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Historical Diseases from a Modern Perspective

The American Experience

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For my wife, Nancy, whose companionship and love have brought joy to my life.

“Fortunate is he whose mind has the power to probe the causes of things and trample underfoot all terrors and inexorable fate.”

Virgil

Introduction

Note to Readers

James A. Shaw

Despite being a medical doctor, student of history, and fan of historical novels, I am often stumped when an author refers to *Ague*, *Ship Fever*, *Blue Death*, *Quincy*, *Scarlatina*, *French Pox*, *Consumption*, *Congestive Fever*, *Black Plague*, *Bronze John*, *Breakbone Fever*, etc., and am forced to make a trip to the Internet for clarification.[1] Not infrequently, ancient diseases and/or symptoms are inadequately or incorrectly described in historical novels and are often afforded superficial context in history books, where they are referred to somewhat peripherally. It is my hope that this short book will provide an informative reference for readers who are similarly puzzled when confronted with an unfamiliar disease in a novel or book of history.

Like COVID-19, the impact that yellow fever, malaria, smallpox, measles, polio, cholera, and 1918 pandemic influenza, among many others, had on Americans was profound and, in some cases, overwhelming. U.S. military campaigns, starting with smallpox in the Revolutionary War, dysentery in the Civil War, influenza in WWI, malaria in WWII, opioids in Vietnam, and sexually transmitted diseases across all wars, markedly impacted troop strength and preparedness. In many instances American physician-scientists identified the origins, transmission vectors, and cures for these diseases, which is fascinating history in and of itself.

I suspect that most readers are vaguely aware of the devastating impact of bubonic plague over the ages in the Old World. But how many realize a plague epidemic occurred in San Francisco in 1900, fortuitously controlled before becoming a pandemic by epidemiologists who identified rats as the reservoir of disease

[1] For example, David Grann refers to "saffron scourge," "bloody flux," "breakbone fever," "blue death," and "ship's fever" within the first chapter of his book, *The Wager: A Tale of Shipwreck, Mutiny and Murder* (Doubleday, New York, NY; 2023).

and fleas as the communicating vector? (A thriller story in its own right!) How many are aware that a few cases of plague still occur in the United States every year and that squirrels are a persistent reservoir of the disease?

How many are aware that smallpox nearly annihilated the Native American population and decimated Revolutionary War soldiers, polio was every parent's nightmare, cholera epidemics plagued U.S. cities, chicken pox "parties" were once common, and the 1918 influenza pandemic may have started in the United States and may have shortened the duration of WWI? I suspect very few realize that leprosy occurred in the United States or are aware of the horrors of pre-antibiotic treatment of this debilitating disease. How many know that the Centers of Disease Control and Prevention (CDC) had its inception in 1946, with one of its foundational missions to stop the spread of malaria across the nation?

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The history of diseases is intrinsically fascinating and may be of particular interest to readers in light of the recent COVID-19 pandemic. Most diseases have many interconnected aspects of historical importance—medical, social, economic, and political—which I have tried to condense into a few summary paragraphs for each disease covered. Intrinsic to such brevity is the risk of oversimplification, which I recognize as a potential concern. That said, any subject the reader finds of interest can be further clarified by an Internet search using any of the references listed at the end of each section, among many others.

The cited references were principally selected for their ready Internet availability, authoritative authorship, and content written at a level understandable by a lay audience. They represent only a small portion of the sources researched during the preparation of this book. Reference numbers appearing within or at the end of sentences refer, specifically, to that sentence's content, generally being a quotation or a disease incidence statistic. Those at the end of paragraphs refer more broadly to the subject matter within the preceding paragraph or paragraphs.

CDC and WHO prevalence and incidence data is cited by virtually all medical historians and researchers and I relied heavily on those two sources throughout the book. The Mayo Clinic, Cleveland Clinic, and Johns Hopkins references are included as authoritative sources of clinical information regarding disease presentation, diagnosis, progression, complications, and treatment. Similarly, the Merck Manual is written by recognized clinical experts and is a relied upon reference in the personal library of virtually every medical student and resident physician. Cited journal articles represent peer-reviewed research or subject reviews and are included for readers who wish a more detailed discussion of a particular aspect of the work summarized in the text.

Biographical profiles of prominent researchers and clinicians, written by the editors of the Encyclopedia Britannica and specialty museum curators, provide interesting historical background information. Lesser credentialed references and Internet videos were critically reviewed for accuracy before listing, and are included,

like others, for their clarity and/or readability. Footnotes list supplemental reading, either historical novels or history books of potential interest to the reader.

All included pictures and figures are drawn from the public domain, based on elapsed time from initial publication or from U.S. government institutions (NIH, CDC, Smithsonian, etc.). All can be found in multiple web sites, with the particular Internet source selected for this book credited in the picture caption as well as the artist and original source, whenever applicable or known.

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The book is divided into chapters, beginning with an introductory chapter outlining historical theories of disease causation, prevention, and cure, which is intended to provide some perspective and contextual understanding for the ensuing disease-specific chapters. Included chapters cover contagious diseases, vector-borne/zoonotic diseases, fecal-oral diseases, sexually transmitted diseases, substance use disorders, parasitic diseases, nutritional diseases, fungal diseases, and soil-related bacterial diseases of major historical impact afflicting Americans in the years predating the current era of disease identification, understanding, and treatment.

Contagious diseases are generally spread person-to-person by bacteria or viruses enveloped in respiration droplets, diffused into the air by an infected person during talking, sneezing, or coughing. Zoonotic diseases are spread from animals to humans by direct contact with the infected animal (or its bodily fluids), ingesting infected meat or animal-contaminated food or water, or by an intermediary vector ("vector-borne") such as mosquitoes, fleas, lice, and ticks.

Fecal-oral diseases are acquired by ingesting water or food contaminated by the feces of an infected individual. Commonly, drinking water is tainted by primitive (or non-existent) sewage systems and food by using human waste for fertilizer. An infected individual can unknowingly spread fecal-oral diseases by handling food or eating/cooking utensils without appropriate handwashing following a bowel movement.

Sexually transmitted diseases are communicated with the exchange of bodily fluids during sexual intercourse or by intimate contact with an open lesion (sore) associated with a particular disease. Substance use disorders are self-inflicted indulgences, often resulting in addictions. The two nutritional diseases discussed in the text are caused by inadequate dietary intake of an essential vitamin, specifically vitamins D and C.

Parasitic diseases are acquired through multiple modes including contact with fecally contaminated soil, insect vectors, ingestion of parasite contaminated food, and sexual intercourse. Fungal diseases are acquired by inhaling environmental fungal spores, contagious contact with infectious skin dermatophytes, or overgrowth of fungi normally inhabiting the skin or vagina. Soil-related bacterial infections are caused by soil contamination of open wounds, or by inhalation, ingestion, or skin contact with soil-indigenous bacterial spores.

Of note, the inclusion of a disease within a particular category is somewhat arbitrary in many cases. Malaria, for example, is listed as a vector-borne disease, which

it clearly is. However, it is a parasite sporozoite that the vector mosquito carries from person-to-person, so it could reasonably be included within the parasitic disease category, as well. Similarly, anthrax is a soil-related bacterial disease, but is most commonly contracted by contact with an infected animal or animal parts so could, alternatively, be included in the zoonotic disease chapter.

Of additional note, dates regarding the introduction of vaccines and antibiotics can be very confusing. There is often a long time period—sometimes spanning decades—between the laboratory identification of a viable vaccine or antibiotic and its licensed approval for general use. I have tried to be specific with respect to the dates identified, but have been purposefully vague in some instances as widespread use frequently predated final licensure, much like the COVID-19 vaccines were in general use under "emergency use authorization" long before final FDA approval.

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A recurring note of concern ends many of the disease sections throughout the text. The concern is the omnipresent threat of disease emergence or re-emergence in localized, epidemic or pandemic forms, potentially impacting the lives of many. The threat is very real and multifactorial, but centers on two principal areas of concern. The first is waning vaccine immunities in much of the world's population, including the U.S., coupled with the current trend of vaccine hesitancy. An unvaccinated or inadequately vaccinated populus is at grave risk, particularly in a global world where disease transmission from one area to the next is an ever-present possibility. Moreover, effective vaccines are not currently available for many diseases, representing a broad area of needed research and development.

The second concern is ever-increasing bacterial resistance to existing antibiotics. The emergence of "superbugs," resistant to multiple or all antibiotics, is almost a daily topic of headline news. Critics note the lack of new antibiotics to combat these organisms and the associated lack of research and development efforts and money to address this area of universal need.

Similarly, the emergence of insecticide resistant mosquitoes and other disease transmitting vectors has limited the ability of the World Health Organization (WHO) and other national and international health organizations to combat malaria and other vector-borne diseases. Climate change has lengthened the breading season and fostered the widespread dissemination of mosquitoes, ticks, and other insect vectors, further complicating international disease prevention efforts.[2] Additionally, the lack of monies committed by the global community for prevention and treatment of diseases has hampered many of the initiatives promoted by the WHO and other agencies.

Enjoy.

[2] The reader might find the article in *The Washington Post* (November 2, 2023) titled "Malaria's Deadly Reach is Growing" of interest. The article, written by Rachel Chason, Kevin Crowe, John Muyskens, and Jahi Chikwendiu, documents the alarming increase in malaria cases in Mozambique, attributed to climate change and the correspondingly longer breeding season for the *Anopheles* mosquito, principal transmitter of malaria between people.

Contents

About the Author

James A. Shaw is a recently retired academic orthopedic surgeon with more than 30 years of teaching, writing, and lecturing experience, accompanying an active clinical practice focused on hand surgery and joint replacement. He has published extensively in peer-reviewed journals, authored orthopedic textbook chapters, and has served on the review boards of several academic journals. He has been an invited speaker, moderator, and presentation commentator at many local, regional, and national/international orthopedic meetings.

Before entering medical school, Dr. Shaw received bachelor's and master's degrees in mechanical engineering from Cornell University and is the designer of two prosthetic knee replacements.

Dr. Shaw is an outdoor enthusiast, lover of travel, student of history, and a fan of historical novels. In addition to his ever-supporting wife, he is blessed with two wonderful daughters, both with PhDs in medically related fields, and three lively grandsons.

Chapter 1
Historical Theories of Disease Causation, Prevention, and Cure

Abstract An imbalance of vital humors (*yellow bile, black bile, phlegm, and blood*), first introduced by Hippocrates (460–370 BCE) and his followers in the fourth- and third-century BCE, remained the principal theory of disease causation well into the nineteenth century. Therapeutic corrections were focused on restoring humoral equilibrium through diet or purging—the latter achieved through bloodletting, emetics, diuretics, poultices, and laxatives. Diseases were felt to be acquired by inhaling foul-smelling air, referred to as the miasma theory of disease. Alcohol- and opioid-laced patent medicines flourished as "cure-alls" for virtually every type of disease.

The germ theory of disease, generally credited to the pioneering works of Louis Pasteur, Joseph Lister, and Robert Koch in the mid-1800s, reduced the understanding of disease to a simple interaction between a microorganism and host. Embraced more rapidly in Europe than America, antiseptic medical and surgical practices soon followed with a marked diminution of iatrogenic infections, as did more widespread attention to personal hygiene. Initially referred to as "non-filterable" disease-causing agents, viruses were definitively identified in the 1930s with the development of the electron microscope.

Vaccines were first introduced by English physician Edward Jenner in 1796 for the prevention of smallpox, followed over ensuing decades by vaccines for a large number of other diseases—many derived from killed or attenuated viruses. In 2020, modified messenger RNA vaccines were introduced, representing a new concept in vaccine development.

In 1909, the arsenic-based compound Salvarsan (arsphenamine) was introduced for the treatment of syphilis. Generally regarded as the first effective antimicrobial agent, Salvarsan was followed several decades later by sulfonamides, penicillin, and vast array of other antibiotics.

Current concerns referable to infectious diseases focus on ever-increasing microbial antibiotic resistance, waning vaccine immunities, vaccine hesitancy, and environmental changes favoring the propagation and spread of disease-transmitting insect vectors.

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Without question, the earliest theories of disease were based on religious or demonic beliefs, linking the misfortunes of man to divine retribution for sins committed—a concept that continues to percolate through the minds of many, to date [1, 2].

Be that as it may, the first to consider that diseases had natural (vs. supernatural) causes was Hippocrates (460–370 BCE) and his followers in the fourth- and third-century BCE. Hippocrates postulated that disease was caused by an imbalance of four vital humors: *yellow bile, black bile, phlegm, and blood*. Illness was thought to occur when there was an excess or deficiency in one of the four humors, a theory that persisted for another 2000 years, well into the nineteenth century [3].

Hippocratic diagnoses were based on observations of a patient's excretions of sweat, urine, blood, vomitus, and stool. Therapeutic corrections of imbalance were focused on restoring equilibrium through diet or purging—the latter achieved through bloodletting, emetics, diuretics, poultices, and laxatives.

Seemingly barbaric and likely harmful from today's perspective, bloodletting was the principal tool in the armamentarium of physicians from the time of the ancient Greeks to the latter part of the nineteenth century. Considered the dominant humor, blood irregularities were felt to be responsible for most illnesses and releasing bad humors through bloodletting was the accepted standard of treatment for virtually all maladies [4, 5].

Bloodletting was performed as a systemic release of bad humors through venesection or arteriotomy or, alternatively, through localized release, by scarification and cupping or by application of leeches. Thumb lancets or pocketknife-like fleams were used to puncture superficial blood vessels, commonly the median cubital vein at the elbow, for a generalized release (Fig. 1.1). Suction cupping techniques or leaches were used to withdraw disease-causing humors from localized lesions such as an infected wound or the bubo of bubonic plague.

A likely example of an unknowing malfeasance was the bloodletting performed on former president George Washington (1732–1799). Following a wintry horseback ride, President Washington came down with a fulminant throat infection, possibly epiglottitis. He died within 24 h and during that time period he endured four

Fig. 1.1 Colorized photograph of bloodletting, Circa 1860. (Picture Source: https://en.wikipedia.org. The Burns Archive)

Fig. 1.2 Washington on his deathbed, circa 1851. Junius Brutus Stearns (1810–1885). (Picture Source: https://www.daytonartinstitute.org. Dayton Art Institute)

bloodlettings, amounting to 2500 ml or approximately 40% of his blood volume (Fig. 1.2). Although unlikely the direct cause of his death, it certainly was of no benefit [4, 6].

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Evolving at some point in the Middle Ages, and persisting until the end of the nineteenth century, was the belief that the source of disease was *miasmas*. Simply put, malodorous vapors emanating from sewage-laden streets and waterways, swamps and wetlands, and putrefied body parts/lesions carried disease. Inhaling these smells caused illness. Emblematic of this concept is the origin of the name "malaria," which was derived from *mala aria*, Italian for "bad air" [7].

Arising from miasma theory were many ineffectual practices such as using smoky bonfires, burning incense, and wearing perfume to ward off diseases. Unwittingly, disease mitigation also benefited from miasma theory. Sewer systems were built, and swamps and wetlands drained to lessen miasmic smells, unknowingly eliminating the disease-causing bacteria which contaminated the drinking water and destroying the mosquito breeding grounds responsible for many vector-borne illnesses.

Although not understood from a modern perspective, the concept of disease contagion was well appreciated from the earliest of times—long before germ theory was first elucidated. In addition to miasmic transmission, early contagion theory suggested that diseases were spread by coming in direct contact with infected

people, clothing, bedding, and food (all considered disease spreading *fomites*) and the most effective control of disease transmission was through quarantine of sick persons.

Early references to quarantine practices include the banishment and isolation of persons afflicted with leprosy (referred to as "unclean") during Biblical times, as depicted in the book of *Leviticus* [8]. Ships suspected of carrying plague were often quarantined offshore for 30–40 days during the Middle Ages, a waiting period known as *quarantinario* from the Italian word for 40 [9]. During the 1793 yellow fever epidemic in Philadelphia (then capital of the USA), federal government personnel isolated themselves by evacuating the city rather than risk contagious infection [9]. Early immigrants to America who were suspected of carrying transmissible diseases were often sent to quarantine from Ellis Island—a practice which continues to date under authority of the CDC's Division of Global Migration and Quarantine [10].

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Germ theory revolutionized the practice of medicine, reducing the understanding of disease to a simple interaction between a microorganism and host. The French chemist and microbiologist Louis Pasteur, English surgeon Joseph Lister, and German physician Robert Koch are generally credited as the founding fathers of germ theory [11].

Louis Pasteur (1822–1895) is best known for his discoveries of microbial fermentation, pasteurization (which carries his name), and the foundational principles of vaccination. Based on a series of experiments on alcohol fermentation in the mid-1850s, Pasteur provided evidence that living organisms, not a series of inherent chemical reactions, caused the fermentation process. In 1865, he patented a method of heat sterilization to prevent spoilage of wine and other liquids. In milk, the process killed harmful bacteria, including the infective bovine tuberculosis organism, *Mycobacterium bovis*—representing a major advance in public health [12–14].

In related studies, Pasteur proposed that environmental microorganisms caused disease and infection, not an internal state of "humoral imbalance," or "spontaneously generated" microorganisms. Remarkably, he also discovered how to make vaccines from weakened/attenuated microorganisms, including the earliest vaccines against fowl cholera, anthrax, and rabies. In 1885, Pasteur and his colleagues successfully prevented a rabies infection in 9-year-old Joseph Meister, who had been bitten by a rabid dog, with a series of inactivated rabbit rabies virus inoculations [12–14].

Expanding on the work of Pasteur, Dr. Joseph Lister (1827–1912) postulated that environmental microorganisms colonized open (compound) fracture wounds, causing infection and sepsis. As a decontaminating germicide, he experimentally applied dilute carbolic acid to open wounds and surgical instruments, introduced weak carbolic acid hand washes for surgical staff, and used watery solutions of carbolic acid spray to reduce the level of germs in the air around the patient (Fig. 1.3). With the addition of these antiseptic adjuncts, infection rates in his practice decreased markedly. Feeling compelled to share the encouraging results of his clinical studies, he published two papers in *The Lancet* in 1867, outlining the technique [15, 16].

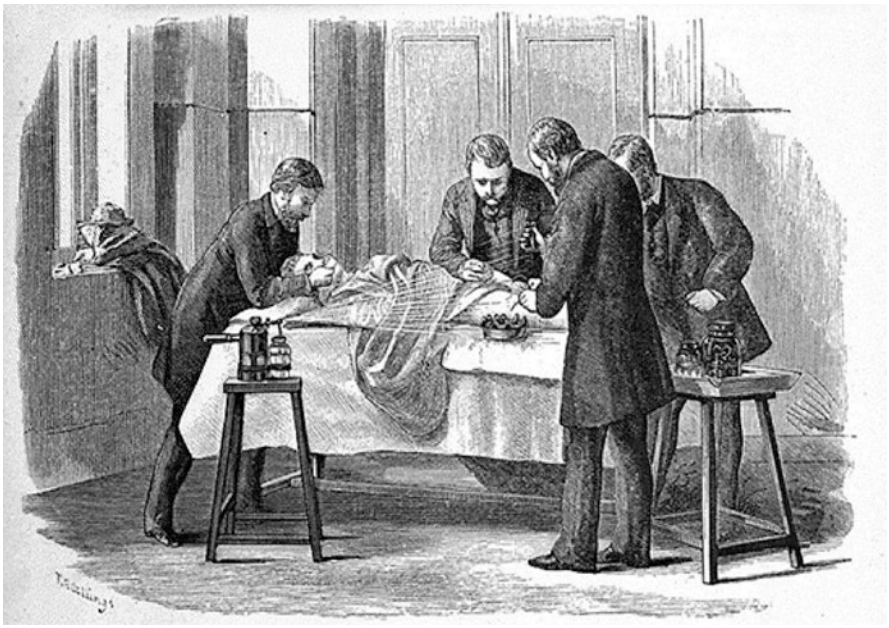

Fig. 1.3 Lister's antiseptic spray in use in an operating room, Circa 1882. (Picture Source: https://www.sciencemuseum.org.uk. *Antiseptic Surgery: Its Principles, Practice, History and Results* by W. Watson Cheyne. Wellcome Collection. Public Domain Mark)

Lister was the first to apply the science of germ theory to surgical practice. His antisepsis principles remain the basis of modern infection control and his revolutionary techniques made surgery much safer and helped to save countless lives.

Although germ theory was accepted relatively quickly in Europe, Lister's aseptic principles were met with cynicism and ignorance for many years in the USA. Bloodstained frocks and unwashed hands and instruments remained common well into the 1870s. Most notably, Dr. Willard Bliss and other attending physicians repeatedly probed President James A. Garfield's (1831–1881) gunshot wound over many weeks with unwashed fingers and instruments in unsuccessful attempts to retrieve the retained bullet after he was shot in an assassination attempt by Charles J. Guiteau on July 2, 1881.[1]

Garfield's gunshot wound was not immediately fatal, but he died of florid sepsis on 19 September 1881, 80 days after being shot. Autopsy findings showed no sign of infection around the retained bullet, itself, but active infection along the multiple soft-tissue tracks formed by probing unsterile fingers and instruments.

[1] The reader might find of interest *The Butchering Art: Joseph Lister's Quest to Transform the Grisly World of Victorian Medicine* (Scientific American/Farrar, Strauss, and Giroux, 2018) by Lindsey Fitzharris.

Subsequent to Garfield's death, Dr. Bliss was severely censured by the medical community for his blatant disregard of aseptic surgical techniques, which had by then become generally accepted principles of medical science and practice. Ridiculed in the press for his ineptitude, the phrase "Ignorance is Bliss" became part of the American lexicon [17].

During his trial, Guiteau argued that Garfield's death was due to medical malpractice, not his gunshot wound. The jury was not convinced and he was convicted of murder on January 5, 1882.

N.B.

Predating the works of Pasteur and Lister by several years—and one of the most historically under acknowledged advances in trauma management and sepsis mitigation—was the use of bromine as an antiseptic agent (anti-putrefaction agent, as then appreciated) in the treatment of gangrenous wounds in the midst of the American Civil War [18].

Although infectious diseases (dysentery, typhoid fever, malaria, measles, etc.) were the principal causes of death during the Civil War, wound infections and sepsis following battlefield injuries took many thousands of lives as well. Faced with a staggering number of extremity wounds, largely caused by the bone-shattering/flesh-tearing impact of the 0.58 caliber Minié Ball, battlefield surgeons frequently opted for the expediency of amputations over attempts at limb salvage, which were then considered to be futile and infection-prone (Fig. 1.4).

Following his fortuitous observation that post-surgical infection rates were lower in recovery wards where bromine was used as a deodorizing spray, Dr. Middleton Goldsmith (1818–1887) began experimenting with bromine as a putrefaction/gangrene inhibitor during his service as a surgeon with the Army of the Cumberland.

In 1863 Goldsmith submitted a detailed report to the Surgeon General relaying his experimental observation that the application of bromine to gangrenous wounds decreased the mortality rate of patients under his care to under 3% from a generally reported average of over 40% [19]. *Following his report, bromine antisepsis (anti-putrefaction) became a standard of care throughout Union military hospitals, with many lives saved.*

Unfortunately, Goldsmith's experimental observations predated the elucidation of germ theory linking microbes to surgical infections. As such, he was unable to explain his clinical results in a scientifically rigorous fashion. That unfortunate fact, coupled with prideful post-war resistance from battle-savvy surgeons and physicians, delayed the acceptance of germ theory and the initiation of aseptic medical and surgical practices in the United States for many years after being acknowledged and routinely embraced in Europe—needlessly costing American lives to sepsis [19].

With respect to Dr. Goldsmith's legacy, bromine continued to be successfully used as a skin and wound antiseptic for many years following the war, but was largely supplanted over time by less tissue-toxic alternatives.

Fig. 1.4 Post-amputation patient with arm gangrene, Circa 1863. Edward Stauch. (Picture Source: https://www.civilwarmed.org. Medical and Surgical History of the War of the Rebellion, Surgical vol. 2, p. 739)

Robert Koch (1843–1910) is regarded as one of the founders of modern bacteriology, having correctly identified the causative organisms of anthrax (*Bacillus anthracis*), cholera (*Vibrio cholerae*), and tuberculosis (*Mycobacterium tuberculosis*), among others [20]. His seminal contribution to germ theory is his list of criteria necessary to establish a microorganism as a causative agent for a specific disease. Still applicable to date, and known as "Koch's postulates," the original criteria state [21]:

- The microorganism must be found in diseased, but not healthy individuals.
- The microorganism must be cultured from the diseased individual.
- Inoculation of a healthy individual [or animal] with the cultured microorganism must recapitulate the disease.
- The microorganism must be re-isolated from the inoculated, diseased individual and matched to the original microorganism.

N.B.

A positive aspect of the germ theory of disease was the introduction of soap and water to the lexicon of personal hygiene and sanitation. Simply put, most people stank through the mid-1800s until a causal link connecting personal cleanliness to disease was first established.

For many centuries preceding the Civil War, soap made from animal fat and ash lye had been used for cleaning clothes, but rarely for bathing. Early soaps were quite caustic to the skin and bathing was considered unhealthy (or immoral) by many. Tainted water was long associated with disease and body oils were felt to be protective. Perfumes were widely used to mask body odor.