Pathology

Pathology is that field of science and medicine concerned with the study of diseases, specifically their initial causes (etiologies), their step-wise progressions (pathogenesis), and their effects on normal structure and function.

Pathogenesis of Bacterial Infection

The pathogenesis of bacterial infection includes:

- Initiation of the infectious process and
- The mechanisms that lead to the development of signs and symptoms of disease.

The biochemical, structural and genetic factors play important roles in bacterial pathogenesis.

Characteristics of bacteria that are pathogens include:

Transmissibility, adherence to host cells, persistence, invasion of host cells and tissues, toxigenicity, and the ability to evade or survive the host's immune system.

Resistance to antimicrobials and disinfectants can also contribute to virulence, or an organism's capacity to cause disease. Many infections caused by bacteria that are commonly considered to be pathogens are inapparent or asymptomatic.

Disease occurs if the bacteria or immunologic reactions to their presence cause sufficient harm to the person.

Identifying Bacteria that Cause Disease

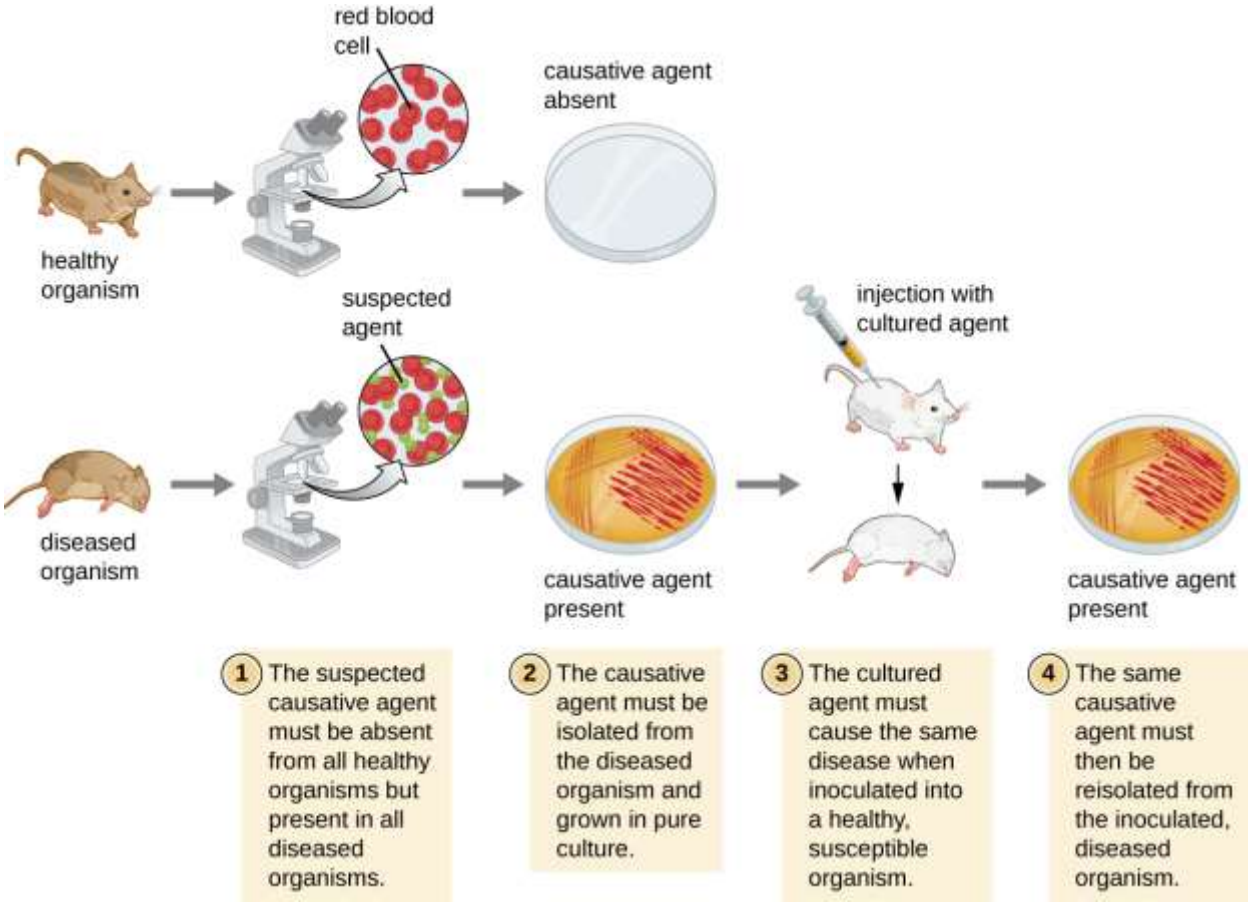
Humans and animals have abundant normal microbiota that usually do not produce disease but achieve a balance that ensures the survival, growth, and propagation.

Some bacteria that are important causes of disease are cultured commonly with the normal microbiota (eg, *Streptococcus pneumoniae*, *Staphylococcus aureus*). Sometimes bacteria that are clearly pathogens (eg, *Salmonella typhi*) are present, but infection remains latent or subclinical and the host is a "carrier" of the bacteria.

It can be difficult to show that a specific bacterial species is the cause of a particular disease. In 1884, Robert Koch proposed a series of postulates that have been applied broadly to link many specific bacterial species with particular diseases.

Koch's postulates: These postulates are summarized as following

1. The suspected pathogen must be found in every case of disease and not be found in healthy individuals.
2. The suspected pathogen can be isolated and grown in pure culture.
3. A healthy test subject infected with the suspected pathogen must develop the same signs and symptoms of disease as seen in postulate.
4. The pathogen must be re-isolated from the new host and must be identical to the pathogen from postulate 2.



Koch's postulates have remained a mainstay of microbiology; however, since the late 19th century, many microorganisms that do not meet the criteria of the postulates have been shown to cause disease.

For example, *Mycobacterium leprae* (leprosy) cannot be grown in vitro; however, there are animal models of infection with these agents.

In another example, *Neisseria gonorrhoeae* (gonorrhea), there is no animal model of infection even though the bacteria can readily be cultured in vitro; experimental infection in humans has been produced which substitutes for an animal model.

The host's immune responses also should be considered when an organism is being investigated as the possible cause of a disease. Thus, development of a rise in specific antibody during recovery from disease is an important helper to Koch's postulates.

Modern-day microbial genetics has opened new borders to study pathogenic bacteria and differentiate them from nonpathogens. Molecular cloning has allowed investigators to isolate and modify specific virulence genes and study them with models of infection. The ability to study genes associated with virulence has led to a proposed form of **molecular Koch's postulates**.

Molecular Koch's postulates: These postulates are summarized as following

1. The phenotype (sign or symptom of disease) should be associated only with pathogenic strains of a species.
2. Inactivation of the suspected gene(s) associated with pathogenicity should result in a measurable loss of pathogenicity.
3. Reversion of the inactive gene should restore the disease phenotype.

Some pathogens are difficult or impossible to grow in culture, and for that reason it is not possible with Koch's postulates or the molecular Koch's postulates to establish the cause of their associated diseases.

The polymerase chain reaction is used to amplify microorganism- specific nucleic acid sequences from host tissues or fluids. The sequences are used to identify the infecting organisms. For this purpose the molecular guidelines for establishing microbial disease causation are proposed. This approach has been used to establish the causes of several diseases, including Whipple's disease (*Tropheryma whipplei*).

The molecular guidelines for establishing microbial disease causation

1. The nucleic acid sequence of a putative pathogen should be present in most cases of an infectious disease, and preferentially in anatomic sites where pathology is evident.
2. Fewer, or no, copies of the pathogen-associated nucleic acid sequences should occur in hosts or tissues without disease.
3. The copy number of a pathogen-associated nucleic acid sequence should decrease or become undetectable with resolution of the disease (eg, with effective treatment) and should increase with relapse or recurrence of disease.
4. The presence of a pathogen-associated nucleic acid sequence in healthy subjects should help predict the subsequent development of disease.
5. The nature of the microorganism inferred from the available sequence should be consistent with the known biological characteristics of that group of organisms.

Analysis of infection and disease through the application of principles such as Koch's postulates leads to classification of bacteria as pathogens, opportunistic pathogens, or nonpathogens.

Some bacterial species are always considered to be **pathogens**, and their presence is abnormal; examples include *Mycobacterium tuberculosis* (tuberculosis). Such bacteria readily meet the criteria of Koch's postulates.

Other species are commonly part of normal microbiota of humans (and animals) but also can frequently cause disease. For example, *Escherichia coli* is part of the gastrointestinal **flora** of normal humans but is also a common cause of urinary tract infections.

Other bacteria (eg, *Pseudomonas species*, and many yeasts and molds) only cause disease in immunosuppressed and debilitated persons and are **opportunistic pathogens**.