure scientific curiosity, not commercial ambition. Yet that curiosity produced one of the most important medical technologies in modern history. It is one of the greatest examples of how fundamental science can change the world.

- **Brock the Extreme Mind:**

Thomas Brock was not only a scientist of extraordinary intellect—he was a man of remarkable discipline, passion, and independence. Colleagues often described him as "bigger than life," a person whose presence filled every room. Jo Handelsman, one of his longtime mentees, said he walked through life with powerful conviction, doing exactly what he believed was right. His mind was adventurous, but his principles were deeply grounded.

After joining the University of Wisconsin–Madison in 1971, Brock shifted part of his attention from Yellowstone's simple thermal systems to the far more complex ecology of Wisconsin lakes, especially Lake Mendota. He believed that since

Wisconsin taxpayers supported his work, he had a responsibility to study and improve Wisconsin's own natural environment. His research on lake ecology, nutrient cycling, and microbial communities led to the important book A Eutrophic Lake: Lake Mendota, Wisconsin and helped establish the North Temperate Lakes Long-Term Ecological Research Network.

Brock was also a prolific author, publishing hundreds of scientific papers and nearly two dozen books. His textbook Biology of Microorganisms remained a standard reference across generations. Alongside his wife Kathie, also a microbiologist, he founded Science Tech Publishers, helping publish scientific monographs and educational works. He also wrote on genealogy, history of science, and even produced a biography of Robert Koch.

Outside the laboratory, Brock was deeply connected to nature and the arts. He loved canoeing, hiking, camping, classical music, literature, opera, and even taught himself German. After retirement, perhaps his greatest personal achievement was ecological restoration. Together with Kathie, he transformed 140 acres of neglected land in Wisconsin's Driftless Area into the beautiful Pleasant Valley Conservancy, restoring oak savanna, prairie, and marshland ecosystems. It became both a scientific model and a living monument to conservation.

Thomas Brock passed away in April 2021 at the age of 94 due to complications from a fall. Yet his legacy remains alive everywhere—from Yellowstone hot springs to hospital diagnostic labs, from microbiology classrooms to DNA testing centres. He proved that the greatest discoveries often begin with simple curiosity. By asking whether life could exist where no one expected it, he helped humanity discover not only new microbes, but new possibilities for science itself.

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