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Review

Pathogenesis of Microbial Disease

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Abstract

Pathogenesis refers to the process through which a disease or illness develops. The majority of infections are caused by a number of microbial species. The average human body contains 10 trillion human cells that include approximately 100 trillion bacteria and other microorganisms. Humans and their naturally occurring microflora have a tangled mutually beneficial symbiotic interaction that is essential for optimal health. Millions of genes of microflora of the human body not only aid in normal human metabolic process but also cause opportunistic infections. The pathogenic microorganisms may be bacteria, virus, or fungi. This article summarizes the general paradigm of microbial disease pathogenesis.

Keywords: Microbial pathogenesis, pathogenicity, transmission

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INTRODUCTION

Pathogenicity is the ability of a microbe to cause disease and inflict damage upon its host. A pathogen is a microorganism that is capable of producing disease. Only few groups of microorganisms in nature are pathogenic. Organisms causing disease only in compromised individuals when their immune system is weak are called opportunistic organisms, as they take the opportunity offered by reduced host defences to cause disease. Usually, these opportunistic microbes are part of the body's immune system. Pathogenicity is qualitative term and the qualitative factors are virulence factors that enhance the ability of the microorganisms to evade the host.

Virulence is the degree of pathogenicity ie., the ability of the organism to invade the tissues of the **host.**

The virulence factors of an organism influence its pathogenicity, its capacity to cause illness. Virulence is a quantitative term and these quantitative factors control the amount of severity of the disease. Virulence is an expanse. At one end the spectrum are organisms are avirulent (not harmful) and on the other organisms that are highly virulent. Highly virulent pathogens leads to disease condition when introduced to the body, may even cause multi-organ and body system failure in healthy individuals. Less virulent pathogens may cause an initial infection, but may not always cause severe illness. Low virulent pathogens would more likely to cause mild signs and symptoms of disease, such as low-grade fever, headache, or muscle aches. Some people might even be asymptomatic. Virulence of a pathogen is usually quantified using controlled experiments with laboratory animals. Two important indicators of virulence are the median infectious dose (ID50) and the median lethal dose (LD50), both of which are typically determined experimentally using animal models. The ID50 is the number of pathogen cells required to cause active infection in 50% of inoculated animals. The LD50 is the number of pathogenic cells, virions, or amount of toxin required to kill 50% of infected animals.

- An infection is when a microorganism establishes itself in a host, has colonized that host.
- A disease is impairment to host function as a result of damage or injury. In terms of infectious disease, the etiologic agent is the microorganism causing that disease.
- Nature of infectious disease:

An acute infection generally progresses through four stages:

a.The incubation period: time between the acquisition of the organism to the commencement of symptoms (this may vary from hours to days to weeks).

b.The prodromal period: non-specific symptoms such as fever, malaise and loss of appetite appear during this period.

c.The acute specific illness: the characteristic signs and symptoms of the disease are evident.

d.The recovery period: the illness subsides and the patient returns to health during this final phase.

- Depending on the degree of incidence and prevalence of an infectious disease in a community, may be :

  i.An endemic infection present at a low level in a specific population (e.g. endemic malaria in some African countries).

  ii.An infection is an epidemic if it occurs much more frequently than usual (e.g. an epidemic of influenza in the winter).

  iii.An infection is a pandemic if it has a worldwide distribution (e.g. COVID-19)

- **KOCH'S POSTULATES**

In 1884, Koch established four postulates that summarized the method for determining whether a particular microorganism was the cause of a particular disease:

1. The suspected organism must be absent in all healthy organisms but present in all diseased organisms.

2. The suspected pathogen should be isolated from the diseased organism and grown in pure culture.

3. The suspected pathogen must develop the same signs and symptoms of disease when inoculated in healthy disease free individual.

4. The pathogen must be able to re-isolate from the new host and must be producing identical effect when grown in culture .

- **MOLECULAR KOCH'S POSTULATES**

In 1988, Stanley Falkow (1934) revised Koch's postulates and called as molecular Koch's postulates.

a) The phenotype (signs and symptoms od the disease) should be associated only with the pathogenic strains of the species.

b)Inactivation of the suspected gene associated with pathogenicity should result in a measurable loss of pathogenicity

c)Reversion of the inactive gene should restore the disease phenotyp

EXPOSURE:

Pathogens can enter the body through the respiratory, gastrointestinal, urinary, or vaginal systems, among other places. Many opportunistic pathogens are found in the normal human flora and serve as a ready source of infection in the infected host (e.g., AIDS

Exposure or contact is the term for coming into contact with a possible pathogen. A pathogen must be able to obtain access to host tissue in order to cause illness. A portal of entrance is an anatomic location via which infections can infiltrate host tissue. These are areas where the host cells have direct contact with the outside world. The skin, mucous membranes, and parenteral routes are all major entry points. Mucosal surfaces are the most significant entrance points for bacteria. The mucous membranes of the respiratory tract,

gastrointestinal system, and genitourinary tract are among them. The environmental adaptations of a pathogen, as well as the enzymes and toxins it secretes, influence its portal specificity. Pathogens can also enter the body as parenteral pathogens. Microorganisms may enter the body through breaches in the skin, such as wounds, insect bites, animal bites, and needle pricks. Microorganisms are normally prevented from passing from the mother to the foetus by the placenta. Only a few pathogens, however, can cross the blood-placental barrier. The abbreviation TORCH refers to pathogens that can get through the placental barrier and infect the foetus.

Table 1: Depicting the entry points of some common pathogens.

Portal of entry	Pathogen	Disease
Skin	Clostridium tetani	Tetanus
	Hepatitis B virus	Hepatitis B
Respiratory tract	Streptococcus pneumoniae	Pneumonia
	Neisseria meningitidis	Meningitis
	Haemophilus influenzae	Meningitis
	Mycobacterium tuberculosis	Tuberculosis
	Influenza virus	Influenza
	Rhinovirus	Common cold
	Epstein–Barr virus	Infectious mononucleosis
Gastrointestinal tract	Shigella dysenteriae	Dysentery

	Salmonella typhi	Typhoid fever
	Vibrio cholerae	Cholera
	Hepatitis A virus	Infectious hepatitis
	Poliovirus	Poliomyelitis
Genital tract	Neisseria gonorrhoeae	Gonorrhoea
	Treponema pallidum	Syphilis
	Human immunodeficiency virus (HIV)	Acquired immune deficiency syndrome (AIDS)
	Candida albicans (fungus)	Vaginitis

ADHESION:

Capacity of pathogenic microorganisms to connect to body cells via adhesion factors is referred to as adhesion, and different pathogens utilise different ways to adhere to host tissue cells. Adhesins are molecules present on the surface of pathogens that attach to particular receptors (glycoproteins) on host cells. They can be proteins or carbohydrates. Adhesins can be found on bacteria's fimbriae and flagella, protozoa's cilia, and viruses' capsids or membranes. Hooks and barbs are also used by protozoans for adherence, and spike proteins on viruses aid viral attachment. Bacterial pathogens may adhere to cells thanks to the development of glycocalyces, which have a high sugar and protein content.

TORCH infections:

	DISEASE	PATHOGEN
T	Toxoplasmosis	*Toxoplasma gondii* (protozoan)
O	Syphilis	*Treponema pallidum* (bacterium)
	Chickenpox	Varicella-zoster virus (human herpesvirus 3)
	Hepatitis B	Hepatitis B virus (hepadnaviral)
	HIV	Retrovirus
	Fifth disease (erythema infectiosum)	Parvovirus B19
R	Rubella (German measles)	Togavirus
C	Cytomegalovirus	Human herpesvirus 5
H	Herpes	Herpes simplex viruses (HSV) 1 and 2

A biofilm is a bacterial population that produces glycocalyx, a polymeric material that permits the biofilm to adhere to a surface. A biofilm is a collection of microorganisms coated in an extracellular polysaccharide matrix that gets adhered to a surface, such as a enture prosthesis or an intravenous catheter. Microbial biofilms are considered to be involved in up to 65% of human illnesses.

INVASION:

The spread of a pathogen across local tissues or the entire body is referred to as invasion. Exoenzymes (toxins) are produced by pathogens and serve as virulence factors, allowing them to invade and harm host tissues as they penetrate deeper into the body. Virulence factors are produced by pathogens to shield them from immune system responses. The degree of tissue damage caused by a disease is determined by its virulence factors. Intracellular pathogens infiltrate the host's cells and reproduce within them. Some pathogens are obligatory intracellular pathogens, whereas others are facultative. Intracellular pathogens are able to circumvent some immune system responses while simultaneously accessing the nutrients in the host cell by infiltrating the host cell. Endocytosis is a method of gaining access to a cell. Some host cells, for eg.,white blood cells and other phagocytes of the immune system, actively endocytose pathogens by the process of pathogen recognition and phagocytosis.

INFECTION:

The infection occurs once the pathogen has successfully invaded the host. Depending on the degree of the illness, infections can be local, focal, or systemic.

- A local infection affects only a small area of the body, usually around the entrance site.
- A localised pathogen, or the toxins it generates, can travel to a secondary area causing focal infection.
- A systemic infection is defined as an illness that has spread throughout the body. The varicella-zoster virus, for example, usually enters the body through a mucous membrane in the upper respiratory system. It then spreads throughout the body, producing in the characteristic red skin lesions of chickenpox. These lesions are symptoms of a systemic infection since they are not the source of the illness.
- A primary infection, or the first infection caused by one pathogen, can sometimes develop to a secondary infection caused by a different pathogen. For eg., a patient's immune system is weakened by HIV infection, rendering him or her more vulnerable to secondary infections such oral thrush and others caused by opportunistic microorganisms. Antibiotic medication aimed at the primary infection harms the normal microbiome, allowing opportunistic bacteria to take advantage.

CONCLUSION

Pathogenic bacteria have perfected their strategies for colonising and multiplying in humans. Similarly, the host has evolved immunological systems that enable it to recognise invading organisms and distinguish between the host and the pathogen. Hence the pathogenic microorganisms must overcome the host's insults in order to establish and sustain an infection.

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