Homage to Ferdinand J. Cohn, Driving Force in the Emergence of Modern Microbiology

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The history of microbiology spans almost 350 years, starting with the discoveries of Robert Hooke and Antoni van Leeuwenhoek in the 17th century (Gest 2004, 2009a). From my studies, I conclude that "modern" microbiology emerged in the late 19th century from the singular efforts of a relatively small number of gifted investigators. Prominent among them were: Ferdinand Cohn (1828-1898), Louis Pasteur (1822-1895), Robert Koch (1843-1910), Martinus Beijerinck (1851-1931), and Sergei Winogradsky (1856-1953). This essay focuses on Cohn, who is not well known to most contemporary microbiologists still active in research. Pasteur and Koch are much more familiar; they are lauded, even in the skimpy historical sections of current textbooks. The important roles of Beijerinck and Winogradsky in developing understanding of microbial ecology, diversity, and chemical activities of microbes in the biosphere are discussed in Gest 2009b and 2009c. Here, I focus on Cohn, who deserves to be remembered and celebrated as a "prime mover" into the modern era.

How important scientific discoveries are made

Cohn was a truly creative scientist in pioneering the development of "modern" microbiology at a particularly important time. "Spontaneous generation" of microbial life was a major topic of current discussion and Cohn's discoveries were crucial in ending the debate. The sources of creativity in science and art was of special interest to Max Perutz (Nobel Laureate 1962), who pinpointed their major features (Perutz 1989): "Great scientists and artists have one [other] trait in common--they both tend to be single-mindedly devoted to their work. Renoir painted every day of his life, and when old age made his fingers too arthritic to hold a brush, he got someone to tie the brush to his hand. Haydn rose early each morning to compose; if ideas failed him, he clasped his rosary and prayed until Heaven sent him fresh inspiration. Tolstoy rewrote *War and Peace* seven times. When Newton was asked how he had arrived at his insights, he answered 'By keeping the problem constantly before my mind.' There is little benefit in following scientists' daily grind but much in tracing the unique combinations of theoretical knowledge and manual

skills, the web of personal encounters and accidental observations , the experience, temperament, moods and clashes that go into the making of discoveries, even though the crucial leap of the mind is often impenetrable." There is no doubt that Cohn had the creative gift, as well as energy, drive, and foresight.

From botany to microbiology

The present article presents an account of Cohn's life and important accomplishments, and also provides references to pertinent literature. I begin with a condensed "biographical notice" from William Bulloch's great classic of 1938…The History of Bacteriology:

"COHN, Ferdinand" (born 1828, died 1898). Great German botanist and one of the founders of bacteriology. Born in Breslau, where he was for many years Prof. of Botany. He early took to the study of microscopic algae and fungi and made many important discoveries. From 1860 onwards devoted himself particularly to the study of bacteria and became the leading authority on the subject. He was one of the first to hold that bacteria can be arranged in genera and species which exhibit a high degree of

constancy. Much of our knowledge is based on his work. He supported Pasteur's ideas on spontaneous generation in opposition to Pouchet and Bastien, and first clearly described bacterial spores. He wrote a great deal and most of it was accurate. He discovered Robert Koch and befriended him. In Cohn's *Beiträge zur Biologie der Pflanzen* appeared many of the classical papers on bacteriology by Cohn, Schroeter, Koch, and others. Cohn was a man of great diligence and talent and personally a fine character."

In discussion of Cohn's research, Bulloch also comments: "His researches were the result of many years laborious work and he was successful in disentangling almost everything that was correct and important out of a mass of confused statements on what at that time was a most difficult subject to study. *His work was entirely modern in its character and expression, and its perusal makes one feel like passing from ancient history to modern times* [my italics]. He was clear, explicit, and fair in his judgment to other workers, and on every page it is apparent that he wrote from first-hand knowledge. In his paper of

1872 he at once raised the fundamental question whether, like other plants or animals, bacteria can be arranged in genera and species."

It is relevant that a number of fundamental aspects of bacterial evolution, classification, and nomenclature are still unresolved (e.g., there is still no generally accepted definition of a bacterial species). In 1946, C.B. van Niel wrote an important essay on these subjects in which he reviewed Cohn's ideas. Van Niel noted "….Cohn appreciated the great significance which attaches to a stable and generally accepted nomenclature," and described Cohn's contributions "for the time he worked, masterly: he furnished sufficiently complete descriptions of several species so that the organisms could be recognized by others, using the same general approach, and he supplied a sort of key for the allocation of a bacterium to one of the six genera which he proposed and consolidated into four tribes."

The first journal that can be understood as a microbiological journal in the modern sense was established and published by Cohn himself…Beiträge zur

Biologie der Pflanzen [i.e., Contributions to the biology of plants]. Volumes 1 and 2, dated 1875-1877, were bound together and contained 235 pages devoted to basic research on bacteria. Cohn was the author of 188 pages, and Robert Koch authored a 31 page paper describing his epoch-making discoveries on the etiology of anthrax. One of Cohn's papers included a section on the behavior of bacteria to "extreme temperatures," foreshadowing current preoccupation with "extremophiles" by about a century.

Cohn's academic career

The following is a composite of accounts based largely on Bulloch (1938), a profile in the Dictionary of Scientific Biography by Geison (1971), and papers by Gerhart Drews (see below).

Cohn began studies of natural sciences (major subject, botany) in Breslau in 1844. His application for the doctoral program at the university was refused because of his Jewish faith. Undaunted, he proceeded to the University of Berlin in 1846 and received his doctorate in botany in 1847, at the age of 19. He returned to Breslau where he completed a second dissertation (Habilitation) and became a lecturer in

1857. Eventually, in 1872, he was promoted to full professor rank. Meanwhile, he had agitated for establishment of an institute of plant physiology. “In 1866, the Breslau authorities finally acceded to Cohn’s long-standing request and acquired a nearby building that had once been a prison. In these inauspicious surroundings Cohn founded the first institute for plant physiology in the world, and soon launched the second great creative period of his career….About 1870, Cohn turned his attention primarily to bacteria, and it is for his researches in this area that he is best known. In 1870 he founded a journal, *Beiträge zur Biologie der Pflanzen*, designed primarily to publish the work that came out of his institute. In this journal appeared the founding papers of modern bacteriology” (Geison 1971).

Cohn and Robert Koch

As indicated earlier, Cohn was instrumental in launching Koch’s transformation from country doctor to great fame (Nobel Prize 1905). Bulloch: “We are introduced to Koch by Ferdinand Cohn (1876), who tells us [*in Beiträge*] that it was with great pleasure that he received

a letter, dated 22 April 1876, from Dr. Koch to the effect that after prolonged investigations he had discovered the complete life-history of the anthrax bacillus, and that he was prepared to come to Breslau to demonstrate his work to Cohn. The meeting took place in Cohn's institute on 30 April 1876, and lasted three days, in which time Koch completely convinced his audience of his discovery. The occasion is historic….Koch's discovery, published (1876) under the aegis of Ferdinand Cohn, immediately became widely known, and it was at once recognized that a great investigator had arisen in the field of bacteriological research. The early hopes raised by Koch's first publication were not frustrated, for, along with Pasteur, he remains to-day the greatest exponent of bacteriological science. In connection with his rise to fame I cannot refrain from adding a tribute to the memory of Ferdinand Cohn, who behaved towards Koch in a most generous way. Along with [Julius] Cohnheim he was largely responsible for giving Koch a proper start in his scientific career, and they did everything in their power to further his worldly interests

and set him free from the hum-drum of medical practice so that he could get scope for his great talents."

The historic 1876 letter from Koch to Cohn is included in the biography of Cohn by his wife Pauline (Cohn, P. 1901). Brock's biography of Koch (1998) gives an English translation of the letter, which follows:
"Honored Professor!

I have found your work on bacteria, published in the *Beiträge zur Biologie der Pflanzen*, very exciting. I have been working for some time on the contagion of anthrax. After many futile attempts I have finally succeeded in discovering the complete life cycle of Bacillus anthracis. I am certain, now, as a result of a large number of experiments, that my conclusions are correct, However, before I publish my work I would like to request, honored professor, that you, as the best expert on bacteria, examine my results and give me your judgment on their validity. Unfortunately, I am not able to send you preparations which would show the various developmental stages [*including spores*] as I have not succeeded in conserving the bacteria in appropriate fluids. Therefore, I earnestly

request that you permit me to visit you in your Institute of Plant Physiology for several days, so that I might show you the essential experiments. If this request is agreeable to you, perhaps you might inform me of a suitable time that I could come to Breslau.

Very sincerely yours,

Dr. Koch, Kreisphysikus"

Koch's title indicates that he was in practice as a District Medical Officer for the province of Wollstein, Prussia.

Cohn's career and contributions reviewed by G. Drews

Two lengthy articles by microbiologist Gerhart Drews (1999, 2000) review Cohn's personal life, scientific career, and impacts on the development of microbiology. The 1999 article covers Cohn's botanical research on plants and microalgae thoroughly; 153 references including a comprehensive list of Cohn's major publications. His 2000 paper has a somewhat different perspective, which is evident from the title; the paper discusses scientific progress in biology and chemistry in the 17th and 18th centuries and then focuses on the 19th century in respect to early classification of microorganisms, concepts of

taxonomy, and the "spontaneous generation of living organisms" controversy. He gives a detailed history of the latter because Cohn played a major role (together with Pasteur and Tyndall) in its demise. One of Cohn's major discoveries was the fact that certain bacteria produce heat resistant spores, especially *Bacillus* species. "The results of Cohn and Tyndall explained many of the controversial results of the advocates and opponents of the doctrine of spontaneous generation, especially the observation that hay infusion, which very often contains heat-resistant spores, resists boiling" (Drews 2000). Bulloch (1938) devotes 58 pages to this topic!

Discovery of spore formation in bacteria

An English translation, by Thomas Brock, of one of Cohn's classic research papers became available in 1961 (see Suggested Reading). Part of one section of the paper describing the formation and generation of spores of *Bacillus subtilis* is an excellent example of Cohn's astute observations and clear writing style:

"The process of spore formation can only be observed by careful observations with very strong immersion systems.

Although the *Bacillus* filaments seem to be without cross walls even under the strongest magnification, this is in reality not the case. The single members which make up the filament are four times as long as wide. In each member a spore develops, which does not fill the cavity completely, but is separated from the empty cell membrane on each side. The spores are 1.5-2.2 microns long and 0.8 microns wide….In their development they seem to resemble those of Nostocaceae (*Cylindrospermum, Nostoc. Spermosira,* etc.) the most. Depending on whether the *Bacillus* filaments are shorter or longer, out of two or more members, we find the spores in a filament arranged in short chains of two or more. By decomposition of the *Bacillus* filaments, single members become isolated which contain only single spores. When these have completely separated from their mother cell, they show a delicate, jelly-like enclosure (spore membrane) and a strongly refracting interior…. With the maturation, release and settling out of the spores, the development of the *Bacillus* is ended and no further changes take place in the hay infusion…."

The same paper gives Cohn's account of the extraordinary visit of Koch to Breslau: "To my great pleasure, I received a letter from Dr, Koch in Wollstein on 22 April. He has been occupied with studies on the anthrax contagium for a long time and has finally been able to discover the complete life cycle of *Bacillus anthracis*. He was willing to demonstrate this to me at my plant physiology institute and obtain my opinion of his discoveries. Dr. Koch came to Breslau from 30 April to 3 May and with anthrax material he had brought along performed in our institute inoculations into living frogs, mice and rabbits. Through this series of experiments I was given the opportunity to convince myself of the complete correctness of his discoveries on development of the anthrax bacillus…. Herr Dr. Koch reports the results of his experiments at the end of this paper and indicates the highly important conclusions which these studies yield for the nature and spread of the anthrax contagium. I will only remark here that the life history of the anthrax bacillus agrees completely with that of the bacillus of hay infusions. Indeed, the anthrax bacillus does not have a motile stage,

but otherwise the similarity with the hay bacillus is so perfect that the drawings of Koch can serve without change for the clarification of my observations, and some of my drawings could serve as illustrations of the of the anthrax rods." *In fact, the figures for the paper by Cohn are on the very same published plate with those of Koch's succeeding paper on B. anthracis.*

Cohn and Charles Darwin

Cohn had an active correspondence with Darwin from 1874 to 1882, largely on botanical subjects. Darwin obviously was impressed by Cohn's wide knowledge and research acumen. Cohn clearly understood the great importance of Darwin's observations and theories, but did not hesitate to criticize certain conclusions of Darwin on plant physiology. Their correspondence has been documented by T. Junker and M. Richmond in the form of telegraphic summaries (in English) of the subject matter of each letter [Charles Darwins Briefwechsel mit Deutschen Naturforschern; Basilisken-Presse, Marburg an der Lahn, 1996]. Some relevant examples follow.

From Cohn, 21 Aug 1875: Acknowledges presentation copy of *Insectivorous plants*. Studying *Drosera* on vacation in Bohemia. Thinks CD has erred in considering 'aggregation' to have occurred in the protoplasm. Suggests it is result of exosmosis of vacuole.

To Cohn, 24 Aug 1875. Thanks for good opinion of *Insectivorous plants.* Responds to FJC's criticism regarding 'aggregation' as it occurs in protoplasm.

To Cohn, 26 Sept 1876. Invites him to visit Down.

From Cohn, 31 Dec 1876. Acknowledges presentation copy of *Cross and self fertilization.* Thanks for visit to Down. Praise for CD's theories. *The visit by Cohn and his wife is described by Mrs. Cohn in her biography of FJC.*

From Cohn, 31 Dec 1877. Sends details of Robert Koch's work on bacteria, including the first photographs. Sanderson's and Koch's collaboration on systemic fever. Thinks movement of Francis Darwin's *Dipsacus* filaments is an artifact.

To Cohn, 3 Jan 1878. Comments on discovery of micro-organisms in disease. Describes experiments carried out by Francis Darwin on the filaments of *Dipsacus.*

From Cohn, 26 Dec 1880. Response to *Movement in plants.* Setting out to confirm CD's experiments. Believes plant cell motion, like that of animals, depends on protoplasm more than water.

Cohn and bacterial species

Drews (1999) summarizes Cohn's conceptions of bacterial species at length. Thus: "The first of his comprehensive articles on bacteria (1875) was a critical evaluation of the available data on shape and properties of the four groups of bacteria he proposed: I. Sphaerobacteria (sphere-shaped) *Micrococcus,* II. Microbacteria (rod-like) *Bacterium,* III. Desmobacteria (filamentous bacteria) *Bacillus, Vibrio,* and IV. Spirobacteria (screw-like bacteria) *Spirillum, Spirochaete*....Cohn designated the new genus *Bacillus* and the formation of endospores (light-scattering bodies) as a possible stage of propagation."

What is a bacterial species?

As a student in van Niel's renowned microbiology course (in 1947), I quickly learned that van Niel (like Cohn) had a clear-cut *practical* understanding of what a species is. He was fond of quoting the famous remark of

mycologist Oscar Brefeld: “If one does not work with pure cultures, you end up only with nonsense and *Penicillium glaucum* (i.e., *blue mold*).” What is a pure culture? It is commonly understood to be a culture of morphologically homogeneous cells, derived from successive single colony transfers, that show a consistent profile of physiological and biochemical characteristics. Such pure cultures gave us the ca. 7000 organisms, regarded as species, which are in bacterial culture collections. Arduous experimental studies of the properties of these organisms provided the basis of a “Mt. Everest” of contemporary molecular biological speculations.

100 years later; *Bacillus* spores, a model system for research in developmental microbiology

The Royal Society of London Leeuwenhoek Lecture for 1975 was delivered by Prof. Joel Mandelstam (1919-2008) on “Bacterial sporulation: a problem in the biochemistry and genetics of a primitive developmental system.” [see Mandelstam 1976]. The lecture summarized an impressive series of investigations by Mandelstam and his colleagues at the University of Oxford [Microbiology

Unit of the Biochemistry Dept.] They analyzed the complex series of morphological, biochemical and genetic events that occur in the formation of spores by *Bacillus subtilis*. Further progress during the following decade in defining the sequence of gene expression in spore formation (regulated by at least 50 operons!) was described by Mandelstam and Errington in 1987. In the same year, Gest and Mandelstam (1987) reported observations on the longevity of bacterial spores in natural environments. We also conducted experiments to test the possibility that the survival of *Bacillus* spores over very long periods of time might be limited by the lethal effects of natural radiations. We concluded that the calculated half-life of the stored *B. subtilis* spore population that we tested would be about 7000 years. "Using this value, and assuming an exponential rate for death resulting from radiation damage, it can be estimated that a population containing 10^{10} spores initially would have a measurable number still viable after 200,000 years."

CODA:

I am indebted to Prof. Donald A. Klein (Colorado State University) for bringing my attention to Cohn's unusual efforts to communicate the latest scientific advances to the public: "In 1872, he wrote a delightful essay for non-specialists entitled 'Bacteria, the smallest living organisms.' An English translation by C.S. Dolley was published by the Johns Hopkins Press in 1939. According to Dolley, this was one of the 'earliest (such) works to be translated into English,' and had a wide-spread influence on making information on the new field of bacteriology available to Americans."

Recognition of Cohn's eminence

Geison (1971) notes a number of honors awarded to Cohn: "Cohn held an honorary doctorate from the faculty of medicine at the University of Tübingen and was named a corresponding member of the Accademia dei Lincei in Rome, the Institut de France in Paris, and the Royal Society of London [*Note: he was named a Foreign Member of the Royal Society in 1897*]. In 1885 he was awarded the Leeuwenhoek Gold Medal and in 1895 the Gold Medal of the Linnean Society."

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