Pathology is the medical discipline dealing with development of disease
- Pathology addresses issues of disease etiology and pathogenesis
  = The etiology of a disease is the mechanism through which it occurs
    • In this course, we are naturally concerned with diseases that exhibit an infectious etiology
    • The etiology of a disease may also be congenital, nutritional, etc.
    • Some of the diseases receiving the greatest attention - cancers, heart disease - exhibit an etiology that is mixed or to some degree unknown
  = Pathogenesis refers to the manner in which a disease develops, especially the structural and functional changes that occur in tissues
- Infection is the invasion or colonization of the body by pathogenic (disease-causing) microorganisms
  = "Infection" implies that the organism is present in tissues where it does normally occur
  = Infection may exist in the absence of detectable disease

All animals, including humans, serve as hosts to a normal microbiota, or "normal flora" (Tortora et al., Figures 14.1, 14.2)
- These are microorganisms that colonize certain tissues and establish more or less permanent residence (Tortora et al., Table 14.1)
- Abundant normal microbiota organisms are found in the nasopharyngeal and oropharyngeal regions of the upper respiratory tract, the digestive tract (especially the large intestine), the vagina, the distal end of the urethra, and the skin (Tortora et al., Figure 14.2)
- The ecological relationship between the normal flora organisms and their host is generally a commensal one in which the microorganisms obtain nutrients from the animal without causing either harm or benefit
  = One "benefit" of the normal flora is the phenomenon of microbial antagonism: By their presence, normal flora organisms prevent colonization by pathogens
  = The importance of microbial antagonism can be seen in increased susceptibility for some infections following antibiotic treatment
    • Vaginitis due to Candida albicans may follow a drop in the bacterial flora of the vagina, which normally maintains a low pH that inhibits growth of C. albicans
    • Antibiotic treatment can also lead to certain gastrointestinal tract infections
  = True mutualism has been suggested in production of certain vitamins by enteric bacteria, but this may not be significant
- Many of the organisms of the normal microbiota are considered opportunistic pathogens
  = These are microorganisms that do not normally cause infectious diseases but will if given the "opportunity" to gain access to normally sterile tissue
    • Staphylococcus epidermidis, the most common resident of human skin, may cause serious infections if it gains access to the bloodstream during cardiac catheterization
    • Pseudomonas aeruginosa is not even a member of the normal microbiota (it normally lives in soil), but commonly infects tissue damaged by burns
  = Opportunistic infections are common in persons whose normal defenses against infection are compromised
    • A person may be compromised by another disease or even by treatment for another disease
    • A person infected by HIV is compromised by the immunodeficiency resulting from the virus infection; thus, opportunistic infections are the leading cause of death in AIDS patients
Interestingly, many true pathogens can be carried by some persons without infectious disease resulting

- This seems especially true for bacteria of the upper respiratory tract, including *Nesseria meningitidis* and *Streptococcus pneumoniae*

- The mechanisms through which such pathogens are normally held “in check”, and how they overcome those mechanisms to cause infectious diseases, are topic of great interest to pathologists

Establishing an infectious etiology for a particular disease is not always straightforward

- Simple association between a disease and the presence of microorganisms is not sufficient

  - Erroneous association between normal flora organisms and various diseases led some 19th century physicians to promote unnecessary surgery

  - The bacterium *Haemophilus influenzae* was named for its association with influenza; pulmonary infection with *H. influenzae* often follows damage caused by the virus that actually causes influenza

- In the late 19th century, Robert Koch established a set of requirements for determining infectious etiology that have come to be known as *Koch’s postulates* (Tortora et al., Figure 14.3).

  - Koch first used this approach to demonstrate that *Bacillus anthracis* was the agent of anthrax

  - According to Koch’s postulates, to implicate a microorganism as the cause of a disease,
    1. The same microorganism must be present in every case of the disease.
    2. The microorganism must be isolated from the diseased host and grown in pure culture
    3. It must be possible to cause the disease by inoculating healthy animals with the pure culture of the suspected pathogen
    4. The pathogen must be isolated from the experimentally infected animals

  - It has not always been possible to satisfy Koch’s postulates

    - "Step 3" is morally indefensible if a serious infection is limited to humans, as is the case in most viral diseases
    - Some pathogens, including *Treponema pallidum*, the agent of syphilis, have never been grown in pure culture

- Despite their limitations, Koch’s postulates should be kept in mind in considering proposals for an infectious etiology for diseases, such as the recent association stomach cancer with infection by *Helicobacter pylori*

Complicating consideration of infectious etiologies is the fact that there is no "one pathogen - one disease" rule

- Some infectious diseases, such as meningitis and pneumonia, may be caused by a variety of bacteria, fungi and viruses

- Some microorganisms may cause a variety of different infectious diseases

Infectious diseases are classified in terms of how they behave within a host and within a population

- **Communicable** diseases are infectious diseases that are spread from one host to another, directly or indirectly

- **Noncommunicable** infections are those not normally spread between hosts

  - Most opportunistic infections are noncommunicable in that they are typically self-acquired

  - Some infectious diseases, including tetanus and *Legionella* pneumonia, are caused by microorganisms that do not normally inhabit the body

Infectious diseases are also classified according to patterns of occurrence

- The incidence of a disease is the fraction of a population that acquires the disease during a particular period of time

- The prevalence of a disease is the fraction of a population affected by the disease during a particular period of time

- The distinction between these two terms is subtle but important; for example, the prevalence of tuberculosis in the United States remains very low, but its rising incidence is a cause for concern
Frequency of occurrence is another criterion used in classification of infectious diseases. Many infectious diseases, including common childhood infections, are endemic within a population. Some infections, such as bacterial conjunctivitis ("pinkeye") occur in sporadic outbreaks. An infection becomes epidemic if its incidence in a population continues to increase over a period of time (as is certainly the case for HIV disease at this time). A worldwide epidemic, as frequently occurs with influenza, is referred to as a pandemic. Infectious diseases may be classified according to their severity or duration. An acute infection is one that develops rapidly but lasts only a short time. A chronic infection may develop more slowly but continue or recur over an extended period of time. A latent infection is one in which the agent remains inactive for a period of time. Infectious diseases can be classified according to the extent of host involvement. In a localized infection, the infecting microorganisms are confined to a limited area of tissue. In a systemic infection, microorganisms or their products are distributed throughout the body, usually through the circulatory system. Bacteremia refers to presence of bacteria in the blood. Septicemia is a condition in which bacteria are actually multiplying in the blood - bad news indeed. Toxemia refers to the presence of toxins in the blood. Viremia refers to the presence of viruses in the blood. The course of an infection may be determined by the state of host resistance. A primary infection results from exposure of a susceptible host to a pathogen. A secondary infection results from invasion of opportunistic pathogens following host damage due to a primary infection; most deaths that occur during influenza epidemics are actually caused by pneumonia due to secondary bacterial infections. Inapparent infections are infections that do not cause any noticeable illness.