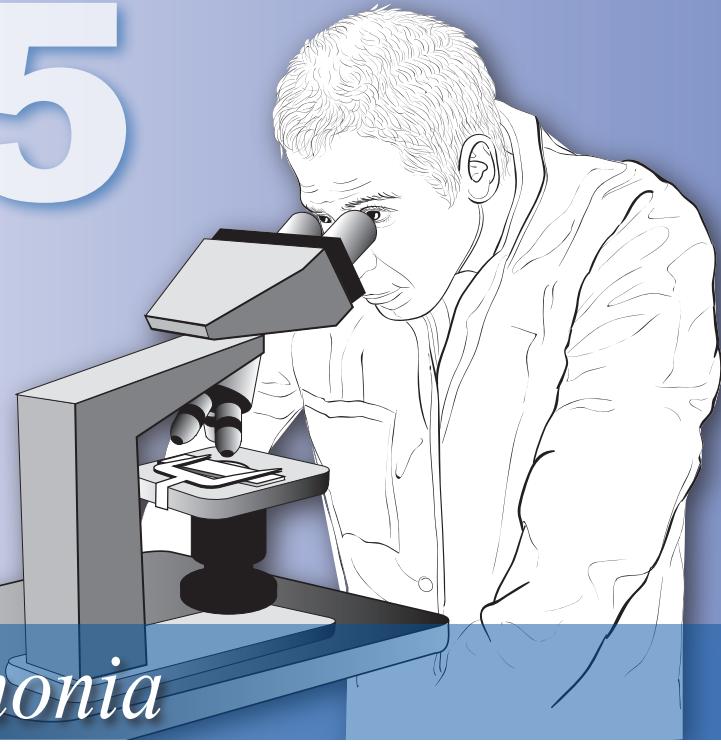


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Pneumonia

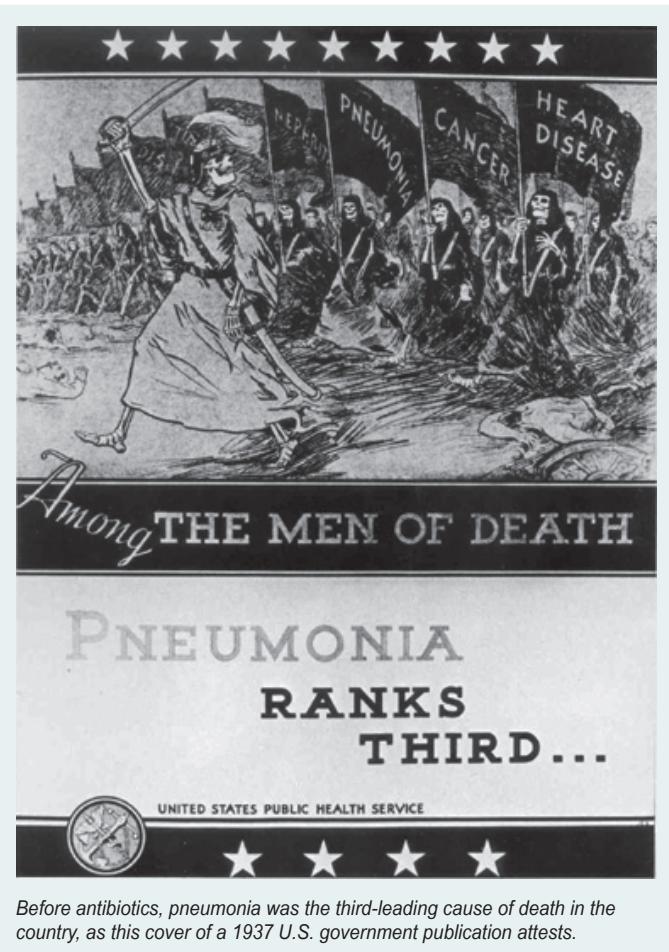


Pneumonia is a lung infection involving the lung alveoli (air sacs) and can be caused by microbes, including bacteria, viruses, or fungi. It is the leading infectious cause of hospitalization and death in the United States and exacts an enormous cost in economic and human terms. Healthy individuals can develop pneumonia, but susceptibility is greatly increased by a variety of personal characteristics.

Whom does it affect?

Epidemiology, prevalence, economic burden, vulnerable populations

Pneumonia was described 2,500 years ago by Hippocrates, the father of medicine. Dr. William Osler, the founder of modern medicine, who studied pneumonia throughout his career, called pneumonia the “captain of the men of death” because of the great toll it exacted on humanity. Pneumonia occurs commonly in individuals living in their home communities (“community-acquired pneumonia”) as well as in individuals who are hospitalized for other reasons (“hospital-acquired pneumonia”). In the 1930s, before the advent of antibiotics, pneumonia was the third-leading cause of death in the United States. Notably, it remains a leading cause of death. In 2006, it was the eighth-leading cause of death,

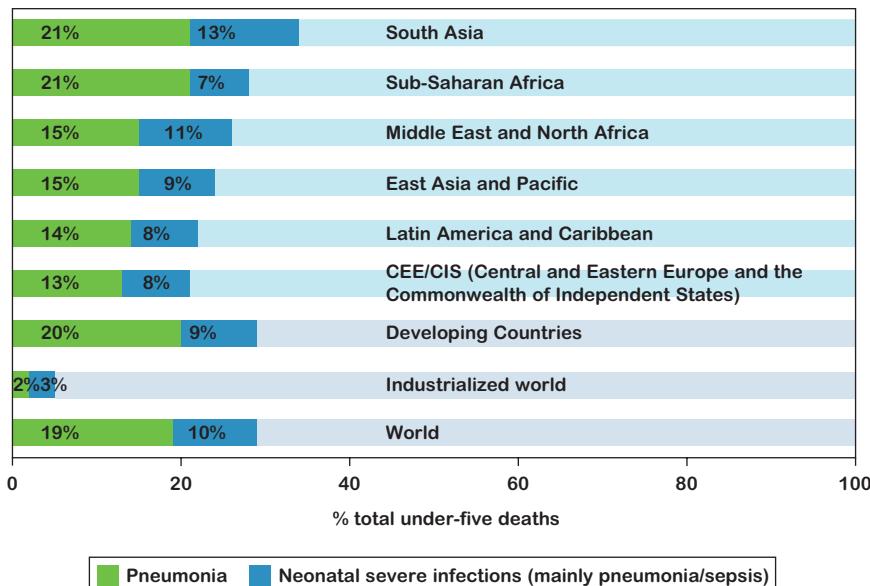


Before antibiotics, pneumonia was the third-leading cause of death in the country, as this cover of a 1937 U.S. government publication attests.

accounting for about 55,000 deaths (1). It is estimated that 4 million cases of community-acquired pneumonia occur annually in the United States, of which 20 to 25 percent are severe enough to warrant hospitalization. Pneumonia is second only to delivering a baby as a cause for hospitalization in the United States today (1).

The human and economic burden of pneumonia is enormous. In fact, World Health Organization data indicate that respiratory infections, a term which in this

Pneumonia is the leading killer of children under the age of five worldwide



This bar chart shows that pneumonia is the leading killer of children under five worldwide. "Pneumonia: The forgotten killer of children," The United Nations Children's Fund (UNICEF)/World Health Organization (WHO), 2006.

context is synonymous with pneumonia, account for more deaths among children worldwide than any other cause and for more disability-adjusted life years lost around the world than any other category of disease, including cancer and cardiovascular disease (2). In the United States alone, total medical expenditures and indirect costs (lost work and productivity) attributed to pneumonia amounted to more than \$40 billion in 2005 (1).

The lungs are particularly susceptible to infection because they interact with the outside environment. They are exposed to about 10,000 liters of air per day, which may contain infectious or toxic agents. The lungs are also connected to the upper airways and are, therefore, frequently exposed to small amounts of saliva and oral secretions that contain bacteria. Furthermore, part of the passageway to the lungs is shared by the stomach, and stomach contents can, on occasion, be regurgitated and aspirated into the lungs.

Although pneumonia can occur in anyone, it occurs with increased frequency in individuals whose immune systems are deficient (3). Human

CASE STUDY

An 85-year-old woman with a history of COPD associated with past smoking complained of fatigue along with increased shortness of breath and white-grey sputum. She had no fever or chest pain. When she arrived at the hospital, she had low blood pressure, low blood oxygen levels, an elevated white blood cell count, and a new shadow on the chest x-ray image of her right lung, which confirmed the diagnosis of pneumonia. She was admitted to the intensive care unit with a diagnosis of community-acquired pneumonia and possible sepsis. (Sepsis is the term used to indicate that the infection has spread throughout the body via the bloodstream.) She was treated with intravenous antibiotics, fluids, blood pressure support medications, and oxygen via a face mask. She improved, but because of a persistent high oxygen requirement, she underwent a computed tomography (CT) scan that revealed a large fluid collection around her right lung. Two needle drainage procedures of this fluid ultimately resulted in improvement in her shortness of breath and her oxygen requirement. She returned home after two weeks in the hospital. No bacteria were ever identified in cultures of her sputum, blood, or fluid around the lung.

Comment

This patient was vulnerable to pneumonia because of her age and her underlying COPD. As in many elderly persons, her pneumonia presented with vague symptoms such as fatigue and confusion. Her lack of fever, which can be seen with pneumonia, reflects an inadequate immune response to the infection and, again, was likely owing to her age. She illustrates serious and common complications of pneumonia. She had a sepsis-like picture with an overwhelming reaction that caused a fall in blood pressure (shock). Sepsis and respiratory failure are major causes of death in pneumonia patients. Fluid collection around the lung (pleural effusion) and low oxygen levels are other common complications. The lack of identified bacteria in cultures of pneumonia patients' blood is common, as bacteria may not be present in the blood at the precise moment when the cultures are drawn, or their growth may be suppressed by prior administration of antibiotics.

immunodeficiency virus (HIV) infection, malnutrition, diabetes, renal failure, cancers, and treatment with immunosuppressive drugs are all risk factors for developing pneumonia. Infants and very young children are highly vulnerable, as are the elderly. At both extremes of age, this increased risk relates in part to impaired immunity. In the United States, individuals older than age 65 account for almost two thirds of hospitalizations and 90 percent of deaths from pneumonia (4).

Patients who smoke or have underlying lung diseases, including chronic obstructive pulmonary disease (COPD), cystic fibrosis, congestive heart failure, and lung cancer, are also vulnerable, owing to abnormalities in lung structure and function. Finally, patients with respiratory failure who are on mechanical ventilators are more prone to pneumonia (3).

What are we learning about this disease?

Pathophysiology, causes: genetic, environment, microbes

Pneumonia can be transmitted when airborne microbes from an infected individual are inhaled by someone else. However, most instances of pneumonia are attributable to self-infection with one or more types of microbes that originate in the nose and mouth. In healthy people, typical upper airway bacterial residents such as *Streptococcus pneumoniae* (commonly referred to as “pneumococcus”) and *Hemophilus influenzae* are the most common bacteria causing community-acquired pneumonia. Hospital-acquired pneumonia is usually caused by more resistant bacteria, such as *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Escherichia coli*. Individuals with a serious impairment of their immune system become susceptible to pneumonia caused by so-called “opportunistic” microbes, such as certain fungi, viruses, and bacteria related to tuberculosis (mycobacteria), that would not ordinarily cause disease in normal individuals (5).

To cope with its constant exposure to potentially infectious microbes, the lung depends on a hierarchy of defense mechanisms (3). Physical mechanisms that can prevent microbes from reaching the alveoli include the structure of the upper airway, the branching of the bronchial tree, the sticky mucus layer lining the airways, the hair-like cilia that propel mucus upward, and the cough reflex. The microbes that do manage to reach the alveoli are usually

destroyed by a variety of immune cells, which is why most pneumonias occur in people with one or more deficiencies in either their mechanical or immune defense mechanisms.

How is it prevented, treated, and managed?

Prevention, treatment, staying healthy, prognosis

Although pneumonia cannot be completely prevented, a variety of strategies can be employed to reduce its incidence. Adequate nutrition, dental hygiene, and not smoking are elements of a healthy lifestyle that reduce a person's risk of getting pneumonia.

For those with lung disease or impaired clearance of mucus, aerobic exercise, deep breathing maneuvers, and cough assist devices can facilitate expectoration and lung hygiene. Immunity to certain common microbes can also be enhanced by immunization of vulnerable populations with specific vaccines. In contrast to the influenza vaccine, which must be administered annually to keep up with the ever-changing strains of influenza virus, the vaccine against *Streptococcus pneumoniae* bacteria typically provides longer-term protection.

Pneumonia is generally diagnosed based on a history of typical symptoms, abnormal breath sounds that can be heard with a stethoscope, a chest radiograph showing characteristic shadows, and, sometimes, laboratory tests (5). Once the disease is recognized, a determination is made as to its severity and whether the patient requires hospitalization. Approximately 75 percent of cases are managed as outpatients with oral antibiotics and fluids; this manifestation is sometimes called "walking pneumonia."

Since the responsible microbe is usually not known initially (and is often never definitively identified), antibacterial agents are selected to cover the most likely culprits. Many viral causes of pneumonia lack effective drug treatments, but fortunately, most healthy patients will recover from either bacterial or viral pneumonia with no long-term consequences.

As the population has aged and as the number of patients with multiple vulnerabilities has increased, the proportion requiring hospitalization for pneumonia and experiencing poor outcomes has grown. Also contributing to adverse outcomes is the growing problem of microbes that are resistant to antibiotics to which they were formerly sensitive. An important factor driving antibiotic

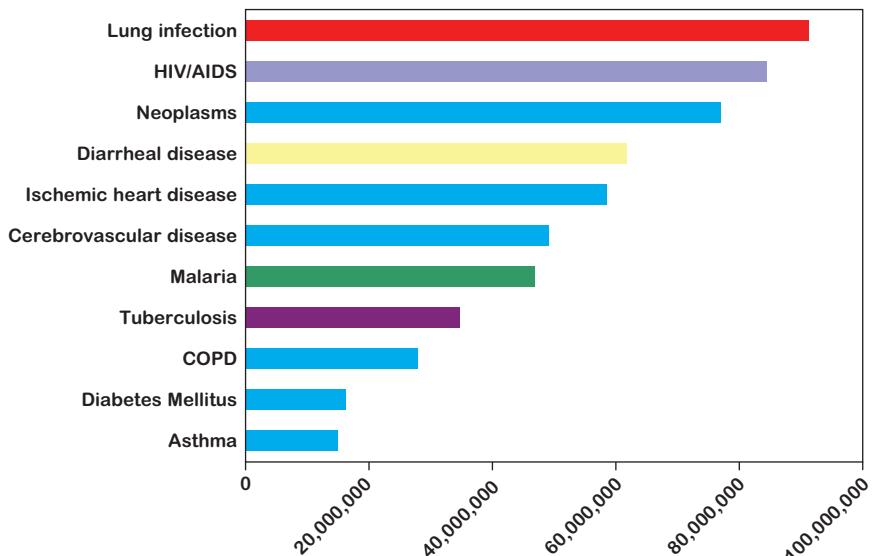
resistance has been the inappropriate use of antibiotics when they are not called for, such as for the common cold.

Are we making a difference?

Research past, present, and future

In almost no area of medicine has a discovery made a greater impact than that of antibiotics for infections. The availability of penicillin starting in the 1940s revolutionized the treatment of patients with pneumococcal pneumonia, which previously had been limited to watchful waiting. This discovery laid the groundwork for the development of additional antibiotics for treatment of other bacterial, viral, and fungal forms of pneumonia. In recent years, research on vaccinations has increased and has already reduced the frequency of the most common forms of pneumonia. The means to diagnose pneumonia have improved with better sampling procedures, such as bronchoscopy, and new methods for rapid laboratory detection of microbial molecules in sputum, blood, and urine.

Global burden of disease (da Lys lost in 2002, worldwide)



Pneumonia causes the greatest burden of any disease when measured by disability-adjusted life years (DALYs) lost. World Health Organization 2002 (3).

Despite these major advances, the dimensions of the clinical problem posed by pneumonia remain enormous. After those early gains achieved with first-generation antibiotics, the mortality rate for pneumonia has not changed appreciably in the last 50 years (6).

What we need to cure or eliminate pneumonia

In order to take the next leap forward to reduce the burden of pneumonia, the following issues must be tackled: 1) new laboratory approaches must be developed that are capable of rapidly identifying the causative microbe so that physicians can more precisely select antimicrobial drugs for treatment of pneumonia; 2) effective antibiotics must be developed against microbes for which there are currently none available; and 3) existing vaccines need to be improved and new vaccines developed.

However, vaccines cannot be developed against every microbe. Old microbes continuously change and new ones emerge. New antibiotics alone will not be enough because microbes develop antibiotic resistance. A substantial investigative effort must be mounted to improve the understanding of lung immunity—how it functions to deal with various infections, how it is influenced by common host factors, and how it can be manipulated for therapeutic gain. To complement antibiotics, an array of immunostimulant strategies that can be intelligently applied in different types of patients is needed. Substances that stimulate immunity could also be employed to enhance the body's response to vaccination.

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6. Wunderink RG, Mutlu GM. Pneumonia: overview and epidemiology. In: Laurent GJ, Shapiro SD, eds. *Encyclopedia of Respiratory Medicine*. Oxford, UK: Elsevier Academic Press; 2006:402–410.

Web sites of interest

Medline Plus

Pneumonia

www.nlm.nih.gov/medlineplus/ency/article/000145.htm

Centers for Disease Control and Prevention

Pneumonia

www.cdc.gov/nchs/FASTATS/pneumonia.htm

American Thoracic Society

Infectious Diseases Society of America/American Thoracic Society Consensus Guidelines on Managing Community-Acquired Pneumonia

www.thoracic.org/statements/resources/mtpi/idsaats-cap.pdf