

BACTERIAL PATHOGENESIS

Most bacteria are harmless or often beneficial, some are pathogenic. For bacteria to cause disease (to be pathogenic) , it needs to have some attributes to help it reach the host and persist within the host and replicate, then causing harm (disease) to the host. Characteristics of bacteria that are pathogens are sometimes referred to as virulence factors .

Stages of bacterial pathogenesis

Most bacterial infections are acquired from an external source. However, some bacterial infections are caused by members of the normal microbiota. A generalized sequence of the stages of infection is as follows:

- (1) Transmission from an external source into the portal of entry.
- (2) Evasion of primary host defenses such as skin or stomach acid.
- (3) Adherence to mucous membranes, usually by bacterial pili.
- (4) Colonization by growth of the bacteria at the site of adherence.
- (5) Disease symptoms caused by toxin production or invasion accompanied by inflammation.
- (6) Host immune response to each of the mentioned stages
- (7) Progression or resolving of disease.

The pathogen: A microorganism capable of causing disease in the host.

Non pathogen: A microorganism that does not cause disease; may be part of the normal microbiota.

Pathogenicity: is the ability of M.O to produce disease in a host.

Opportunistic pathogens: are those that rarely, cause disease in immunocompetent people but can cause serious infection in immunocompromised patients. These opportunists are frequent members of the body's normal microbiota.

Virulence: is the quantitative measure of pathogenicity, which is measured by the number of organisms required to cause disease.

Virulent agents cause disease when introduced into the host in small numbers. Virulence involves adherence, persistence, invasion, and toxigenicity.

Infection: Multiplication of an infectious agent within the body.

Multiplication of the bacteria that are part of the normal microbiota of the gastrointestinal tract, skin, and so on, is generally not considered an infection; on the other hand, multiplication of pathogenic bacteria (eg, Salmonella species) even if the person is asymptomatic is deemed an infection.

The infectious dose: an organism required to cause disease varies among the pathogenic bacteria. For example, Shigella and Salmonella both cause diarrhea by infecting the gastrointestinal tract, but the infectious dose of Shigella is less than 100 organisms, whereas the infectious dose of Salmonella is on the order of 100,000 organisms.

Pathogenicity islands (PAIs)

Pathogenicity islands (PAIs) are a distinct class of genomic islands acquired by microorganisms through horizontal gene transfer. They are incorporated in the genome of pathogenic organisms, but are usually absent from those nonpathogenic organisms of the same or closely related species. These mobile genetic elements may range from 10-200 kb and encode genes which contribute to the virulence of the respective pathogen. Typical examples are adherence factors, toxins, iron uptake systems, invasion factors, and secretion systems. Pathogenicity islands are discrete genetic units flanked by direct repeats, insertion sequences or tRNA genes, which act as sites for recombination into the DNA. Cryptic mobility genes may also be present, indicating the provenance as transduction. One species of bacteria may have more than one PAI (i.e. Salmonella has at least 5). They are transferred through horizontal gene transfer events such as transfer by a plasmid, phage, or conjugative transposon.

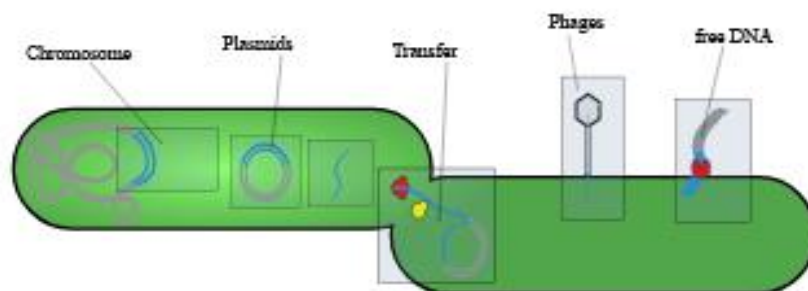


Figure: Horizontal Transfer: Pathogenicity islands are transferred horizontally, this details some of the ways that occurs.

Pathogenicity islands carry genes encoding one or more virulence factors, including, but not limited to, adhesins, toxins, or invasins. They may be located on a bacterial chromosome or may be transferred within a plasmid. The GC-content of pathogenicity islands often differs from that of the rest of the genome, potentially aiding in their detection within a given DNA sequence. PAIs are flanked by direct repeats; the sequence of bases at two ends of the inserted sequence is the same. They carry functional genes, such as integrases, transposases, or part of insertion sequences, to enable insertion into host DNA. PAIs are often associated with tRNA genes, which target sites for this integration event. They can be transferred as a single unit to new bacterial cells, thus conferring virulence to formerly benign strains.

The major properties of PAIs are as follows:

- They have one or more virulence genes
- They are present in the genome of pathogenic members of a species but absent in the nonpathogenic members
- They are large
- They typically have a different guanine plus cytosine (G + C) content than the rest of the bacterial genome
- They often have genetic instability
- Pathogenicity islands are found in many Gram-negative rods, such as *E. coli*, *Salmonella*, *Shigella*, *Pseudomonas*, and *Vibrio cholerae*, and in Gram-positive cocci, such as *S. pneumoniae*.