

Pasteur–Koch: Distinctive Ways of Thinking about Infectious Diseases

Linguistic misunderstandings along with genuine scientific differences over virulence and immunity drove the two geniuses apart

Agnes Ullmann

Louis Pasteur and Robert Koch are considered the founders of medical bacteriology. Their paths crossed only a few times but, as often happens for such geniuses, those encounters evinced polemics and controversy. Was this due to their different backgrounds? Robert Koch was a physician, 20 years younger than Pasteur, a chemist and microbiologist. Neither man understood the other's language.

Yet their contributions to microbiology were so complementary that it is difficult to imagine one without the other. To better understand the Pasteur–Koch clash, it seems useful first to re-

view several of their major achievements before they crossed paths.

Pasteur Approach to Microbiology Was Both Theoretical and Practical

Pasteur, whose interests touched on many scientific areas, was a keen observer and especially adept at integrating relevant observations into his conceptual schemes. Born in 1822, Pasteur was admitted in 1843 to the scientific section of the *École Normale Supérieure* in Paris, where he was trained to become a professor in chemistry.

At the age of 24, studying the crystal structure of organic molecules, he discovered molecular asymmetry. Ten more years of crystallographic studies convinced Pasteur that one of the fundamental characteristics of living matter was its asymmetric nature at the molecular level.

In 1854, Pasteur was appointed professor of chemistry and dean of the Science Faculty in Lille. There he started to study alcoholic fermentation in response to a request for him to deal with problems that arose in a distillery in Lille. This proved the first of several occasions when he was asked to study specific problems from a practical as well as an economic point of view. Often, his insights led to successful practical solutions, while also providing new, more theoretical insights. In this case, his realization that organisms participate in fermentations led him later to formulate the germ theory of infectious disease.

When Pasteur later studied wine diseases, he showed that specific wine diseases are

Summary

- Louis Pasteur, a keen observer who was adept at integrating relevant observations into his conceptual schemes, studied specific problems from a practical and sometimes economic point of view.
- Robert Koch, a physician, developed a systematic approach for establishing the causal relationship between a particular microorganism and a specific disease.
- An overlapping interest in anthrax led to an intense rivalry between Pasteur and Koch, with Koch and his followers embracing a rigid belief in the specificity and permanence of microbial characteristics, while Pasteur recognized that pathogens attenuate, making them useful in vaccines.
- Despite a friendly encounter at a London meeting in 1881, Pasteur and Koch were soon in open conflict—in part, because of a mistranslated phrase.

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Pasteur

associated with particular microorganisms. Moreover, heating wine to 55°C is sufficient to keep its quality intact. This experience led to the process of partial sterilization, subsequently called “pasteurization” and now applied widely to many different foods and beverages.

Pasteur was never satisfied merely to formulate the theoretical basis for a given process. Instead, he took an active interest in its industrial development and practical applications. “There are no such things as pure and applied science,” he said. “There are only science

and the application of science.”

Darwin’s *Origin of Species*, Pasteur’s Debunking of Spontaneous Generation

Darwin published *The Origin of Species* in 1859, the same year that controversy over spontaneous generation reignited. Responding to that controversy and using very simple devices, Pasteur showed that, provided that germs are completely excluded, “spontaneous generation” does not occur. These simple experiments settled once and for all not only a philosophical problem, proving that life is not spontaneously generated from dead matter, but it also served to establish the new science of microbiology, basing it in part on specialized techniques, including sterilization and aseptic manipulation.

Toward the middle of the 19th century, a mysterious disease began to attack French silkworm nurseries. The disease then spread elsewhere in Europe and then to China and Japan. By 1865 the silkworm industry was decimated in Western Europe. Although Pasteur knew nothing about silkworms, he was asked to take charge of this problem in France. Intrigued through his interest in experimental pathology, he accepted the challenge. Soon, in less than a year, Pasteur became an expert breeder of silkworms and, through these studies, came into contact with some of the complexities of infectious processes. He also established some new selection techniques useful for silkworm specialists that gained wide recognition and were soon being applied throughout Europe.

The silkworm efforts plunged Pasteur more broadly into infectious diseases research. For instance, he developed some practices that became the foundations of modern epidemiology, providing investigative approaches that served him years later when he was asked to deal with very different animal and human diseases.

Koch’s Career Took Shape with Anthrax Studies begun during the 1860s

In 1860 Pasteur branched out from studying fermentation and putrefaction to investigating various specific diseases. At about the same time, Robert Koch was earning his medical degree at the University of Göttingen in Germany. Born in 1843, he became a medical doctor in 1866 and, at the age of 29, became a District Medical Officer, or *Kreisphysikus*.

Besides these public health-related official duties, Koch had an extensive medical practice. Moreover, working on his own, he began doing experiments with bacteria while also investigating a disease called anthrax that was worrying farmers all over Europe. In 1873, he began using microscopes to inspect blood from sheep that died from anthrax. He observed the same rod-shaped structures that the French scientist, Davaine, had named “bacteridia” in an 1863 report.

By 1874, Koch made a crucial finding while observing cultured bacteridia. He learned that they go through a cycle, with motionless rod-shaped cells changing into spores. His discovery of spores helped to explain findings by Davaine and others that sheep become sick with anthrax not only after being exposed to other infected animals but also when exposed to soil, where spores can be harbored for years.

Working in a primitive laboratory that he constructed at home, Koch obtained cultures of bacteria from blood of infected animals, then determined that anthrax can be transmitted from one mouse to another, reproducibly causing typical lesions. This work laid the methodological foundations for Koch’s postulates, a systematic approach for establishing the causal relationship between a particular microorganism and a specific disease.

Within a few years, Koch developed a number of original experimental and diagnostic procedures, making him the leader of the German school of bacteriology. He achieved im-

mortal fame by isolating the tubercle bacillus in 1882 and the cholera vibrio the following year.

Overlapping Interests in Anthrax Grow into an Intense Rivalry

Their overlapping interest in anthrax was the beginning of an intense rivalry between Pasteur and Koch. When Koch's paper on the etiology of anthrax appeared in 1876, Pasteur was 54 and widely known for his work on spontaneous generation and on the germ theory of fermentation.

Between 1878 and 1880 Pasteur published a number of papers on anthrax. In doing so, he consistently used Davaine's terminology for the bacterium—bacteridia—rather than Koch's term, *Bacillus anthracis*. However, in a single footnote, Pasteur acknowledged Koch's work by referring to "*Bacillus anthracis* of the Germans."

Fortunately, well before this rivalry grew more virulent, Koch and Pasteur continued to work on anthrax independently, providing further experimental evidence that the anthrax bacillus is responsible for causing anthrax. The germ theory of disease was thus firmly established, becoming the fundamental concept on which medical microbiology was built.

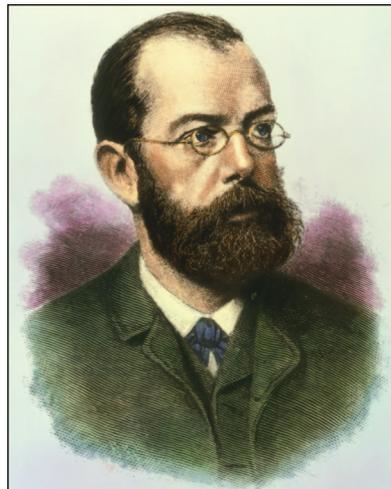
Those who were considered members of the German school of bacteriology discovered many bacterial agents of disease, due mainly to the mastery of Koch and the disciples he trained. In general, they developed and used standardized techniques for isolating and identifying microbial species by growing them in cultures. The germ theory of fermentation and of disease was based mainly on a belief of specificity and permanence of the characteristics of microbial species. Under the influence of Koch, this concept became a rigid doctrine. It held that the properties and forms of each microorganism remained unchanged under all circumstances.

Meanwhile, members of the French school of bacteriology, who were under the dominating influence of Pasteur, focused on another aspect of infectious diseases—immunity. For example, Pasteur investigated chicken cholera, caused by an agent now called *Pasteurella*, late during the 1870s. By chance, he noticed that cultures of chicken cholera sometimes lose their ability to produce disease and then retain this modified or

"attenuated" character through many generations.

Based on these observations, Pasteur inoculated chickens with the attenuated chicken cholera cultures and rendered them resistant to a fully virulent strain. From there on, Pasteur directed much of his experimental work toward understanding and improving such immunizations, striving to obtain attenuated cultures of anthrax with which to vaccinate animals.

In early 1881, Pasteur conducted a large-scale test of anthrax immunization in Pouilly-le-Fort. About 70 sheep were vaccinated in two steps: first they were inoculated with a low-virulence culture; 12 days later, they were vaccinated again, but with a less-attenuated culture. After another two weeks, the vaccinated and unvaccinated sheep were inoculated with a virulent anthrax strain. After a few days all the unvaccinated sheep were dead, while all the vaccinated animals remained healthy.



Koch

When Koch and Pasteur Meet in London, their Rivalry Flares

Joseph Lister invited Koch to attend the Seventh International Medical Congress, which was held in London during the summer of 1881. Earlier, as a surgeon in Glasgow, Lister fell under the influence of Pasteur and admired his work on fermentation and spontaneous generation. Those interests led Lister to develop the use of antiseptic techniques in surgery.

Pasteur also attended the medical congress in London, where he presented a paper on his results on anthrax attenuation and the successful sheep vaccination that were conducted earlier that spring. Koch presented a laboratory demonstration on his plate technique and methods for staining bacteria. Pasteur attended this demonstration session and said with admiration, "C'est un grand progrès, Monsieur." This praise was a great triumph for Koch, who was 20 years younger than Pasteur. Further, Koch knew that Pasteur could not forget that France had lost the Franco-German war of 1870.

Despite their friendly encounter at the London meeting, however, Pasteur and Koch were



soon in open conflict. A few months after the London meeting, in the first volume of the “*Mitteilungen aus dem Kaiserlichen Gesundheitsamte*,” Koch and his students Gaffky and Loeffler published several articles attacking Pasteur’s work on attenuating anthrax, accusing him of having impure cultures and of making errors during his inoculation studies. “Of these conclusions of Pasteur on the etiology of anthrax, there is little which is new, and that which is new is erroneous. . . Up to now, Pasteur’s work on anthrax has led to nothing,” Koch and his collaborators asserted (translated from the original German).

Pasteur answered Koch in detail at the fourth International Congress of Hygiene and Demography, held in Geneva in September 1882. At this memorable meeting, Koch was in the audience when Pasteur presented his speech on attenuation and vaccination. By this time, Koch was at the height of his fame after having reported the discovery of the tubercle bacillus a few months earlier. Koch’s response after Pasteur’s speech was unexpectedly aggressive, leading to an embarrassing situation.

As usual, their personal and national rivalries were mixed in whatever they did or said. This time, however, a translation problem apparently provoked Koch’s unexpectedly aggressive answer, according to a document held at the Museum of the Pasteur Institute in Paris. The problem was that the two men did not speak or understand one another’s language. Pasteur referred to published work of Koch as “*recueil allemand*,” meaning collection or compilation of German works. Professor Lichtheim, who sat next to Koch and was rapidly converting Pasteur’s French into German, incorrectly translated “*recueil allemand*” as “*orgeuil allemand*,” which means “German arrogance.” Not surprisingly, then, Koch angrily protested this unintended insult, while Pasteur—unaware that his innocuous phrase had, mistakenly, been turned into a stinging insult—remained preternaturally calm.

Koch’s written response to Pasteur was published in a paper, “On inoculation against anthrax. A reply to Pasteur’s lecture in Geneva.” In it, Koch attacked Pasteur in a highly insulting manner. Among other insults, Koch wrote, “. . . Concerning inoculation against anthrax, all what we heard was some completely useless data,” “he [Pasteur] is not even a physician,”

and “all this material served only as a vehicle for a violent polemic directed against me.” In his answer, in a long and emotional letter, Pasteur expressed surprise at the virulence of Koch’s attack and reviewed his own contributions to medicine and to science in general.

On top of the personal and scientific antagonisms between Pasteur and Koch, both were passionate patriots. Thus, the 1870–1871 war between France and Germany exacerbated their respective chauvinisms, which colored their broader behaviors. In 1871, for example, Pasteur returned with words of anger and contempt the honorary degree that he received from the University of Bonn.

When Pasteur published his results on rabies vaccination in 1885, Koch opposed use of the vaccine and again minimized the significance of Pasteur’s work. However, a few years later, Koch reversed this tack, using Pasteur’s methods to develop a similar vaccine to protect against rabies. When Koch established the Institute for Infectious Diseases in Berlin, its was designed to be like the Institut Pasteur in Paris.

The Koch-Pasteur Disputes Had Broad Implications

Koch’s refusal to recognize the value of Pasteur’s attenuation procedure had both practical and theoretical implications. Moreover, Koch believed that the biological and chemical characteristics of a microbial species were not only specific but also permanent. These views contradicted Pasteur’s concept that microbial virulence is not constant but, instead, is a variable property of microbial species—a property that can be lost but also recovered.

Pasteur believed that such variations were of great importance and could help to explain the epidemiology of various infectious diseases. He suggested that epidemics might arise because of a temporary or short-term increase in virulence of a particular microorganism. Further, such changes in virulence might arise when a particular microbe acquired virulence that enabled it to infect a previously unsusceptible animal species. Pasteur wrote:

Thus, virulence appears in a new light, which may be disturbing for the future of humanity, unless nature, in its long evolution, has already experienced the occasions to produce all possible contagious diseases—a very unlikely as-

sumption. What is a microorganism that is innocuous for man or for a given animal species? It is a living being which does not possess the capacity to multiply in our body or in the body of the animal. But nothing proves that if the same microorganism should chance to come into contact with some other of the thousands of animal species in the Creation, it might invade it, and render it sick. Its virulence might increase by repeated passages through that species, and might eventually adapt it to man or domesticated animals. Thus might be brought about a new virulence and new contagions. I am much inclined to believe that such mechanisms explain how smallpox, syphilis, plague, yellow fever, etc. have come about in the course of the ages, and how certain great epidemics appear from time to time.

These historical remarks continue to be relevant, and are especially applicable to HIV/AIDS and other emergent diseases.

The Pasteur-Koch controversy reflected, in part, then-contemporary political antagonism between France and Germany. On a more personal level, the Pasteur and Koch schools of microbiology adhered to different methods and philosophies. Pasteur was deeply interested in questions of immunity and in developing specific means to protect humans or other animal species against specific infectious diseases. By contrast, Koch favored public health measures for controlling infectious diseases. Pasteur's approach was to vaccinate individuals, whereas Koch's approach was to rely on sanitary methods to protect populations. Despite both Koch and Pasteur being impatient and intolerant and despite their bitter personal and nationalistic differences, both men defended truth and devoted their intellectual powers and their hearts in service to humanity.

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