Friedrich Loeffler and His History of Bacteriology

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The first history of bacteriology was written by Friedrich Loeffler, who in 1887 published a slender volume entitled Vorlesungen über die geschichtliche Entwicklung der Lehre von den Bacterien (17). The book was based on a series of lectures covering the historical developments in the field of bacteriology which he presented during the winter semester of 1886-87 at the University of Berlin, where he had just been appointed a lecturer in hygiene (for additional biographical material on Loeffler, see references 3 and 13). The work appeared as part 1 and covered the subject up to 1878. He intended that there be a part 2 to bring the subject up to the year 1887, but it never appeared, and it seems likely that his appointment as professor of hygiene at the University of Greifswald in 1888 prevented him from carrying out his intention. (The University Greifswald was reorganized in 1946 as Ernst-Moritz-Arndt-Universitat, Greifswald, German Democratic Republic.)

The part that was published is a remarkable document, which, although not rare, is available in only a few biomedical libraries. A cursory search revealed 15 copies of the German edition scattered in various university and medical libraries throughout the United States. No doubt there are others. I have prepared an English translation of the work (in press with Coronado Press, Lawrence, Kans.) from a photocopy of the volume (17) kept at the National Library of Medicine, National Institutes of Health, Bethesda, Md. During some portions of my research a second copy was consulted at the library of the Wellcome Institute for the History of Medicine, London, England. In many instances Loeffler recorded investigations which were conducted in his own lifetime, sometimes only a few years before he wrote of them. It is, therefore, a fascinating experience to reexamine well-known events in the history of bacteriology through the writings of a 19th-century scholar of considerable merit.

Merits and Shortcomings

It is not certain what amount of time Loeffler devoted to the prodigious library research apparent in his study, nor is it known how long he spent in preparing the lectures, but it would seem from his comments in the foreword to the German edition that the decision to publish and the readying of the manuscript must have been accomplished in a relatively short time. Thus, the errors in fact and referencing which have been detected (it has been said that Loeffler’s book is flawed by many errors [11]) are at least understandable. More importantly, there is no lack of errors in assessment and interpretation.

No doubt Loeffler would have corrected the errors in fact and interpretation himself had he devoted any time to a revision of part 1 or the completion of part 2 of his project. But this he did not do. Nevertheless, in spite of its limitations, the work abounds in numerous examples of instances in which Loeffler points out the key issue in a controversy and recognizes the criteria necessary for decisive conclusions. He does not always do this succinctly, and frequently goes on quite at length only to show ultimately that a whole series of experiments was worthless because of a crucial flaw in technique or interpretation. But in spite of occasional ponderousness, the book is of considerable value and great interest, even though as a source book it is not as reliable as more recent works (Grainger [11], for example, recommends the admirable account by Bulloch [4]).

It is astonishing to see how often Loeffler, when confronted with a welter of conflicting experimental data, often based on subtly inadequate techniques, arrived at a conclusion or an evaluation with which modern scholarship completely agrees. But then, I suppose, if he had...
not, he would not be remembered as one of the substantial contributors to 19th-century bacteriology, and this work would then take its place alongside other long-forgotten tomes of that period (examples of massive works on 19th-century bacteriology which are now ignored because of the mistaken ideas they contain include that of Billroth[2] and the extensive writings of Ernest Hallier [for a listing, see reference 4, p. 321-322]).

**Loeffler’s Purpose**

Loeffler’s book is divided into 16 chapters, or lectures, as he termed them. As a physician and professor of hygiene, Loeffler’s predominant interest was in the role of bacteria in disease. Thus, he describes those findings which support the concept that disease is caused by living agents. In tracing this aspect of the history of bacteriology, Loeffler repeatedly confronts the major obstacle to a convincing argument for a “viable contagion,” viz., the indistinguishableness of bacterial forms.

In a letter to Henry Oldenburg, secretary of the Royal Society of London, dated 9 October 1676, Antony van Leeuwenhoek related those microscopical observations which are now generally acknowledged to constitute the original discovery of bacteria (19). Throughout the remainder of his life, Leeuwenhoek observed and described numerous protozoan and bacterial forms with sufficient clarity that many of them can easily be recognized today. Leeuwenhoek’s protozoological findings were quickly confirmed by others (5), but, curiously, the bacteria, which he had also described and figured quite plainly, were almost totally ignored for nearly 150 years after their discovery. A part of this neglect was no doubt due to spherical and chromatic aberrations in the images produced by the lenses of microscopes available throughout the 18th and early 19th centuries. Corrections for chromatic aberrations of microscope lenses were first made in the early 19th century, and when Joseph Jackson Lister showed, in 1829, how this could be accomplished for spherical aberrations as well, the compound microscope became an instrument with which steady advances in the field of bacteriology could be made (23).

Although Leeuwenhoek never suggested that his “animalcules” had anything to do with the etiology of infectious diseases, such an application was immediately made by others. Speculations about “living germs,” which attained notable expression in the writings of Athanasius Kircher (5), were seemingly strengthened by Leeuwenhoek’s discoveries. After the improvements in the design of the microscope, there was an enormous increase in the number of reports on finding microbes of all sorts in morbid processes. Loeffler clearly recognized that in order to make sense of these observations, distinctions between different sorts of microbes had to be made. Yet it was at precisely this point that 19th-century bacteriology, for a time, faltered; advances in the establishment of the etiology of diseases were precluded by an inability to distinguish bacterial forms which were dreadfully similar microscopically. This situation was further complicated by the idea, reiterated several times, that all bacteria were basically the same and simply behaved differently or even looked somewhat different in response to their environment. Accordingly, the dominant concern of Loeffler’s work was to trace the historical development of knowledge about distinctiveness among microbes. Loeffler adopted a predominantly chronological approach to the subject and therefore, with a few notable exceptions, obscured the more important topical subdivision of his work.

Loeffler sought evidence of distinctiveness among the bacteria in three different areas: (i) taxonomic consideration, founded mainly on the shape and motility of microbial forms; (ii) manifestations of biochemical activities, such as fermentations produced in liquids or pigments formed during growth on solid substrates; and (iii) demonstrable associations of distinguishable microbes with distinctive morbid processes.

**Micr0bial Shape and Motility**

Linnaeus (1707-78) was the first to attempt a classification of the animalcules discovered by Leeuwenhoek and others; the “infusorians” (bacteria) were lumped into a single species, Chaos infusorium (see reference 4, p. 37). The earliest fruitful effort at a taxonomy of microbes was that of the Danish naturalist Otto Friedrich Müller, who in 1786 described several species of bacteria, none of which can be identified with certainty today, and attempted a classification of them. Müller’s nomenclature was adopted and extended by C. G. Ehrenberg, who based his system of classification of microbes on shape and motility. The French zoologist Felix Dujardin presented a much simpler system, and somewhat later Maximilian Perty suggested a new classification, which was marred by unclear descriptions and confused ideas. At about this time Ferdinand Cohn began to publish his important observations. Following in the footsteps of Müller, Ehrenberg, Dujardin, and Perty, he arranged bacteria according to form: spherical (Micrococcus), short rods (Bacterium), long rods (Bacillus), wavy rods (Vibrio), flexible spiral forms (Spirochaete), and inflexible spiral forms (Spirillum). Loeffler clearly recognizes the importance of Cohn’s work by devoting one entire lecture (lecture 9) to a consideration of his taxonomic system and by repeatedly referring to his decisive observations which resolve controversies based on the inconclusive researches of others.

Cohn’s views exerted a considerable influence on the opinions held by his contemporaries, and he is now recognized as one of the founders of modern bacteriological doctrines. In marked contrast was the work of Ernst Hallier, a professor of botany in Jena. Hallier had been strongly influenced by the careful studies of Anton DeBary and of C. Tulasne and E. L. R. Tulasne, who had established the fact of polymorphism among certain fungi, notably, the parasites of cereals (for a detailed discussion of the development of the concept of polymorphism among fungi, see reference 1). The term
polymorphism denoted the ability of one fungus to appear in several different forms. This concept came to be applied to the bacteria, and its major protagonist was Hallier, who maintained that all microscopic forms, including micrococci, bacteria, bacilli, and yeasts, were merely stages in the development of more complicated fungi and that transformation of one form into another was based on alteration of cultural conditions. Hallier had arrived at his conclusions after a long series of observations based on absurd culture techniques. He ignored DeBary’s injunction that before one can affirm that one form of microscopic life derives from another, one must be assured that both were not present in the original material. Thus was Hallier led astray, and all his observations on bacteria are now forgotten, but the confusion engendered at the time was painfully obvious to Loeffler.

Edwin Ray Lankester was also among those who denied the constancy of form among bacteria. His studies on a peach-colored bacterium (Beggioota roseo-persicina) were often used in support of a concept of bacterial polymorphism. But of greater overall influence were the writings of the Viennese surgeon Theodor Billroth. He presented a huge series of observations by which he attempted to prove that all spherical and rod-shaped bacteria were stages of a single organism, which he called Cocccobacteria septica (2). The species name indicates that he consistently discovered the bacterium in various sorts of putrefying materials, including infected wounds, of which he considered it to be the cause. Many of Billroth’s descriptive terms have survived, e.g., micrococcus, diplococcus, streptococcus, but his major doctrine is fallacious. Again, it was the rigorous reexamination of materials by Cohn which terminated further serious acceptance of Lankester’s or Billroth’s conclusions about polymorphism among microbial forms.

**Microbial Behavior**

A second approach to distinguishing microbes, apart from their shape and motility, consisted in definitive descriptions of microbial behavior. Perhaps no manifestation of the presence of bacteria was more obvious to early microscopists than their growth in various sorts of infusions. Loeffler points out (lecture 2) that aqueous concoctions of all manner of plant and animal products were used as a convenient source of animalcules by naturalists. The origin of such infusorians became a question of central importance to biologists of the 19th century.

No single subject so captivated the attention of experimentalists as the controversy over the putative spontaneous generation of microbes in putrid fluids (see references 6, 8-10, and 24). In his treatment of the subject, Loeffler focuses on the influence of air on the appearances of microbes in putrescible materials. After outlining the early work of Lazzaro Spallanzani, L. Joblot, and John Turberville Needham in the 18th century, he describes the experiments which F. Schulze conducted in 1838 to determine whether or not air was necessary to vivify an organic infusion. These experiments, in which air had to pass through a strong acid before entering flasks of heated infusions, were hard for others unequivocally to repeat and were followed by those of Theodor Schwann, in which air was allowed to enter flasks of sterilized infusions only after it had been heated.

Proponents of spontaneous generation could object to the experiments of Schulze and to those of Schwann on the basis that the vigorous chemical (acid) and physical (heat) means used to rid the air of germs could just as likely destroy its nonviable but vivifying ability. H. Schroeder and T. von Dusch countered this objection by filtering the air entering their experimental flasks through cotton wool. Although such experiments would seem to answer all possible objections of the heterogeneticists, a series of studies by Hoffman and by Pasteur finally ended the air controversy and proved that air by itself could not activate a sterile infusion to produce life. These studies involved the use of containers whose necks were drawn out and bent down. The heated infusions in such containers thus had free access to air, but the microbes within the air could not ascend the neck.

With these decisive experiments, Loeffler ends his brief treatment of spontaneous generation and does not return to the topic.

The appearance of blood-red spots on wheat products must have startled early observers. I first heard the phrase “drops of Christ’s blood on the communion wafers” used by O. A. Bushnell (University of Hawaii) to describe these spots in a lecture to beginning students of bacteriology at the University of California at Los Angeles in the summer of 1953; the drops of blood on the wafers were caused by the red-pigment-producing bacterium Serratia marcescens, whose history has been recorded in reference 12. Such distinctive colors led easily to speculations about the specificity of their causes, but efforts to establish such speculations on solid cultural grounds were rarely successful and may have been convincingly accomplished only by Joseph Schroeter in some of his classical studies on pigment-forming bacteria (lecture 8) (4, p. 220).

Of more far-reaching significance to a concept of separateness of bacteria was the monumental work of L. Pasteur on various types of fermentation and on undesirable taste or texture changes in beer and wine. Pasteur’s work, and much has been written about it and about him (see reference 7). Loeffler presents (lecture 5) an overview of Pasteur’s research on the specific causative agents of various fermentations, putrefactions, and diseases of wines. Rather than provide a comprehensive coverage of Pasteur’s work, Loeffler describes just enough to bolster his argument for distinctiveness among microbes as manifested by the different sorts of fermentation they produce.

**Microbes in Morbid Processes**

The third source of information regarding distinctness among bacteria was derived from studies on their
relation to morbid processes. The doctrine of a *contagium animatum* had its origin long before the invention of the microscope or the first glimpse of a bacterium by Leeuwenhoek (5, p. 372-373). Although Leeuwenhoek himself made no application of his microbes to a doctrine of contagion (a point emphasized by Loeffler in lecture 1), this connection was soon made by others (5, p. 373). Thus, Leeuwenhoek’s “little animals” became likely candidates for etiological agents of disease. This remained largely speculative until Agostino Bassi, in 1835, established that the muscardine of silkworms was caused by a fungus now known as *Beauveria bassiana* (1; 4, p. 159-161). This convincing demonstration of the causation of a specific disease by a distinctive microbe undoubtedly encouraged further work.

One example of such work noted by Loeffler was that of Alfred Donne on the occurrence of spirochetes in syphilitic chancres. Although Donne was unable to reach any conclusions about the significance of the organisms observed in syphilitic discharges, his observations had some influence on the development of thought in that period. However, a far greater impact was made by the writings of Jacob Henle, who, according to Loeffler, stated that for a microbe to be considered the cause of a disease, it must be (i) consistently found in association with the disease, (ii) isolated from the disease, and (iii) able to produce the disease in its isolated state. These precepts, which came to be more commonly known as Koch’s postulates because of the definitive way in which he used them in his studies on wound infections (15) and on tuberculosis (16), are clearly ascribed to Henle by Loeffler, who asserts that Henle’s statements were an important prelude to subsequent work on pathogenic bacteria. Other historians have agreed with him in this assessment (see, for example, reference 4, p. 165). However, a recent reappraisal of Henle’s contribution to concepts about the pathogenesis of contagious diseases suggests that he has received unmerited praise for his speculations (14). In fact, it is difficult to see how Loeffler derives the “3 criteria of etiologic significance” which he does from the vague writings of Henle quoted.

From 1850 onward, the number of observations in support of the concept of a living contagion increased greatly, and with this growth came also increasing confusion, founded largely on the inability of investigators to distinguish among microbes observed in pathological processes. Only the spirochete of relapsing fever observed by Otto Obermeier in 1873 and the remarkable *Sarcina ventriculi* discovered by John Goodsir in the vomit of some of his patients had forms sufficiently distinctive to be recognized by everyone. Of course, certain highly distinctive fungi had been associated with various dermatoses (1, p. 168-171; 4, p. 166), but the vast majority of morbid processes were colonized by forms no more distinctive than “dots” and “dashes.” The history of the resolution of this problem was Loeffler’s major concern.

The single disease which for a number of years occupied the attention of the greatest number of experimentalists was anthrax, a fatal disease of cattle and sheep caused by *Bacillus anthracis*. The rod-shaped anthrax bacillus was first seen by P. F. 0. Rayer in 1850 and, independently, by F. A. A. Pollender in 1849. Subsequently in 1875, C. J. Davaine claimed he had actually first seen the rods, which he called bacteridia, and had told Rayer (with whom he was seemingly associated) of the observation, which the latter included in his report to the Société de Biologie in 1850 (4, p. 179 ff).

Be that as it may, it is unquestionably true that the bacteridia found in the blood of animals with anthrax gained considerable notoriety largely through the research of Davaine, who from 1863 onward worked almost exclusively on the topic. His views aroused a great deal of interest, and several investigators criticized his conclusions because they were unable to repeat his findings. Principal among such detractors were E.-C. Leplat and P.-F. Jalliard (4, p. 181-182). These two investigators injected experimental animals with anthrax blood which contained organisms that resembled Davaine’s bacteridium, but although the animals died of what they called anthrax, the blood from the dead animals did not contain bacteridia. Therefore, they denied that the rod-shaped organisms described by Davaine were actually the cause of anthrax.

Further doubt was raised by Paul Bert, who concluded from his experiments that a toxin was involved in anthrax and that the bacteridium was not the actual cause. At this time (1877) Pasteur and J. Joubert began their studies on anthrax. They cleared up some of the difficulties by showing that unless carefully obtained, anthrax blood became putrid. Thus, in experimental infections one might observe anthrax with bacteridia, anthrax and sepsis with other sorts of bacteria, or even sepsis alone with no bacteridium. In the meantime, R. Koch had begun his work on anthrax. In a letter to F. Cohn, dated 22 April 1876, he related the complete life cycle of the anthrax bacillus, established its etiological role in anthrax, and showed how the resistant endospores which it formed could explain certain puzzling aspects of the epidemiology of the disease.

The anthrax saga has been told elaborately by others (4, p. 179 ff; 21; 22), but it is still fascinating to read it again as related by Loeffler, who concludes part 1 of his work in 1878, just 2 years after Koch’s classic work on anthrax was published.

In addition to these studies on anthrax, the concept of living agents of disease received considerable bolstering from the exhaustive studies of Pasteur on the disease of silkworms known as pebrine and from the extensive applied studies of the English surgeon Joseph Lister. Acting on the research of Pasteur on spontaneous generation, Lister practically single-handedly developed the antiseptic approach to combating surgical sepsis. Actually, as Loeffler points out, Jules Lemaire had suggested the use of phenol to control sepsis before Lister, but it is the latter who established the usefulness of the procedure in the surgical amphitheater.
Apart from the few cited examples of infectious diseases successfully investigated, most of the efforts with other disease entities had been frustrated by ambiguity, confusion, and bitter, unresolved controversy. Hallier’s culture work, alluded to above, had led him to conclude that the fundamental element of infectious fungi was a small micrococcus, and structures interpreted to be these small cocci were subsequently found in all manner of disease by eager investigators. However, it was soon realized that unstained morbid tissues abounded with structures which could easily be mistaken for viable particles. Moreover, researchers were embroiled in the controversy over whether it was the micrococi, i.e., the particles themselves, or substances (toxins) that they elaborated which were the fundamental causes of disease.

A. Chauveau, by means of an ingenious series of experiments described in some detail by Loeffler, established that the activity of smallpox vaccine was associated with the solid particles rather than the fluid. However, others asserted that the ability of putrid fluids to cause experimentally injected animals to sicken was due to an extractable toxin or poison rather than the microbes contained therein. Such contradictions led to efforts to cultivate the microbes separately and use “pure” cultures in animal studies.

The first attempts to obtain separate cultures of pathogens were made by E. Klebs in 1873. His culture studies are described in elaborate detail by Loeffler (lecture 7). In spite of the great energy which Klebs expended, he never obtained pure cultures, and his culture work, like that of so many others who tried, was made useless by his inability to avoid external contamination or the impossibility of extracting a single form from the mixtures of organisms with which he had to begin.

The frustration of investigators over unrepeatable experiments, such as those of Hallier, Billroth, and Klebs, led ultimately to a rejection of the idea that microbes were etiological agents of disease and to the assertion that the bacteria were the consequence, not the cause, of disease.

Nevertheless, although their significance was debated, bacteria were indeed found in morbid processes, and they were seemingly identical to forms seen by microscopists in putrid infusions. The history of the doctrine of contagium animatum has no more confused chapter than that in which conclusions were derived from experiments involving the injection of putrid materials into experimental animals. Such an experimental approach arose from a consideration of the fact that wounds become infected and putrefied, and that this putrefaction resembled in appearance, odor, and microbial content that seen in other sorts of materials undergoing the putrid process. But putrefaction was considered to be a single microbial process, and the effects of injecting putrid materials were diverse. How was one to explain the origin of these differences? Either the bacteria themselves must have been different, for which there was little compelling morphological evidence, or they must have elaborated various chemical poisons which differed quantitatively and qualitatively.

Loeffler presents (lectures 13 through 16) a fascinating view of this welter of confusion, including arguments over the augmented virulence of blood passed in animals, Billroth’s phlogistic zymoid, further experiments on separating bacteria from the fluid in which they had grown, the controversy over whether or not bacteria are found in normal tissues, and many other issues. Loeffler finally concludes his survey and resolves the confusion with the definitive work of Koch on the etiology of traumatic wound infection. Koch described six different infectious diseases, two in mice and four in rabbits, which followed the injection of putrid fluids. He proved that each of these diseases was caused by a specific bacterium which had definite and distinguishable morphological and biological properties, he established that there were pathogenic and nonpathogenic bacteria which had in common only the fact that they occurred in the same fluid, and he showed that the concept of augmented virulence of blood specimens upon passage in experimental animals was incorrect and that blood achieved maximum virulence when the bacteria were in pure culture within it, usually after one or two passages.

The precise work of Koch, which laid the foundation for the extraordinary succession of discoveries of etiological agents of disease made in the last quarter of the 19th century, was based to a considerable degree on major advances which he made in methods for fixing, staining, and photographing bacteria. It is with these studies that Loeffler concludes his book. In a few more years Koch would go on to develop methods of pure cultivation that would totally revolutionize the study of infectious disease. Loeffler simply hints at these advances and implies they will appear in part 2 of his work. Alas, it never came out, and we are left with the hint and with his description of Lister’s dilution method for obtaining pure cultures, still used in modified form in some procedures (20), and Salomonsen’s capillary culture tube method for separating bacteria in putrid blood (4, p. 225).

Conclusion

These are the major elements of Loeffler’s work, a monumental summary of a vast literature of his time, in which inadequacy of techniques often contributed to the welter of conflicting ideas. Loeffler dealt effectively with this confusion and presents to us a reasoned document which reveals what it was like at the frontiers of mid- to late-19th-century microbiology.

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