

## The Historical Development of Medical Bacteriology

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If one were to review the early historical developments of medical bacteriology one would readily note that its forerunners were the ancient ideas of superstition. Primitive man regarded disease as an evil spirit to be cajoled by burnt offerings and sacrifices. Symptoms were nothing more than outward manifestations of the activity of the supernatural agents.

Scientific development of medicine begins with the great Greek physician, Hippocrates (460-370 B.C.) who postulated disease as the improper mixture of the four bodily humors; blood, phlegm, yellow and black bile. Because Hippocrates gave the science of medicine its ethical ideals and virtually founded the bedside method, by common consent, he is known as the "Father of Medicine". Hippocrates' teachings were dominant all through the middle ages although supplanted to some extent in the 17th century by the theories of Homeopathy of Samuel Hahnemann (1755-1843). Disease according to this theory "is a spiritual dynamic derangement of a spiritual vital principle". He believed that medicines enhanced in strength by diluting, especially if the dilution was accompanied by shaking and that some drugs gained in potency by pounding. Accordingly, Hahnemann diluted his tinctures fifty times, these were again diluted fifty times and so on even to the thirteenth dilution to which he ascribed the highest potentiality.

The greatest scientist after Hippocrates was Aristotle (384-322 B.C.), the great Greek philosopher and a student of Plato. He introduced the beginnings of zoology, comparative anatomy and embryology to medicine.

Theophrastus of Eresus (372-287 B.C.), the "Father of Botany", a pupil of Aristotle, put the loose plant-lore of the woodmen into a systematic treatise.

Aretaeus, the Cappadocian, a Greek physician who lived at Rome in the second half of the second century A.D., applying the method of Hippocrates, developed clinical medicine and presented us with graphic accurate pictures of such diseases as pneumonia, diabetes, lock-jaw and diphtheria.

Caius Pliny (23-79 A.D.), the natural historian, gave us all that was known in his time of geography, meteorology, anthropology, botany, zoology and mineralogy.

The next great figure of this ancient period was Claudius Galen (131-201 A.D.). He was the first experimental physiologist. He also gave us the classic symptoms of inflammation, differentiated pleurisy from pneumonia and described the different forms of tuberculosis.

The outstanding individual after Galen and before Harvey undoubtedly was Andreas Vesalius (1514-64) who established anatomy as a working science.

By far the greatest name of the seventeenth century is that of William Harvey (1578-1657) who in 1626 discovered the circulation of the blood. Following the announcement of this theory of circulation his practice dwindled, the ignorant regarding him as crack-brained. He died, however, an appreciated and honored man.

It was impossible to see the causative agents of infectious diseases without a microscope. The first glimpses into the mysteries of this unknown realm were, of course, simultaneous with the discovery of the microscope. The English monk, Roger Bacon (1214-94), in 1276, appears to have been the first to recognize the peculiar properties of a lens and applied it to the construction of spectacles. It was not, however, until the beginning of the 17th century that the microscope was sufficiently perfected to bring about the existence of microscopic life. The discovery of the compound microscope may be said to have been made by the Italian astronomer, Galilei Galileo (1564-1642), in 1610, although it is probable, that others may have antedated him by a few years.

The earliest one to investigate this invisible world was a Jesuit priest by the name of Athanasius Kircher (1602-80). To him we owe the first clearly presented germ theory of disease, though, the Italian physician Girolamo Fracastor (1483-1553) in 1546, published his ideas on the theory of contagion. In 1660 bubonic plague was raging in London and was common in Europe. Kircher announced that he had seen the organisms in the blood of pest victims. With his very crude 32-power microscope he at best only saw pus or blood cells. The plague germ was not discovered until 1894.

The early compound microscope consisted of a single lens for an objective and of another single lens for an eye-piece. Such an instrument necessarily gave very imperfect results. However, the real value of the microscope as an aid in scientific research dates from the time Charles Chevalier of Paris (1804-59) introduced the method of correcting chromatic aberration in 1825. Antony van Leeuwenhoek (1632-1723), the "Father of Microscopy", who definitely laid the foundations for bacteriology, attracted wide attention by his expertness in lens grinding and did much in developing the microscope into a workable instrument. He made some four hundred biconvex lenses some of which magnified about three hundred diameters. He observed yeast cells in fermenting liquids and swarming organisms in putrid masses. He believed that fermentation and putrefaction was the work of these microorganisms. He was made a fellow in the Royal Society in 1680.

A mechanical genius by the name of Robert Hooke (1635-1703) was another early worker with the microscope. In 1665 he published his famous *Micrographia* and stimulated much interest in microscopy.

One of the greatest microscopists was Marcello Malpighi (1628-94), known as the founder of histology. He accomplished much by his microscopic investigations of the embryology of the chick and visera in general.

The microscopic world was unknown to the great Swedish botanist, Carolus Linnaeus (1707-78), who systematized the classification of plants and animals. He discovered a disease, anthrax, in Siberian reindeer and said it was caused by a living contagion.

A Viennese physician, Marcus Plenciz (1705-86), carrying on the work of van Leeuwenhoek, in 1762 published his theory in which he stated that every disease had its own particular set or agent. Proof of these facts, however, had to wait over 100 years.

The next great naturalist interested in this field was the Danish zoologist, Otto Müller (1730-84). Because of his masterly pioneering work, "Animalcula infusoria" in which he excellently illustrated many microorganisms, their motility and other unique characteristics, he is referred to as the first scientific microscopist.

Hundreds of years before Christ, artificial immunization was practiced in folk-medicine against smallpox. Lady Mary Wortley Montagu (1680-1762) introduced it in London from Constantinople in 1720. It eventually led to one of the greatest triumphs in the history of medicine, the successful introduction of preventive inoculation, came toward the end of the eighteenth century. Edward Jenner (1749-1823) observed that dairy maids who had contracted cowpox from milking did not take smallpox. He mentioned this to the renowned Dr. John Hunter (1728-93), who on August 2, 1775 made his famous reply; "I think your solution is just; but why think? Why not try the experiment?" On May 14, 1796, he performed his first vaccination upon a country boy, Thomas Phipps, using material from the arm of the milk-maid, Sarah Nelmes, who was suffering from cowpox. On July 1st, Phipps was inoculated with smallpox virus and the immunization proved successful, for Phipps did not come down with smallpox.

The year 1837 was memorable in many ways. It was the first time in history that an organism was shown to be the cause of disease. Agostino Bassi (1773-1856), an Italian, demonstrated that the disease, known as muscardine affecting silkworms was caused by a fungus and was transmitted from the diseased to the healthy worm. Later, in the same year Charles Cagniard de la Latour (1777-1859) and Theodor Schwann (1810-82) independently, proved that the yeast cell produced alcoholic fermentation. It will be recalled that the renowned chemist, Justus von Liebig (1830-73) bitterly opposed this theory, stating that the so-called cells were by-products of a chemical phenomenon.

Christian Ehrenberg (1795-1876) published his systematic classification of microorganisms in 1838. He was the first to observe spores or eggs possessed by bacteria.

Matthias Schleiden (1804-81) and Schwann in 1836 announced their cellular unit of life theory. This expounds that tissues of all plants and animals are composed of units called cells and according to this theory a life composed of a single cell could not have organs comparable to those found in large multicellular creatures.

In 1842, at the time cholera was raging in Europe, the brilliant anatomist, Jacob Henle (1809-85) formulated rules which were independently stated by Robert Koch in 1881, whereby, the germ theory of disease could be demonstrated.

Ferdinand Cohn (1828-98), one of the founders of bacteriology, classified bacteria accentually the same as Ehrenberg. It was Cohn who discovered and encouraged Robert Koch.

It will be noted that the scientific advancements kept pace with the perfection of the microscope. The vast development along biologic lines at this time was mainly due to the theories of Darwin (1809-82). His "Origin of Species by Means of Natural Selection" was perhaps one of the outstanding pieces of research in the history of science out of which came the sciences of cellular pathology, bacteriology and parasitology.

The advancement of modern medical science is inseparably connected with the name of Rudolf Virchow (1821-92), the founder of cellular pathology. He succeeded Johannes Müller (1801-1858), medical naturalist, under whom he received his training as did Schwann and Henle, as the dominating figure in German medicine.

Aided by the discoveries of Pasteur, Lord Joseph Lister (1827-1912) was able to announce his principles of antiseptic surgery in 1867 which revolutionized surgery. He was not aware, however, of the work of Ignaz Philipp Semmelweiss (1818-65), who in 1846, 21 years previous to Lister's announcement, by the insistence of washing the hands with chlorinated lime before all examinations were made in maternity cases, caused death from infection pertaining to child-birth to fall to one-tenth of that in previous years. Semmelweiss was ahead of his time, was persecuted and died insane. The development of antiseptic surgery was necessarily one of the first triumphs of modern medicine.

The brilliant, adventurous and courageous Louis Pasteur (1822-95), the great French chemist and bacteriologist, is memorable for his work in 1848 on the optical activity of tartaric acid; the overthrowal in 1860-1 of the ancient theory of spontaneous generation; fermentation in 1857; research on anthrax and chicken cholera in 1877 and his preventive vaccination in 1880, particularly of rabies in 1885. His researches are the beginning of modern bacteriology. The Pasteur Institute was founded in Paris in 1888.

His contemporary, the meticulous, ingenious and patient Robert Koch (1843-1910), an obscure country physician, a student of Henle, in 1876 presented his methods of preparing and staining bacterial films. In the same year, he published his classical research on anthrax. In 1882, he announced his discovery of the causative agent of tuberculosis which was responsible for about one-seventh of all deaths. One of the greatest aids to the advancement of bacteriology was the introduction of his gelatin plate method of obtaining pure cultures of microorganisms in 1887. Koch received the Nobel prize in 1905. The establishment of modern practical bacteriology dates from his experiments. Following the announcement of his new isolation technique, bacteriology developed rapidly.

Georg Gaffky (1850-1918), the successor of Robert Koch in Berlin, along with Koch in 1883 found that the "comma bacillus" caused cholera and discovered how it was transmitted. In 1884 he was the first one to cultivate the typhoid bacillus on cultural media.

The beginning of serology and immunology was due mainly to Emil von Behring (1854-1917) and Sibasaburo Kitasato (1852-1931), who in 1890 were the discoverers of antitoxin. Kitasato, also, was the first to cultivate the bacillus of tetanus in 1889. Emile Roux (1853-1933) and Alexander Yersin (1863-1943), in 1888-90 discovered diphtheria toxin.

Roux was the first to use the horse to produce antitoxin on a large scale. Yersin and Kitasato working independently discovered the plague bacillus in 1894.

Friedrick Loeffler (1852-1915) and Paul Frosch (1860-1928) associates of Koch, in 1892 recognized the filter-passing character of the virus of foot and mouth disease. This was the beginning of searches for the nature of viruses, their peculiarities and immunological and serological reactions and the development of special techniques in dealing with this group of infectious agents. In 1884, Loeffler isolated the diphtheria bacillus and showed its etiological relation to the disease, although, Klebs in the previous year, described the bacillus which bears their names. Loeffler founded the "Centralblatt für Bacteriologie" in 1892.

Vaccinotherapy was originated by Metchnikoff, Wright and others. Elie Metchnikoff (1845-1916), a Russian zoologist, succeeded Pasteur as director of the Pasteur Institute in 1895. He formulated the theory of phagocytosis. In 1908, he was awarded the Nobel prize.

Sir Almroth Wright (1861-1946), demonstrated that blood contained substances (opsonins) that prepared bacteria for phagocytic ingestion and originated anti-typhoid vaccination.

In 1902, Charles Richet (1850-1935) and his associates first called attention to the vast subject known as "hypersensitiveness"—anaphylaxis, allergy, or idiosyncrasy, though, observations of this peculiar phenomenon appeared in the literature as early as 1835-37. Richet coined the term anaphylaxis (against protection) for this reaction. He was made Nobel prizeman in 1913.

Bordet and Wasserman introduced serodiagnosis. Jules Bordet (1870-1946), a Belgian, is known for his work on theoretical immunology and with Octave Gengou (1875-19-), discovered the phenomenon of complement-fixation. In 1919, the Nobel prize was awarded him. These bacteriologists discovered the causative agent of whooping-cough in 1906, which is known as the Bordet-Gengou bacillus. Bordet in 1898 discovered the phenomenon of hemolysis. August Wassermann (1866-1925), director of experimental therapy and biochemistry of the Koch Institute for Infectious Diseases, in 1906, attained great fame by developing the test for the diagnosis of syphilis which bears his name.

Paul Ehrlich (1845-1915), a Nobel prize Winner in 1908, and his followers, who laid the foundation for chemotherapy against parasitic infections, also pioneered in modern immunology. He presented the "Sidechain" theory of immunity; standardized diphtheria antitoxin and synthesized arsphenamine ("606").

Karl Landsteiner (1868-1946) was born and studied medicine in Vienna. Since 1922, he was associated with the Rockefeller Institute. He is especially known for his work in blood groupings and immunology and naturally, he contributed much in the field of medical bacteriology. He, too, was made a Nobel prizeman in 1930.

And so we can say that although diseases were known hundreds of years before Christ and much notable research has been attained, it, however, required such geniuses as Louis Pasteur and Robert Koch to develop methods whereby one could correlate and associate the micro-

organisms revealed by the microscope to the phenomenon they produced. Thus, the establishment and recognition of bacteriology as a cardinal modern practical science.