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## Infectious Diseases and Famous People Who Succumbed to Them

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### Abstract

I remember when I first announced to my family that I would go to Houston to study to become a clinical microbiologist. My grandfather told me that my great grandfather, Isaac Schauer, died in New York City during the 1918 influenza pandemic. He had been a healthy man in his early 40s prior to contracting this disease. Shortly thereafter, I discovered that Eleanor Roosevelt had died of tuberculosis. These early encounters with relatives or historical figures who succumbed to infectious diseases led me to a career-long fascination with death from infectious diseases and history. This article examines seven illnesses — tuberculosis, influenza, infectious diarrhea, syphilis, bacterial pneumonia, bacterial sepsis, and malaria, and the individuals throughout history who contracted and died from them.

### Introduction

The last half of the 20th century and the first part of the 21st century have seen the scourge of infectious disease brought under control in the developed world by antibacterial, antiviral, antifungal, and antiparasitic agents and vaccines. Therefore, it is hard to realize that some of history's most famous figures succumbed to a variety of microorganisms. From sexually transmitted diseases to diarrhea, the poor soldier and the rich and famous contracted these conditions at a time when there were few treatment options.

### Pneumonia

Throughout the course of history, many people have succumbed to pneumonia, an acute, inflammatory infection of the lungs. Bacteria are the most common etiological agents, with *Streptococcus pneumoniae* being the primary cause of community-acquired pneumo-

nia. There can be primary viral infections and secondary bacterial infections following viral pneumonias, such as influenza. Medical historians cite pneumonia as the most common infectious disease, accounting for greater than 50% of all cases of these illnesses. Thus, for historical figures who succumbed to pneumonia (Table 1), it is difficult to say with certainty whether each of the individuals actually died of bacterial or viral pneumonia.

### Influenza

Influenza virus is an orthomyxovirus, which means it belongs to the family *Orthomyxoviridae*. Two major structural proteins, the matrix protein, (M) and nucleoprotein (NP) are used to separate the influenza virus into three types, (A, B, and C) (1,2). Influenza A virus is further classified into subtypes based upon the characteristics of the two major surface glycoproteins, hemagglutinin (HA) and neuraminidase (NA). There are 16 distinct hemagglutinins (numbered 1 to 16), and nine distinct neuraminidases (numbered 1 to 9). However, only three HA subtypes (H1, H2, and H3) and two NA subtypes (N1 and N2) have caused influenza epidemics.

Influenza virus is unique among the respiratory viruses in its ability to reassort its genetic material. This is because its genetic material is single-stranded RNA that is present in the virion as separate small pieces.

As the genome reassorts, minor changes in the configuration of the surface antigens occurs with influenza A, B, and C viruses. This is called antigenic drift. Major changes in the surface antigens occurs only with influenza A virus; this is called antigenic shift.

Influenza viruses cause annual epidemics in areas with temperate climates.

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These epidemics generally occur between December and March in the Northern Hemisphere and between May and August in the Southern Hemisphere. Epidemics occur only with influenza A or B virus, however.

Global epidemics are called pandemics. Pandemics occur only with influenza A virus. Pandemics occur following the emergence of an influenza A virus that has undergone antigenic shift. Pandemic strains develop due to gene reassortment following co-infection with another human strain or an avian or swine virus. The 1918 pandemic was caused by an H1N1 strain that reassorted with an avian strain (the so-called bird flu). The 2009 pandemic is caused by an H1N1 strain that reassorted with a swine strain (the so-called swine flu).

As we have seen with the current pandemic, influenza A virus is capable of spreading across the world in just a few months. In fact, more people have died from influenza in short periods of time than from any other infectious disease (2).

The disease influenza is characterized by a febrile respiratory illness. Influenza C virus causes a mild upper respiratory tract infection in both children and adults. Influenza A virus has the highest morbidity and mortality rate. It is most severe in pregnant women during their second or third trimester, the very young, the elderly, and immunosuppressed individuals. Influenza is often complicated by secondary bacterial pneumonias, which many times are caused by *Staphylococcus aureus*. This is one reason that the CDC is recommending treatment with oseltamivir (3), an antiviral, and evaluation of patients for concurrent antibacterial therapy if a secondary bacterial infection is suspected. Actually, it is impossible to know who died specifically of influenza prior

to the latter part of the 20th century, since no diagnostic test was available. Thus, some of the famous people listed in Table 1 who died of pneumonia may have, in fact, also had influenza. Argentinean President Juan Peron, author Lewis Carroll, actress Tallulah Bankhead, and United States President Martin Van Buren are said to have died of influenza (4).

The 1918 Spanish influenza pandemic killed more people worldwide than there were soldiers killed in combat during World War I. This was the case with a number of infectious diseases discussed below.

### Tuberculosis

Individuals are assumed to have contracted and died from *Mycobacterium tuberculosis* infection as long ago as 15,000 years (4,5). The oldest fossil records are from Africa. In 1882, Robert Koch, who discovered the tubercle bacillus, estimated that one in seven deaths in Berlin was caused by tuberculosis. Today, about one-third of the world's population is infected with *M. tuberculosis*. Eight million people develop the disease each year. Of these, approximately 2 million die annually, with most of the deaths occurring in developing countries.

The story of tuberculosis, also called the "white plague," is the story of the first modern day clinical trial. Selman Waksman was the first to discover that streptomycin was effective against *M. tuberculosis*; he subsequently won a Nobel Prize in medicine for this work. The history of tuberculosis is also the history of sanatoriums, where tuberculosis patients went to "take the cure" before anti-tuberculous therapy was available. These special hospitals allowed *M. tuberculosis* patients to breathe fresh, clean air; eat nutritious

**Table 1. Historical figures thought to have died of pneumonia<sup>a</sup>**

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Albert Schweitzer
Andrew Carnegie
Andrew W. Mellon
Aristotle Onassis
Armand Cardinal de Richelieu
Benjamin Franklin
Boris Karloff
Charlemagne
Charles H. Mayo
Conrad Hilton
"Duke" Ellington
Eli Lilly
Enrico Caruso
Eugene O'Neill
Florence Ziegfeld
Franz Liszt
Geronimo
"Groucho" Marx
U.S. President Herbert Hoover
Ivan Pavlov
John Ringling
Leo Tolstoy
Louis C. Tiffany
Mario Lanza
Otto von Bismarck
Pope Pius X
Pope Pius XI
René Descartes
Robert E. Lee
Texas President Sam Houston
Simon Guggenheim
Sinclair Lewis
Sir Francis Bacon
Stonewall Jackson
Tsar Nicholas I
Victor Hugo
U.S. President William Henry Harrison
William Tecumseh Sherman
William Wordsworth

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<sup>a</sup>Compiled from reference 8.

foods; and rest. The introduction of isoniazid in 1954 finally led to the closing of sanatoriums.

Famous individuals who have died of tuberculosis are shown in Table 2. Death by tuberculosis was also a popular theme in opera. Mimi (La Bohème) and Violetta (La Traviata) are two operatic heroines who succumbed to the disease.

### Syphilis

Syphilis is a sexually transmitted disease caused by the spirochete *Treponema pallidum*. Because the disease was originally linked to the French army, syphilis was called the “French disease” (6). There are three stages of the disease, known as primary, secondary, and tertiary syphilis. Primary syphilis is characterized by the appearance of an asymptomatic, nonpainful ulcer called a chancre at the site of inoculation. Since the advent of penicillin, to which *T. pallidum* remains exquisitely susceptible, syphilis has been highly treatable at this stage. However, left untreated, the chancre will heal within a few weeks to months. By that time, however, the treponemes have spread hematogenously to every organ, including the central nervous system. This stage is known as secondary syphilis and is also over within a few weeks or months. *T. pallidum* is extremely slow growing, and the next phase is known as the latent period. This period can last from a few years to as long as 25 years, and the patient is asymptomatic. In the final stage of the disease, called tertiary syphilis, victims exhibit effects of a chronic neurodegenerative state, i.e., personality changes, hyperactive reflexes, and changes in intellect and judgment. Medical historians have used these final symptoms to assess whether historical figures have actually had syphilis. This is because, prior to the development of the Wasserman complement fixation test for the serodiagnosis of the disease, there was no way to definitely prove that an individual had the disease.

Table 3 lists the individuals whom historians have determined died of syphilis (7).

### Infectious Diarrhea

The story of infectious diarrhea is the 500-pound gorilla on the battlefield when one studies the history of war. The Union army lost over 81,000 troops

to typhoid fever and dysentery during the Civil War (8,9). The poet Walt Whitman visited soldiers hospitalized in Washington, DC, and wrote that war was “about nine hundred and ninety-nine parts diarrhea and one part glory” (7). Similarly, by the end of the Boer War, 13,000 British soldiers had died of typhoid fever, while only 8,000 had died in battle. The two most common types of dysentery were typhoid fever (caused by *Salmonella enterica* serovar Typhi) and cholera (caused by *Vibrio cholerae*). Prince Albert (Queen Victoria’s consort) died of typhoid fever. Peter Ilich Tchaikovsky (as well as his mother) died of cholera, as did Brigham Young and U.S. Presidents Zachary Taylor and James Polk.

### Sepsis

Sepsis means putrefaction in Greek (8). This term was coined to describe the situation in which tissue was destroyed by a purulent infection. Spread of an infection was called “blood poisoning,” or “pyemia.” There were no antibiotics, so topical agents, such as bromine, iodine, or carbolic acid, were applied to putrefying tissue; these agents were termed “antiseptics.” Although we no longer apply most of these chemicals to infected tissue, the terms sepsis and antiseptic are still used.

Lucretia Borgia died in childbirth from what we now know was probably beta-hemolytic streptococci. Ignaz Semmelweis, the physician who figured out that death following childbirth could be prevented by hand washing, himself died of sepsis following an injury to his finger. Willa Cather, the American author, died after pricking herself with a hat pin.

### Malaria

Malaria, caused by *Plasmodium* spp., is a parasitic blood disease characterized by chills and intermittent fevers. It claimed the lives of many soldiers in the Civil War (8). Quinine was actually used to treat these fevers because of its nonspecific antipyretic effects. Quinine was also used prophylactically to prevent malaria, although getting soldiers to take it was not easy. Some commanders allowed physicians to mix the quinine with whiskey to encourage the troops to drink it (8). Deaths from malaria throughout history are shown in Table 4. Many other individuals have suffered

**Table 2. Historical figures who died of tuberculosis<sup>a</sup>**

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Amadeo Modigliani
Cardinal Richelieu
Caroline Harrison (U.S. First Lady)
C. P. E. Bach
D. H. Lawrence
Edgar Allan Poe
Eleanor Roosevelt
Elizabeth Barrett Browning
Elizabeth Monroe (U.S. First Lady)
Emily Bronte
Franz Kafka
Frédéric Chopin
George Orwell
Hannah Van Buren (U.S. First Lady)
Henry Clay
Henry David Thoreau
Jane Pierce (U.S. First Lady)
John Keats
Karl Marx
King Tutankhamen of Egypt
Martha Jefferson (U.S. First Lady)
O. Henry
Robert Louis Stevenson
Simon Bolivar
Vivian Leigh
Walt Whitman

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<sup>a</sup>Compiled from References 3 and 8.

**Table 3. Historical figures thought to have contracted syphilis<sup>a</sup>**

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Al Capone
Erasmus
Ferdinand Magellan <sup>b</sup>
Florence Nightingale <sup>b</sup>
Giovanni Casanova
Gustave Flaubert
Ivan the Terrible <sup>b</sup>
John Keats <sup>b</sup>
King Henry VIII of England <sup>b</sup>
Lord Randolph Churchill (Winston Churchill’s father)
Ludwig van Beethoven <sup>b</sup>
Napoleon Bonaparte <sup>b</sup>
Paul Gauguin
Vincent van Gogh <sup>b</sup>

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<sup>a</sup>Compiled from reference 8.

<sup>b</sup>Medical historians have most often based the attribution of these deaths to syphilis on clinical symptoms compatible with tertiary syphilis.

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from malaria. In fact, 13 U.S. Presidents have had malaria, which Berger and Edberg (4) speculate may be the most common infection of our Commanders-in-Chief.

### Summary

The last 70 years have seen a revolution in the treatment of infectious diseases. Today, we stand at the beginning of a new period that some people are calling the “post-antibiotic era.” As microorganisms develop resistance to all current chemotherapeutics, will we again see people dying of formerly treatable illnesses? Stay tuned.

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### Table 4. Historical figures thought to have died of malaria

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Alexander the Great

Martha Washington (U.S. First Lady)

Oliver Cromwell

Pope Innocent III

Pope Leo X

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