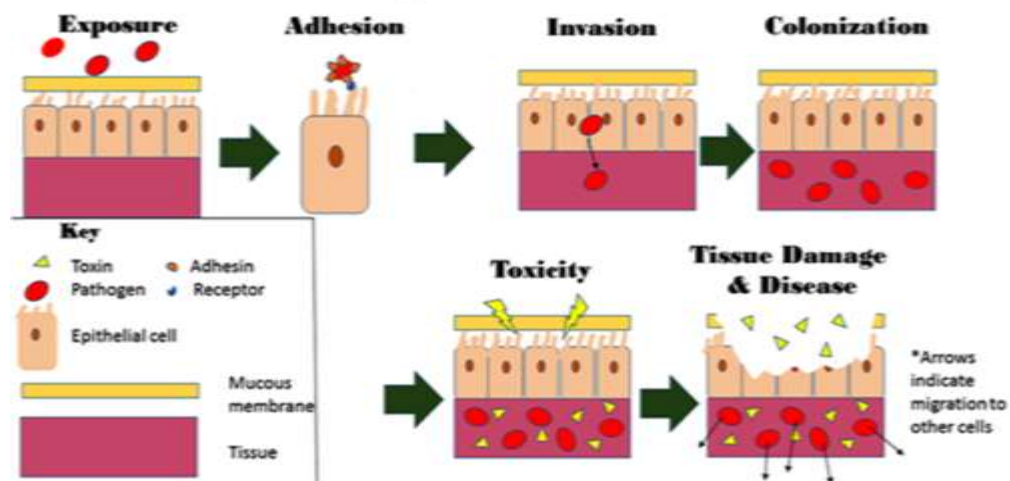


Stages of Pathogenesis

A pathogen must complete four stages of pathogenesis to cause disease: exposure, adhesion, invasion, and infection. The pathogen must enter the host, travel to where it can establish an infection, evade or overcome the host's immune response, and cause disease.



1. Exposure

Contact with a pathogen is called exposure. The food we eat and the objects we handle are all ways that we can come into contact with potential. However, not all contacts cause infection and disease. To cause disease, a pathogen must enter host tissue.

The term "**portal of entry**" refers to an anatomic location where pathogens can enter host tissue. These are locations where the host cells are in direct contact with the external environment.

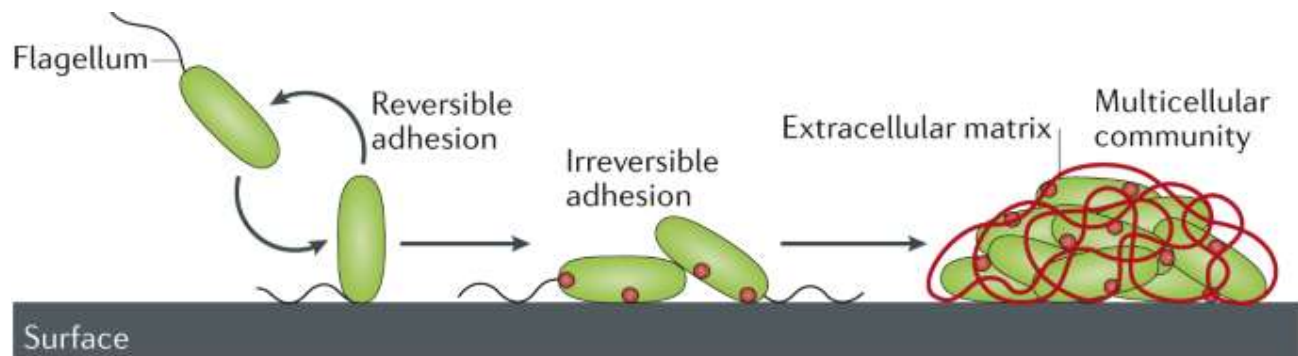
Mucosal surfaces are the most important portals of entry for microbes; these include the mucous membranes of the respiratory tract, the gastrointestinal tract, and the genitourinary tract. Although most mucosal surfaces are in the interior of the body, some are adjacent with the external skin at various body openings, including the eyes, nose, mouth, urethra, and anus.

Pathogens can also enter through skin and mucous membrane breaks. Pathogens that enter the body in this way are said to enter by **the parenteral route**. For example, the skin is a good natural barrier to pathogens, but breaks in the skin (e.g., wounds, insect bites, animal bites, needle pricks) can provide a parenteral portal of entry for microorganisms.

2. Adhesion

The term adhesion refers to the capability of pathogenic microbes to attach to the cells of the body using adhesion factors, and different pathogens use various mechanisms to adhere to the cells of host tissues.

Molecules (either proteins or carbohydrates) called adhesins are found on the surface of certain pathogens and bind to specific receptors (glycoproteins) on host cells. Adhesins are present on the fimbriae and flagella of bacteria, the cilia of protozoa, and the capsids or membranes of viruses. The production of glycocalyx (slime layers and capsules) with their high sugar and protein content, can also allow certain bacterial pathogens to attach to cells.



3. Invasion

Invasion involves the spreading of a pathogen throughout local tissues or the body.

Pathogens may produce exoenzymes or toxins as virulence factors to colonize and damage host tissues. Pathogens may also produce virulence factors that protect them from the immune system.

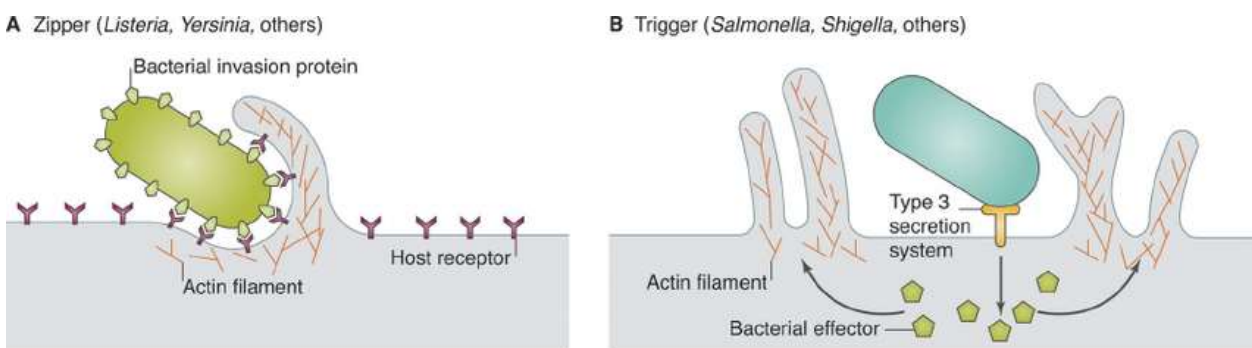
Intracellular pathogens achieve invasion by entering the host's cells and reproducing.

- Some are obligate intracellular pathogens (meaning they can only reproduce inside of host cells) and
- Others are facultative intracellular pathogens (meaning they can reproduce either inside or outside of host cells).

By entering the host cells, intracellular pathogens are able to evade some mechanisms of the immune system while also exploiting the nutrients in the host cell.

Entry to a cell can occur by endocytosis. For most kinds of host cells, pathogens use one of two different mechanisms for endocytosis and entry.

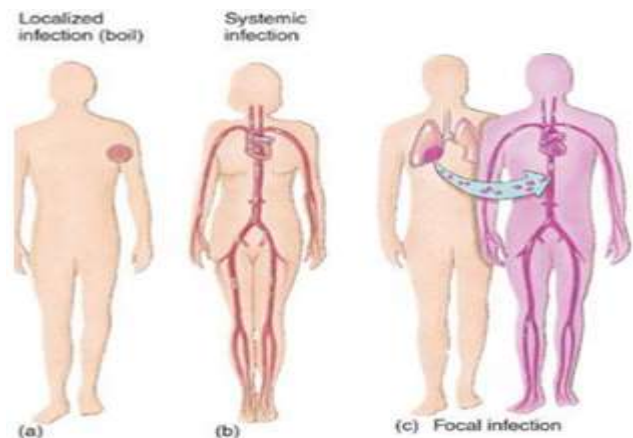
- One mechanism (Zipper) relies on surface proteins expressed on the pathogen that bind to receptors on the host cell, resulting in entry. For example, *Yersinia pseudotuberculosis* produces a surface protein known as invasin that binds to beta-1 integrins expressed on the surface of host cells.
- The second mechanism (Trigger) relies on effector proteins secreted by the pathogen resulting in entry. This is the method that *Salmonella* and *Shigella* use when invading intestinal epithelial cells. They secrete effector molecules that cause protrusions of membrane ruffles that bring the bacterial cell in. This process is called membrane ruffling.



4. Infection

Following invasion, successful multiplication of the pathogen leads to infection. Infections can be described as local, focal, or systemic, depending on the extent of the infection.

1. A local infection is restricted to a small area of the body, typically near the portal of entry.
2. In a focal infection, a localized pathogen, or the toxins it produces, can spread to a secondary location.
3. A systemic infection occurs when an infection spreads throughout the body.



Sometimes a primary infection, the initial infection caused by one pathogen, can lead to a secondary infection by another pathogen. For example, a primary infection by Influenzavirus damages and decreases the defense mechanisms of the lungs, making patients more susceptible to a secondary pneumonia by a bacterial pathogen like *Haemophilus influenzae*.

Transmission of Infection

Bacteria adapt to the environment, including animals and humans, where they normally reside. By producing asymptomatic infection or mild disease, rather than death of the host, microorganisms that normally live in people increase the possibility of transmission from one person to another. Some bacteria that commonly cause disease in humans exist primarily in animals and incidentally infect humans. For example

- 1- *Yersinia pestis* (plague) has a well-established life cycle in rodents and rodent fleas, and transmission by the fleas to humans;
- 2- *Bacillus anthracis* (anthrax) lives in the environment, occasionally infects animals, and is transmitted to humans by products such as raw hair from infected animals.
- 3- The *Clostridium* species are transmitted to humans by ingestion and wound contaminated by soil (eg, *C. perfringens* gastroenteritis and (gas gangrene), *C. botulinum* [botulism]) and when wounds are contaminated by soil *C. tetani* [tetanus]).

The clinical manifestations of diseases (eg, diarrhea, cough, genital discharge) produced by microorganisms often promote transmission of the agents. Examples of clinical syndromes and how they enhance transmission of the causative bacteria are as follows:

- 1- *Vibrio cholerae* can cause voluminous diarrhea which may contaminate salt and fresh water; drinking water or seafood such as oysters and crabs may be contaminated; ingestion of contaminated water or seafood can produce infection and disease
- 2- *Mycobacterium tuberculosis* (tuberculosis) naturally infects only humans; it produces respiratory disease with cough and production of aerosols, resulting in transmission of the bacteria from one person to another.
- 3- Many bacteria are transmitted from one person to another on hands. A person with *S. aureus* carriage in the anterior nares may rub his nose, pick up the staphylococci on the hands, and spread the bacteria to other parts of the body or to another person, where infection results.
- 4- Many opportunistic pathogens that cause nosocomial infections are transmitted from one patient to another on the hands of hospital personnel. Hand washing is thus an important component of infection control.

During birth, infectious diseases can be passed from mother to baby. Babies whose mothers have active chlamydia or gonorrhea infections may be exposed to vaginal pathogens that cause blindness. Infants receive antibiotic eye drops shortly after birth to prevent this.