Section B and C

Volume-06

Contents

4. CELL COMMUNICATION AND CELL SIGNALING

A. HOST PARASITE INTERACTION

Host-Microbe Interactions: The Process of Infection

Infectious diseases occur as the result of interactions between pathogenic (disease-producing) microorganisms and the host. All infectious diseases begin at some surface of the host, whether it may be the external surfaceucous membranes of the respiratory tract, intestine, or urogenital tract. Many pathogens can selectively attach to particular host surface. In most infectious diseases the pathogenic microorganism penetrates the body surface and gains access to the internal tissues. In some kinds of infections the pathogen may remain localized, growing near its point of entry into the body. In other instances it may be transported to some other body site. Some pathogens may cause generalized infections, in which the microorganism becomes widely distributed and grows throughout the body. Some pathogens may be capable of growth within the cells of the host, causing severe disruption of normal physiological processes. In other infections the pathogen may grow extracellularly; here, damage to body cells usually occurs as the result of elaboration of poisonous substance (toxins) by the microorganisms.

If a host is to recover from an infection, it must eradicate the pathogenic microorganisms. However, termed virulence factors, that can combat the various defence mechanisms of the host; each species of pathogen possesses only one or a few of these factors. Thus, an infection represents a battle between the defences mounted by the host and the particular armamentarium of virulence factors produced by the pathogen. Often the infection proves lethal to the host; however it is to the microbe's advantage if the battle is somewhat indecisive, i.e., if the disease the pathogen causes is not so severe as to kill the most. Killing the host would diminish the pathogen's chance of survival; consequently, host-microbe interactions that result in chronic, long-lasting infections are regarded as being more highly evolved than interactions that are acute, i.e., have a short and relatively severe course.

Pathogenicity, virulence and infection

Pathogencicity is the capability of a microbial species to cause disease. However, various strains of a pathogenic species may differ with regard to their degree of pathogenicity, i.e., with regard to their virulence. For instance, some strains are highly virulent: only a few bacterial cells from a highly virulent strain are needed to cause disease in a host. Other strains may be less virulent, and larger numbers of cells of such strains are needed to cause the disease. Some strains may be avirulent, incapable of causing the disease even when large numbers of cells are inoculated into the host. Virulent strains of many pathogens, when repeatedly cultured onl laboratory media or grown in vivo in hosts other than their normal hosts, may lose their virulence: such avirulent strains are called attenuated strains and are widely used as vaccines to elicit immunity to various diseases.

The virulence of a pathogen is usually measured by determining its LD_{50} dose for a particular type of laboratory animal. The LD_{50} dose is defined as that number of organisms which, when administered to a number of laboratory animals, will kill 50% of them. For example, an LD_{50} dose of 10 cells of strain X compared with 100,000 cells of strain Y would indicate that X is 10,000 times more virulent than Y. The LD_{50} dose can be determined more

precisely than other endpoints such as the dose that kills 100% of the animals (LD_{50} dose, sometimes also termed minimum lethal dose or MLD) because the rate of change in mortality versus change in dose is greatest around the point of 50% mortality.

Infection represents the most intimate way in which a microorganism may cause disease: the host is invaded by the microorganisms which subsequently multiply in close association with the host's tissues. Most, but not all, microbially caused diseases are infections. An example of one that is not is a type of food poisoning called botulism, in which there is no invasion of the body by the causative microorganims; rather, the disease is contracted by ingesting the poison (toxin) in a food in which the bacterium Clostridium botulinum has previously grown.

In order to cause infectious disease a pathogen must accomplish the following:

1. It must enter the host.
2. It must metabolize and multiply on or in the host tissue.
3. It must resist host defences.
4. It must damage the host.

Each process is complex and all four processes must be fulfilled to produce infectious disease. Some infection may result in only a very minor amount of damage to the host, so minor that there are no detectable clinical symptoms of the infection; such infections are called subclinical infections. Other infections vary in regard to severity, location and the number of microbial species involved (see Table 1).

Table 1: Some Types of Infections

Definition	**Example**
Acute: Has a short and relatively severe course	Streptococcal pharyngitis (sore throat caused by *Streptococus pyogenes*)
Chronic: Has a long duration	Tuberculosis
Fulminating: Occurs suddenly and with severe intensity	Cerebrospinal meningitis caused by *Neisseria meningitidis*
Localized: Restricted to a limited area of the body	Urinary tract infection caused by *Escherichia coli*
Generalized: Affects many or all parts of the body	Blood infections, such as typhoid fever
Mixed or polymicrobial: More than one kind of microorganism contributes to the infection	Gaseous gangrene, in which a combination of *Clostridium* may occur
Primary: An initial localized infection	*Viral influenza*

that decreases resistance and thus paves the way for further invasion by the same microorganism or other microorganisms	
Secondary: Infection that is established after a primary infection has caused a decreased resistance	*Pneumococcal pneumonia* following viral influenza

Microbial Adherence

Unless a pathogen is introduced directly into the tissues (as by a wound, injection by an arthropod, or other similar means), the first step in initiation of infection is usually adherence or attachment of the pathogen to some surface of the host. Such surfaces represent hostile environments and the microorganism must compete with normal flora organisms for surface attachment. Moreover, the attachment is selective: various pathogens attach only to certain tissues. For most pathogens, the precise means of attachment are not yet understood, particularly for pathogenic and protozoa.

Examples of Adherence of Pathogenic Bacteria

Neisseria gonorrhoeae, the causative agent of gonorrhea, adheres specifically to the epithelial cell layer of the human cervix, urethra, and conjunctiva by means of pili and thus avoids being washed away by the flow of mucus or tears. *Escherichia coli* strains that cause "scours," a diarrheal disease of newborn pigs, also possess pili that allow the bacteria to attach firmly to the mucosal lining of the small intestine. *Vibrio cholerae* adheres to the epithelial layer of the small intestine of humans; although the bacterial surface component responsible for the attachment is not yet certain, it may be a hemagglutinin (so named because it also permits attachment to erythrocytes in laboratory experiments). In another example, certain proteins located on the outer surface of the bacterial cell wall have been shown to be essential for the initiation of infection. For instance, Streptococcus pyogenes, the causative agent of streptococcal sore throat, attaches specifically to the epithelial cells of the throat by means of cell-wall proteins called M proteins.

Examples of Adherence of Viruses

The surface of influenza virus particles is studded with hemagglutinin spikes that can cause attachment of the virus to specific mucoprotein receptors on the surface of host cells. Neuraminidase spikes on the virion surface also may possibly aid attachment by degrading the protective mucus layers of mucous membranes and allowing viral attachment to the underlying epithelial cells. Another example is a protein on the surface of poliovirus, which seems to be critical for attachment of the virus to lipid and glycoprotein-containing receptors on host cells; the attachment is specific for cells of the intestinal tract and the central nervous system, and subsequent infection of the latter can lead to paralysis. In this regard, it is interesting that the attenuated strains of poliovirus used for vaccination against poliomyelitis can attach to the gastrointestinal tract as the wild-type poliovirus does; however because of mutation in the genes

for the viral surface proteins, these attenuated strains have lost the ability to attach to cells of the central nervous system and thus do not cause the paralysis that is characteristic polomyelitis.

Penetration of Epithelial Cell Layers

Although penetration of the epithelial layer follows adherence in most infections, this is not always a prerequisite to infection. The microorganisms may merely multiply on the epithelial surface and cause damage without penetration into the body. For example, *V. cholerae*, the causative agent of the severe diarrheal disease known as cholera, multiples on the epithelial layer of the small intestine where it produces a toxin that causes the loss of fluid from the epithelial cells and kills the cells.

Passive Penetration into the Body

It should be emphasized that penetration of body surfaces may be achieved not only actively (i.e. by the adherence and penetration mechanisms of the pathogen itself) but also passively, by mechanisms having nothing to do with the properties of the microorganism. Any mechanically caused breach in the body surface can introduce pathogens directly into the underlying tissues. Wounds or burns represent one passive mechanism. For example, soldiers wounded on the battlefield may develop gas gangrene if the wound becomes contaminated by Clostridium perfringens present in soil and fecal matter. Burns often become infected by Pseudomonas aeruginosa or other aerobic or facultatively anaerobic bacteria from the surrounding environment. Another mode of passive penetration is by arthropods. For example, Borellia species cause relapsing fever in humans when the spirochetes are introduced through the bite of a tick or a body louse.

Active Penetration into the Body

Some pathogenic microorganisms are capable of penetrating the epithelial layer to which they have become attached. For example, in bacillary dysentery, Shigella bacteria penetrate into and kill the epithelial cells of the colon, then spread to adjacent cells, which are in turn killed. The result is the formation of lesions (areas of damage) known as ulcers, i.e., areas on the intestinal wall which have disintegrating or necrotic (dead) tissue. In another example, the influenza virus penetrates the epithelial cells lining the nasopharynx, trachea, and bronchi. The virus then undergoes replication, and new viral progeny are subsequently liberated from the infected cell. The severity of influenza depends mainly on the degree of host cell destruction during viral multiplication.

After penetration through or between the epithelial cells, some pathogens may penetrate into the deeper tissues of the body and may even become widely disseminated throughout the ……

Continued with...Page 5 Onwards…. It's So Goooood!!!, Buy it now…!