Characterizing a "New" Disease: Epizootic and Epidemic Anthrax, 1769–1780

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In 1876, Robert Koch established anthrax as the first disease linked to a microbial agent. But Koch's efforts had followed more than 150 years of scientific progress in characterizing anthrax as a specific human and veterinary disease.

Focusing on France and the period between 1769 and 1780, this brief review examines noteworthy early events in the characterization of anthrax. It suggests that some "new" diseases like anthrax might be "discovered" not only by luck, brilliance, or new technologies, but by clinical/epidemiological "puzzle-fitting," which can assemble a cohesive picture of a seemingly specific disease entity.

If such processes have operated over 2 or more centuries, studying them may yield clues about desirable interactions between epidemiology/public health and experimental science in the characterization of new diseases.

"So much the better that . . . God leaves free field in the world to opinions and arguments and with equal indifference permits diversity of systems in the . . . sciences."

C. F. Cogrossi,[1] 1714

ROBERT KOCH'S 1876 "discovery" of anthrax[2] is an event familiar to physicians, veterinarians, microbiologists, and public health professionals. Anthrax was the first infectious disease linked to a microbial agent, and Koch's anthrax discoveries confirmed the centuries-old "germ theory," legitimized the new field of microbiology, and led to the development of numerous preventive vaccines for passive and active immunotherapy for other diseases. It was also Koch's anthrax discovery that prompted his colleague Edwin Klebs (1834–1913) to set down the "Henle–Koch postulates" for establishing microbial causes of disease,[3,4] leading to acceptance of infectious agents as the causes of tuberculosis (1882), cholera (1883), and many others.[5]

But Koch's discovery was not serendipitous. Characterization of anthrax was the result of a long series of critical observations and experiments extending over decades. Some of these events have been occasionally remembered in the context of early microbiology[6–10] (Table 1), especially the many serial studies conducted separately by Henri-Mamert-Onésime Delafond (1805–1861) and Casimir Davaine (1812–1882).

Almost completely forgotten, however, is what might be called the "early discovery" of anthrax, which took place in the premicrobial era, a century before Koch. By "early discovery" I mean the characterization of anthrax as a distinct and specific disease, transmitted and acquired by specific (if multiple) means. It can be argued that this early discovery of anthrax, which occurred in the context of veterinary and human public health responses rather than experimental science, is just as important as Koch's later triumph. Without it, the breakthroughs of experimental microbiology in the next century, which culminated in Koch's success, may not have occurred when they did.

The following examination of the early characterization of anthrax focuses on a small group of French observers working over a 12-year period (1769–1780) amid devastating epizootics that produced many fatal human cases. It looks also at the unique confluence of political and social determinants that made characterization of anthrax possible.

BACKGROUND

Epizootic Appearance

Anthrax and several other sporadic and epizootic diseases of domestic animals had probably been prevalent since ancient times, but they had not been well distinguished from each other. In early 18th-century Europe, fatal epizootics in cattle and other farm animals had seldom been recognized and apparently were small in scale. Sheep pox and glanders were gradually becoming recognized, but these did not cause widespread devastation.

In 1709, the first of many disastrous cattle epizootics appeared in Europe, ushering in a century of almost constant epizootic prevalence and economic disaster. At the time, the causes of these epizootics were unknown; historians later came to believe that most were caused by only 3 infectious diseases.[11] Rinderpest, a highly fatal and highly contagious disease of cattle caused by a measles-related paramyxovirus, appeared first and caused Europe's most infamous panzootic from 1709 to 1713. Thereafter, rinderpest (then referred to nonspecifically as *"la maladie pestilentielle des bêtes à cornes"* and later in England as "cattle plague") remained in one locale or another throughout the 18th century, undergoing panzootic recrudescences in the 1740s and again during most of the 1770s.

Epizootic anthrax appeared almost simultaneously with rinderpest, in 1712. It caused a European panzootic and then settled down to frequent small-scale outbreaks, punctuated by further panzootics in the periods 1757 to 1763, 1774 to 1780, and 1786 to 1793.

The third epizootic disease, foot-and-mouth disease, caused by a picornavirus related to the human enteroviruses, appeared suddenly in 1755 and caused a brisk European panzootic. It reappeared sporadically over the next half century, including panzootics in 1763 to 1764 and 1776 to 1779.

The economic impact of these epizootics was enormous. In Western Europe, over 200 million cattle died of rinderpest alone between 1709 and 1769, said to be equivalent to an annual loss of 20% of all dairy cows continuously over a 60-year period.[12]

Differentiating Between Enzootic and Epizootic Diseases

Although we would now regard the clinical-epizootiological picture of these 3 cattle diseases as being distinct, they were not easily differentiated by contemporary observers. Until the early 18th century, there was no coherent germ theory more sophisticated than the barely remembered notions of Fracastoro, published 165 years earlier,[13] nor were epidemiological principles of transmission/acquisition appreciated. Without such knowledge, it was impossible even for contagionists to conceptualize a carrier state, asymptomatic shedding, or environmental persistence of a transmissible agent, making it difficult to explain how, for example, animals might become ill without having been near other ill animals. Epizootics occurred in the countryside, where they were observed mainly by lay persons. There were farriers, but no professional veterinarians. Well-trained physicians were few, tended to be located in cities and towns, and focused their observations and ministrations mainly on human diseases associated with animal contact, not on the overall behavior of zoonotic diseases. In fact, the notion of a zoonotic disease did not then exist.

That all 3 epizootic diseases noted above—rinderpest, anthrax, and foot-and-mouth disease—predominantly affected cattle, that 2 of them affected humans in close contact with cattle (at least occasionally), and that they were often coprevalent, all tended to reinforce the belief that the 3 diseases were variants of the same. In place of disease specificity—the modern notion that different "causes" (e.g., microorganisms) produce different diseases—observers of the time were more likely to conclude that epizootics and epidemics alike took on different characteristics and exhibited different behaviors—from time to time and place to place—not because of inherently different causes, but under the influence of modifying "local" climatic, environmental, and meteorological cofactors. This was a century-old notion of Guillaume de Baillou (1538–1616),[14] adapted from Hippocratic doctrine and referred to by Thomas Sydenham (1624–1689) as an "epidemic constitution."[15]

Epizootic Responses

The rinderpest panzootic of 1709 to 1713, observed and studied by some of the great proto-epidemiologists of the day, began to break down Baillou's concept. It is fortunate that rinderpest was studied carefully by Bernardino Ramazzini (1633–1714), who was primarily an expert in occupational diseases. Some of the occupational diseases had known physical causes, while no infectious diseases did. Ramazzini's consequent ability to observe true cause-and-effect sequences in occupational diseases led him to realize that studying the "behaviors" of diseases in populations could provide clues to their causes. He was so impressed by rinderpest's behavior, including its apparent specificity and its smallpoxlike contagion,[16] that he immediately suggested immunization, a concept so new in Europe that few physicians were probably familiar with it. (Immunization did not become generally recognized until nearly a

TABLE 1—Representative Observational and Experimental Associations of *Bacillus anthracis* With Disease in the Early "Microbial Era," 1849–1876

Year	Investigator	Event
1849	Pollender[6]	*B anthracis* seen in blood of dead animals
1857	Brauell[7]	*B anthracis* seen in blood of living animals
1860	Delafond[8]	*B anthracis* cultivated; spores predicted
1863	Davaine[9]	Transmission of *B anthracis* and disease production
1873	Davaine[10]	Transmission prevented by bacterial removal
1876	Koch[2]	*B anthracis* artificially cultivated to produce disease

decade later, when variolation to prevent smallpox was introduced into Europe.)

Impressed by the recent appreciation of the contagionlike transmission of scabies and mange,[17] Ramazzini's contemporary Carlo Cogrossi (1682–1769) derived from rinderpest observations the most advanced germ theory proposed to that date, noting in 1714 that "in spite of all the assistance of microscopes which . . . reinforce my conjectures and suspicions . . . the idea [of contagion] would not be unreasonable even if . . . it were impossible to discover [detect] insects [communicable agents]."[1]

The European response to rinderpest was orchestrated at the highest levels of government. The Pope's physician, Giovanni Lancisi (1654–1720), arrived at the same general conclusions about rinderpest as had Ramazzini, and proposed an aggressive public health response that featured destruction of all ill and suspect animals (but not exposed healthy animals), followed by cremation, burial, and disinfection.[18] In England, farmers were indemnified for government-destroyed cattle.[19] In France, King Louis XIV's 1714 *arrêts du Conseil* drew up powerful veterinary public health measures. Friedrich Wilhelm of Prussia even ordered health certificates for all transported cattle, along with the carving of an "FW" on the right horns of imported cattle.[20]

By 1716, seven years of epizootic rinderpest had led to a great awakening of the old contagion theory, to a dawning realization that diseases of domestic animals seemed to obey the same rules (however poorly understood) as diseases of humans, and to a more sophisticated and more aggressive preventive approach by kings, princes, and modernizing states.

ANTHRAX AS A DISTINCT DISEASE

Up to this time, anthrax had not been extensively studied. Unlike rinderpest (from which it had not yet been clearly differentiated), anthrax was clinically and epidemiologically confusing, as reflected in hundreds of publications in the medical literature of the time that appear, in retrospect, to correspond to anthrax. The reasons, apparent to us today, could not have been apparent 200 years ago. Anthrax cannot normally be transmitted from animal to animal by aerosol (like rinderpest) but can be transmitted by blood, body fluids, and the carcasses, flesh, and hides of dead animals, as well as by contaminated earth and fomites (i.e., inanimate objects capable of transmitting infection). It affects many animals as well as man, and it produces different clinical pictures in different hosts, as well as different diseases in the same host, depending on its mode of acquisition (e.g., the clinically distinct pictures of cutaneous, gastrointestinal, and inhalational anthrax in man).

Clinical Experiences

After roughly 1720, an increasing number of observations about anthrax were made in Europe, and especially in France, but none were published in a truly organized form until 1769. In that year, an elderly retired physician from Dijon set down the observations made in his youth about a condition that seems to correspond to human anthrax.

As a young physician, Nicolas Fournier (c. 1700–1781) had been sent to investigate one of the most devastating events of the century, the infamous *"peste de Marseille,"*[21] a bubonic plague epidemic that killed 80,000 people between 1720 and 1722. Returning to one of Dijon's major hospitals, Fournier began to see and treat a disease that appeared similar to what he had seen in Marseille, so-called *charbon malin* ("malignant charcoal"). Having little clinical success, Fournier sought the advice of an older practitioner, a Dr Verny, whose successes with *charbon malin* had likewise been few, but who had at least made progress in distinguishing it from similar conditions like *charbon simple* and *clou charbonneux* (a darkened carbuncle).

Fournier began private research on this challenging disease. By 1727, he had begun to investigate *charbon malin* outbreaks in villages around Montpellier. He now also saw cases of fatal internal *charbon* associated with consumption of the meat of ill animals. He marveled at the terror that seized a community struck by even a single *charbon* case, noting the inevitable response of villagers, who would drag off the victims from their families, place them in isolation in far-off places, under guard, and wait until they died.

Fournier was soon able to go beyond Verny's observations by differentiating charbon from additional conditions like "erysipelatous" *charbon*, which only spread superficially on the surface of the body (as he had seen in the "*peste de Marseille*"), *charbon ordinaire, "phlegmon charbonneux," "le clou,"* furuncles, complications of smallpox, and scorpion bites. Believing he was observing a spectrum of conditions larger than just cutaneous *charbon malin*, Fournier developed a classification system for them. Deviating from the standard symptom-based classifications then in vogue in France and much of Europe, as promulgated by France's influential nosologist Boissier de la Croix de Sauvages,[22] Fournier's classification was based on (presumed) means of acquisition and on severity.

Fournier's Classification of Human Anthrax

Fournier's system supposed 2 basic forms of human "charbonous" disease: "spontaneous" and "contagious." The spontaneous form, an occupational disease producing skin lesions, typically affected peasants who worked out in the fields. Although it appears to correspond largely to sporadic cutaneous anthrax, Fournier speculated that spontaneous *charbon* was caused by work under the hot sun (anthrax was a summer disease), "putrid exhalations" (from the ground, decaying matter, etc.), unhealthy food and drink, and dirty clothes (all common enough in the peasants who contracted it).

The second form, contagious *charbon*, was defined primarily by its means of acquisition and existed in 2 clinical varieties: (1) one associated with a single cutaneous lesion and a lesser tendency to become systemic and (2) an "internal" variety that was rapidly fatal. Both of these clinical varieties were contagious, Fournier indicated, because they occurred only after touching or eating the meat, wool, or hides of animals. Indeed, he clearly described human anthrax acquired from handling wool long after it had (presumably) been contaminated, an early appreciation of transmission by fomites. He did not specifically describe inhalational anthrax.

Fournier's treatise was an important advance in conceptualizing anthrax as a specific disease. Although the association of human with animal disease was not fully characterized, and the clinical spectrum not fully described, Fournier did describe the basic clinical and epidemiological characteristics of a human-acquired zoonosis, distinguished it from other diseases, categorized it into different clinical/epidemiological varieties, and loosely identified the 2 main clinical/epidemiological forms recognized today: cutaneous and gastrointestinal anthrax.

Anthrax Epizootic Explosion

Although unappreciated at first, the 1769 publication[23] of Fournier's lifetime observations and reflections was timely. Within a year, anthrax broke out in the wealthy French colony of Saint-Domingue (modern Haiti), where a massive cattle epizootic led to 15,000 human deaths from gastrointestinal anthrax, the largest anthrax epidemic ever recorded.[24,25] Anthrax reappeared in Saint-Domingue in 1772 and spread elsewhere in the French West Indies.

Major epizootics and epidemics now began to explode. In Saint-Domingue, Regnaudot reported epizootic anthrax in horses, mules, and cattle in 1772, 1773, and 1774.[26] Worlock described epizootic anthrax imported into Saint-Domingue from North American horses.[27] These observations documented multispecies involvement in single epizootics, as well as contagious importation into new areas that provided a "fertile soil."

Félix Vicq-d'Azyr (1748–1794), protoepidemiologist and physician to Louis XVI. Image courtesy of the National Library of Medicine, National Institutes of Health.

> *"Vicq-d'Azyr, Bourgelat, and Bertin, for example, were all "hands on" investigators who promoted firsthand experience over theoretical knowledge and book learning."*

Claude Bourgelat (1719–1779), director of the World's first veterinary school in Lyon. Image courtesy of the National Library of Medicine, National Institutes of Health.

A 1774 Guadeloupe epizootic was reported in great clinical and epidemiological detail by Henri-Léonard-Jean-Baptiste Bertin (1719–1792), who documented not only the specific means of transmission from animals to humans but also the absence of secondary spread between human index cases and their close contacts.[28] A careful observer, Bertin documented numerous instances of anthrax lesions on the hands and lower arms of slaves who opened animal carcasses, performed animal autopsies, or administered animal enemas. (The administration of enemas, a common treatment for a variety of veterinary conditions, involved inserting the hands and arms far up into the animal's rectum.) Bertin also observed intestinal anthrax in humans who consumed the meat of ill animals. He performed autopsies, verifying the gross pathological similarity of intestinal lesions in animals to those in humans.

The return of epizootic anthrax to Saint-Domingue in 1774 and 1775 was recorded by an obscure physician named Baradat, but written up and interpreted by proto-epidemiologist Félix Vicq-d'Azyr[29] and later by his colonial colleague Charles Arthaud.[30] The 1774–1775 epizootic affected not only cattle, horses, and mules but also goats, sheep, pigs, dogs, cats, and chickens. Once again, many slaves were infected and died, and once again the means of human acquisition were as Bertin had described[28]: opening animal carcasses and administering enemas to farm animals (both practices causing cutaneous lesions only on exposed surfaces) or eating infected meat (causing fatal gastrointestinal disease).

Proto-Epidemiology and Proto-Epizootiology Begin to Coalesce

An epizootic–epidemic disease pattern was beginning to emerge, but the various diverse pieces of the puzzle needed to be fit together. During the 1760s and 1770s, France was undergoing dramatic social changes as the *ancien régime* grew in size and complexity, liberal ideas began to flower, and the state assumed increasing responsibility for the health and welfare of its citizens. The social and economic importance of agriculture was becoming apparent as well, leading to an evolving consensus that it was the responsibility of the state to provide not only for the well-being of its citizens but also for their economic health. It was in this climate that innovations in veterinary and human public health were promoted by a small group of government officials and royally sponsored scientists.

Henri Bertin, the author of the key 1774 anthrax epidemic investigation report in Guadeloupe,[28] was a nobleman and horse fancier who had been *intendant* of Lyon from 1754 to 1757. In that powerful position he had become passionately devoted to the agricultural life of the region, and increasingly concerned about the social and economic impact of the recurring epizootics that threatened it.

In 1759, Bertin had been appointed comptroller general of France under Louis XV. Within 2 years, he had engineered an *arrêt du Conseil* authorizing establishment of France's (and the world's) first veterinary school, in his old hometown of Lyon. Bertin placed the new school under the supervision of his friend Claude Bourgelat (1712–1779), the director of the local horsemanship academy and a renowned *philosophe*. By 1764, Bertin's influence was such that he convinced the king to upgrade the Lyon school to an école *royale vétérinaire* and to name Bourgelat director and inspector general.

No sooner had the Lyon school opened, in 1762, than small groups of its veterinary students were sent out to investigate epizootics, which they were credited with controlling.[31,32] Another *intendant*, Anne-Robert-Jacques Turgot (1727–1781), was soon networking with Bertin to create a second school in Limoges, in his own region of Limousin. When this effort failed, Bertin and Turgot conceived a more ambitious plan, successfully establishing their second veterinary school at Charenton, and soon moving it to the nearby Chateau d'Alfort, on the outskirts of Paris.

Vicq-d'Azyr Links Human Medicine, Veterinary Medicine, and Proto-Epidemiology

In 1774, when *intendent* Turgot succeeded Bertin as comptroller general, he brought to court the brilliant 26-year-old physician and comparative anatomist Félix Vicq-d'Azyr (1748–1794). At Turgot's behest, Vicq-d'Azyr spent the better part of 2 years (1774–1776) traveling throughout France, investigating epizootics and issuing instructions for prevention and outbreak control.[33–35] (As it turned out, these epizootics were mostly caused by rinderpest, although anthrax and foot-and-mouth disease were also prevailing at the time. Vicq-d'Azyr was highly successful in epizootic control, typically bringing large numbers of armed troops into affected areas to maintain *cordons sanitaires*, find and destroy ill herds, collect data, and shoot stray animals.)

Vicq-d'Azyr's successes came at a critical time. In 1776, when Turgot and others convinced the new king (Louis XVI) to establish a *Société royale de médecine*—partly as a progressive youth-oriented alternative to the privilege-obsessed Paris Faculty of Medicine—Louis named Paris Faculty member Vicq-d'Azyr "permanent secretary," a role providing nearly total control over the society's day-to-day operations.

Vicq-d'Azyr was quick to set up a national system of human and veterinary disease surveillance and outbreak investigation throughout France and in her overseas colonies.[36,37] He immediately began interacting on a regular basis with those few physicians and scientists interested in epidemic and epizootic diseases, many of whom were members of the same royal societies (e.g., Vicq-d'Azyr, Bourgelat, and Alfort's future director, Philibert Chabert, were all members of the societies for medicine, sciences, and agriculture). Vicq-d'Azyr worked closely with his own protégé, Alfort's chemistry professor Antoine-François de Fourcroy (1755–1809). In 1782, when national veterinary education was placed under the direction of the powerful *intendant* of Paris, Louis-Bénigne-François Bertier de Sauvigny (1737–1789), Vicq-d'Azyr himself was appointed an Alfort professor.

Scientific and Public Health Networks Are Created

Although confusing, these new political and organizational networks were probably of great importance to the characterization of anthrax: they drew together a medical and veterinary corps of privileged and exceptionally talented men interested in epidemic and epizootic diseases, and they created a system for quickly assembling knowledge from far-flung sources throughout the empire. Moreover, they added a strong focus of scientific observation and experimental investigation. Vicq-d'Azyr, Bourgelat, and Bertin, for example, were all "hands on" investigators who promoted firsthand experience over theoretical knowledge and book learning. In outbreak investigations, Vicq-d'Azyr repeatedly argued the importance of careful observation and careful assembly of facts, including construction of daily "line lists," and he insisted on performing careful autopsies in fatal cases. A contagionist with a strong intuitive sense of a germ theory, Vicq-d'Azyr conducted numerous challenge experiments in animals to elucidate the modes and determinants of disease transmission.[38] (So keen was his scientific focus that he was once temporarily relieved of his Alfort professorship when students complained that he spent too much time conducting experiments in his laboratory and too little time teaching.)

It was under Vicq-d'Azyr's leadership, and with his considerable organizational skills, that a fuller picture of anthrax was assembled from the input of his Alfort colleagues and his "correspondents" in the national disease surveillance system. The most important outbreak reports from the French West Indies, for example, saw the light of day under Vicq-d'Azyr. Several of the outbreaks were published in some detail by Vicq-d'Azyr in 1776,[34] the most significant report being that of the 1774 Guadeloupe epizootic conducted by Bertin and the 1774–1775 Saint-Domingue epizootic recorded by Baradat.

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Vicq-d'Azyr was also able to draw into his circle the independent veterinary investigator Jean-Jacques Paulet (1740–1826), a member of the conservative and competitive Paris faculty and author of a comprehensive treatise on epizootiology[39] that was published, possibly with Vicq-d'Azyr's help, a few months before a similar work by Vicq-d'Azyr himself.[34] Considering the frequency with which the evolving data and conclusions of various observers were presented, discussed, published, and republished by their colleagues, it seems clear that new observations about anthrax circulated intensely through the small group of Alfort's professors and Vicq-d'Azyr's proto-epidemiology correspondents.

Philibert Chabert and the Characterization of Anthrax

In 1780, the Academy of Sciences of Dijon announced a prize competition for manuscripts that could identify the cause and optimal treatment of *charbon*. The best of these, written by cavalry surgeon-major Jean-François Thomassin (1750–1828),[40] assembled several decades' worth of historical information, much of it unpublished, into a comprehensible whole, organized in the puzzle-fitting style now familiar to epidemiologists and historians. It may have been the national visibility of this competition that convinced Alfort's director to write his own paper on anthrax. Philibert Chabert (1737–1814), a farrier and professional administrator, did so that same year.[41]

Chabert's 1780 work is often cited as the first true description of anthrax as a specific disease. Compared with similar works of the era, it is written with admirable exactness, objectively examining clinical and pathological findings. But it draws strongly on the preexisting knowledge of his colleagues, focuses on treatment rather than disease characterization, and is devoted only to veterinary anthrax, omitting discussion of human disease. Chabert's division of veterinary anthrax into 3 basic forms—essential (localized cutaneous), symptomatic (systemic), and interior (gastrointestinal)—seems to be derived from some of Fournier's observations in human beings.

In any case, the sudden attention to veterinary diseases in France received worldwide attention. By 1780, veterinary schools had been set up in Italy, Germany, Denmark, the Austrian Empire, and Sweden. Anthrax had been essentially characterized clinically and epidemiologically as the veterinary and human disease recognized today. Very little new information about anthrax was added over the next 4 decades. In 1823, an Alfort professor, Éloy Barthélemy (1783–1850; known as "Barthélemy aîné" to distinguish him from his veterinarian brother), picked up Vicq-d'Azyr's line of research to show that anthrax could be transmitted experimentally by blood and material from lesions.[42] In 1837, inhalation anthrax was recognized.[43] In 1860, the first experimental microscopic studies of *Bacillus anthracis*,[8] conducted by Delafond, who had been a prize-winning first-year Alfort student under Barthélemy in the year Barthélemy first proved anthrax transmission,[42] ushered in the microbial era that led to Koch's definitive "discovery" 16 years later.[2]

The End of an Era

That early steps in the "discovery" of anthrax have been largely forgotten may be due in some measure to the events of 1789 to 1794, which wiped away the *ancien régime*, most of its systems, and many of the men who led it. Some, like Bourgelat and Turgot, had already died of natural causes, but others were not so lucky. Arthaud had stayed on in Saint-Domingue to become a valuable correspondent in Vicq-d'Azyr's surveillance system. Nominated as physician to the king, his promotion was overtaken by the revolution.

Bertier de Sauvigny, who directed Alfort during Vicq-d'Azyr's entire professorship there, was lynched and then decapitated shortly after the fall of the Bastille. de Fourcroy, another Alfort professor and Vicq-d'Azyr's chief protégé, survived the revolution as a radical Jacobin. After the assassination of the murderous physician-revolutionary Jean-Paul Marat (1743–1793), de Fourcroy succeeded him in the Convention. (Despite his brilliance as a speaker, de Fourcroy wisely avoided Marat's extreme positions and generally kept quiet).

Chabert, denounced and imprisoned during the Terror, escaped the guillotine owing to the intervention of one of his students, Jean Girard (entering veterinary class of 1790). To save Chabert, Girard may have risked his own life in an appeal to Georges Couthon (1756–1794), a Jacobin member of the rabid Committee of Public Safety, who nevertheless succeeded in gaining the beloved professor's release. (Couthon joined his colleagues Robespierre, Saint-Just, and 80 others at the guillotine during a bloody purge 2 years later. Girard went on to become an acclaimed Alfort professor.)

Bertin was thrust into obscurity by the revolution and died of unknown causes at the height of it, in 1792. With the death of the *Société royale de médecine* and the national disease surveillance system, Vicq-d'Azyr, now "second physician" to Louis XVI and principal physician to Marie Antoinette, was stripped of his powers. Wandering the poorer quarters of Paris, ministering to the disadvantaged, he was present at the queen's execution. He died shortly thereafter, possibly from bovine tuberculosis.

DISCUSSION

Despite the relative obscurity of these early anthrax investigations, they set the stage for later events that led to Koch's "discovery." It could not have been an accident that *Bacillus anthracis* was the first microorganism to be linked to a transmissible disease, because its clinical appearance, natural history, and modes of transmission in nature had been largely worked out for its most common hosts.

In the modern era, it has been proposed that some "new" infectious diseases have been elucidated by a particular type of "disease discovery process" that begins with clinical description and proceeds to clinical differentiation, epidemiological/epizootiological characterization, generation of a hypothesis about the disease's etiology, epidemiological "fitting," and finally to experimental proof of etiology.[44] Such a process would obviously require a healthy and well-supported scientific and public health infrastructure.

The characterization of anthrax appears to fit such a modern "discovery process" scenario. If such processes are found to span centuries and survive radical changes in science—a possibility that probably deserves further consideration—it may be important to examine them more carefully. Understanding the means by which diseases are characterized and "discovered" may help us support key systems involved in various critical steps, so that public health/epidemiology and experimental science can better meet the challenges of new and emerging diseases. The "discovery" of anthrax may also suggest the value of both breadth and depth in scientific and societal approaches, as well as the importance of maintaining strong links between clinical medicine, epidemiology/epizootiology, public health, and experimental science. ■

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This article was accepted December 6, 2002.

Acknowledgments

I thank the many individuals on the staff of the History of Medicine Division, National Library of Medicine, National Institutes of Health, for help in manuscript retrieval and interpretation.

References

1. Cogrossi CF. Nuova idea male contagioso de' buoi. In: Cogrossi CF, Vallisnieri A. *Pensieri filosofoci Stesi in una Lettera fisicomedica del dottor Antonio Vallisnieri Intorno all corrente Epidemia del Bue.* Milan: Marc'Antonio Pandolfo Malatesta; 1714.
2. Koch R. Die Aetiologie der Milzbrand-Krankheit, begründet auf die Entwicklungsgeschichte des Bacillus Anthracis. *Beiträge zur Biologie der Pflanzen* 1876;2:277–310, 11 figures.
3. Klebs TAE. Ueber die Umgestaltung der medicinischen Anschauungen in den letzten drei Jahrzehnten. In: *Tageblatt der 50 Versammlung der Gesellschaft deutscher Naturforscher und Aertze.* Munich: F. Straub; 1877:41–45.
4. Carter KC. Koch's postulates in relation to the work of Jacob Henle and Edwin Klebs. *Med Hist.* 1985;29: 353–374.
5. Ackerknecht EH. Microbiology. In: Ackerknecht EH. *A Short History of Medicine.* Rev ed. Baltimore, Md: Johns Hopkins University Press; 1982:175–185.
6. Pollender FAA. Mikroskopische und mikrochemische Untersuchung des Milzbrandblutes, so wie über Wesen und Kur des Milzbrandes. *Vierteljahrsschrift für gerichtliche und öffentliche Medicin.* 1855;8:103–114.
7. Brauell FA. Versuche und Untersuchungen betreffend den Milzbrand des Menschen und der Thiere. *Archiv für pathologische Anatomie und Physiologie und für klinische Medicin.* Neue Folge. 1857;11:132–144.
8. Delafond H-M-O. [Untitled discussions "sur la maladie régnante," séances de 22 mars et 10 mai 1860.] *Recueil de médecine vétérinaire.* 1860;37:574, 726–748.
9. Davaine CJ. Recherches sur les infusoires du sang dans la maladie connue sous le nom de sang de rate. *Comptes rendus hebdomadaires des séances de l'Académie des Sciences (Paris).* 1863;57:220–223.
10. Davaine CJ. Recherches relatives à l'action des substances dites antiseptiques sur le virus charbonneux. *Comptes rendus hebdomadaires des séances de l'Académie des Sciences (Paris).* 1873;77:821–825.
11. Fleming G. Period from A.D. 1746 to A.D. 1774. In: Fleming G. *Animal Plagues: History, Nature, and Prevention.* Vol 1. London: Bailliere, Tindall and Cox; 1871:382–464.
12. Smithcors JF. Cattle plagues. In: Smithcors JF. *Evolution of the Veterinary Art. A Narrative Account to 1850.* Kansas City, Mo: Veterinary Medicine Publishing Co; 1957:229–246.
13. Fracastoro G. *De sympathia et antipathia rerum liber unus. De contagione et contagiosis morbis et curatione.* Venice: L. Iuntae; 1546.
14. de Baillou G. *Epidemiorum et ephemeridum libri duo.* Paris: Jacobum Quesnel; 1640.
15. Garrison FH. The seventeenth century: the age of individual scientific endeavor. In: Garrison FH. *An Introduction to the History of Medicine, With Medical Chronology, Suggestions for Study and Biographic Data.* 4th ed. Philadelphia, Pa: WB. Saunders; 1929:245–309.
16. Ramazzini B. *De contagiosa epidemia, quæ in Patavino Agro, & tota ferè Veneta. Ditione in Boves irrepsit. Dissertatio habita in Pavatino Lyceo A' Bernardino Ramazzini, Practicæ Medicinæ Professore Primario. Die IX. Novembris MDCCXI.* Padua: Jo. Baptistae Conzatti; 1712.
17. Wilkinson L. Rinderpest and mainstream infectious disease concepts in the eighteenth century. *Med Hist.* 1984;28:129–150.
18. Lancisi GM. *Dissertatio historica de bovilla peste, ex Campaniæ finibus anno MDCCXIII.* Rome: Joannis Mariæ Salvioni; 1715.
19. Bates T. A brief account of the contagious disease which raged among the milch cows near London, in the year 1714. And the methods that were taken for suppressing it. *Philosophical Transactions [of the Royal Society of London].* 1718;30:872–885.
20. Leclainche E. Les maladies contagieuses du quinzième au dix-huitième siècle. In: Leclainche E, ed. *Histoire de la médecine vétérinaire.* Toulouse, France: Office du livre; 1936:187–195.
21. Hecker JFC. *Der schwarze Tod im vierzehnten Jahrhundert.* Berlin: Friedrich August Herbig; 1832.
22. Boissier de la Croix de Sauvages F. *Nosologia methodica sistens morborum classes juxta Sydenhami botanicorem ordinem.* Amsterdam: fratrum de Tournes; 1768.
23. Fournier N. *Observations et expériences sur le charbon malin, avec une méthode assurée de la guérir.* Dijon: Defay; 1769.
24. Justin M-P. Livre troisième. In: Justin M-P. *Histoire politique et statistique de l'île d'Hayti, Saint-Domingue, écrite sur les documents officiels et des notes communiqués par Sir James Barskett.* Paris: Brière; 1826:109–125.
25. Morens DM. Epidemic anthrax in the eighteenth century, the Americas. *Emerg Infect Dis.* 2002;10:1160–1162.
26. Regnaudot. Extrait d'un mémoire qui a pour titre: "Description d'une maladie épizootique qui a régne à Saint-Domingue, dans la dépendence du Cap-François, dans les années 1772, 1773 & 1774." In: Arthaud C, Cercle des Philadelphes, eds. *Recherches, mémoires et observations sur les maladies épizootiques de Saint-Domingue, recueillis & publiés par le Cercle des Philadelphes du Cap-François.* Cap-François, Saint-Domingue: Imprimerie royale; 1788:196–205.
27. Worlock. Mémoire sur la maladie épizootique pestilentielle de l'île Saint-Domingue. In: Arthaud C, Cercle des Philadelphes, eds. *Recherches, mémoires et observations sur les maladies épizootiques de Saint-Domingue, recueillis & publiés par le Cercle des Philadelphes du Cap-François.* Cap-François, Saint-Domingue: Imprimerie royale; 1788:162–170.
28. Bertin H-L-J-B. Relation de quelques accidens extraordinaires, observés à la Guadeloupe, sur les Nègres du quartier de la Capesterre à la suite de l'usage qu'ils ont fait de la chair des animaux morts d'une maladie épizootique. In: de Montigny É-M. *Instructions et avis aux habitans des provinces méridionales de la France, sur la maladie putride et pestilentielle qui détruit le bétail.* Paris: Imprimerie royale; 1775:49–70.
29. Vicq-d'Azyr F. Épizootie en Guadeloupe en 1774. In: Vicq-d'Azyr F. *Exposé des moyens curatifs & preservatifs qui peuvent être employées contre les maladies pestilentielles des bêtes à cornes.* Paris: Mérigot l'aîné; 1776:162–173.
30. Arthaud C. Épizootie de Saint-Domingue en 1774 & 1775. In: Arthaud C, Cercle des Philadelphes, eds. *Recherches, mémoires et observations sur les maladies épizootiques de Saint-Domingue, recueillis & publiés par le Cercle des Philadelphes du Cap-François.* Cap-François, Saint-Domingue: Imprimerie royale; 1788:11–18.
31. Railliet ALJ, Moulé LT. Maladies contagieuses et police sanitaire. In: Railliet ALJ, Moulé LT. *Histoire de l'École d'Alfort. Deuxième partie. Organization générale et enseignement. Chapitre II. L'enseignement théorique.* Paris, France: Asselin et Houzeau; 1908:367–373.
32. Railliet ALJ, Moulé LT. Bourgelat et Bertin. Les premières Écoles vétérinaires: Lyon, Limoges. In: Railliet ALJ, Moulé LT. *Histoire de l'École d'Alfort. Première partie. Les origines de l'École.* Chapitre II. Paris, France: Asselin et Houzeau; 1908:7–15.
33. Vicq-d'Azyr F. *Observations sur les moyens que l'on peut employer pour préserver les animaux sains de la contagion, et pour en arrêter les progrès.* Bordeaux: M. Racle; 1774.
34. Vicq-d'Azyr F. *Instruction sur la manière de désinfecter les étables où il y a eu anciennement des bestiaux attaqués de l'épizootie.* Paris: Imprimerie royale; 1776.
35. Vicq-d'Azyr F. *Exposé des moyens curatifs & preservatifs qui peuvent être employées contre les maladies pestilentielles des bêtes à cornes.* Paris: Mérigot l'aîné; 1776.
36. Meyer J. L'enquête de l'Académie de médecine sur les épidémies 1774–1794. In: Desaive J-P, Goubert J-P, Le Roy Ladurie E, Meyer J, Muller O, Peter J-P. *Médecins, climat et épidémies à la fin du XVIIIe siècle.* Paris, France: Mouton et C^ie^; 1972:9–20.
37. Hanaway CC. The Société royale de médecine and epidemics in the ancien régime. *Bull Hist Med.* 1972;46: 257–273.
38. Vicq-d'Azyr F. Considérations relatives à un parallèle entre les symptômes des épizooties et ceux de la peste humaine. In: Moreau de la Sarthe J-L, ed. *Œuvres de Vicq-d'Azyr, recueillies et publiées avec des notes et un discours sur sa vie et ses ouvrages. Tome cinquième.* Paris: Imprimerie de Baudouin; 1805: 140–159.
39. Paulet J-J. *Recherches historiques & physiques sur les maladies épizootiques, avec les moyens d'y remédier, dans tous les cas.* Paris: Ruault; 1775.
40. Thomassin J-F. *Dissertation sur la charbon malin de la Bourgogne, ou la pustule maligne.* Dijon: Antoine Benoit; 1780.
41. Chabert P. *Description et traitement du charbon dans les animaux.* Paris: Imprimerie royale; 1780.
42. Raimbert L-A. Introduction. II. Affections charbonneuses des animaux. In: Raimbert L-A. *Traité des maladies charbonneuses.* Paris: Victor Masson; 1859:9–26.
43. Ravenel M. Anthrax. In: Osler W, McCrae T, eds. *Modern Medicine: Its Theory and Practice in Original Contributions by American and Foreign Authors.* Vol 3. Philadelphia, Pa: Lea Brothers; 1907:42–51.
44. Morens DM, Katz AR. The "fourth disease" of childhood: reevaluation of a non-existent disease. *Am J Epidemiol.* 1991;134:628–640.