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Pathogen

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Synonyms

Disease-causing agent; Infectious agent; Infectious particle

Definition

Pathogenic microbes, or *pathogens*, have an ability to produce harm in a host organism and exhibit a parasitic or predatory relationship with the host. Pathogens cause infectious diseases such as streptococcal pharyngitis, influenza, botulism, rabies, gastroenteritis, and Creutzfeldt-Jakob disease.

Introduction

Microorganisms, or microbes, are unicellular or multicellular organisms too small to be seen with the unaided eye (Cowan 2018). Microbes are ubiquitous in the internal and external environments of humans and animals; thus, humans and animals often act as host organisms for microbes. While many microbes in a host's microbiome are harmless or beneficial to the host, the relationship between a microbe and a host can be a complicated one. Animal hosts can exhibit mutualistic, commensal, cooperative, parasitic, or predatory relationships with microbes. An animal host and microbe that exhibit reciprocal benefits and dependency upon each other share a mutualistic relationship. In the event that a host or microbe benefit from the relationship while the other is unharmed, they are said to share a commensal relationship. Cooperative relationships are beneficial to both the host and microbe, but the relationship is not required for survival. Parasitic and predatory relationships are those in which either the host or microbe will benefit at the expense of the other. The difference between parasitic and predatory relationships is difficult to define. However, parasitic relationships require a coexistence of host and microbe for at least some period of time, while predatory relationships do not (Willey et al. 2017). Parasitic or predatory microorganisms that produce direct or indirect harm to a host are said to be pathogens.

Classification of Pathogens

Pathogens may be cellular or acellular entities. Cellular pathogens exist across all three domains of life, including *Bacteria*, *Archaea*, and *Eukarya*. However, most cellular pathogenic organisms belong to the domain *Bacteria*. Acellular pathogens include both viruses and prions (infectious proteins). All pathogens are capable of producing harm, disease, or infection in the host. The term

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pathogenicity refers to the ability of a microbe to produce illness in a host, while *virulence* of a pathogen refers to the degree of pathogenicity. Many pathogens are classified by the severity and type of damage it can inflict upon a host, with host-specific considerations such as health of host, taken into account. For instance, some pathogens are able to produce disease in a healthy host and are termed *true* (*primary*) *pathogens*. Other pathogens are able to cause disease only in immunocompromised hosts and are termed *opportunistic pathogens* (Talaro and Chess 2012). Pathogens may also be classified by their location within the host. *Extracellular pathogens* remain in the extracellular fluid surrounding the host cells but do not enter the cells. *Intracellular pathogens* grow and divide inside host cells (Willey et al. 2017). There are also practical classifications for pathogens. The biosafety levels (BLS) are aimed at promoting worker safety when handling infectious microorganisms; the BLS of an infectious agent takes into account virulence and transmission route in safe-handling protocols (Biosafety in Microbiological and Biomedical Laboratories 2019).

Pathogen-Host Interactions

The cells, tissues, organs, and fluids of animals represent ideal growth conditions for animal pathogens. Yet, the interior of the animal body is generally sterile. This is achieved by use of biological defenses, such as innate and adaptive immune defenses. Innate defenses are composed of anatomical barriers (i.e., skin and mucous membranes), sensor systems recognizing molecular patterns of pathogens or tissue damage, immune surveillance, phagocytosis, and inflammation. Adaptive immunity is a defense mechanism utilized by vertebrates to allow for more sophisticated protection from infection. For instance, adaptive immunity relies on the ability of the immune system to recognize a specific pathogen, mount an immune response to destroy the pathogen, and remember the pathogen. Such a process confers the host *immunity*, or resistance to infection or disease caused by that pathogen. All types of body defenses rely upon distinguishing between self (host) and nonself (pathogen). Antigens are membrane-localized glycoproteins or glycolipids (Nester 2012) utilized by organisms for recognition of self vs. nonself. Additionally, pathogen-associated molecular patterns (PAMPs), such as cell wall components, flagellin molecules, and viral RNA, are expressed by pathogens and can trigger host defenses (Nester 2012). Host immune cells express pattern recognition receptors (PRRs) that bind or detect PAMPs, thereby aiding in the host's detection of a pathogen.

Characteristics and Strategies of Pathogens

If a pathogen penetrates the first line of defense (i.e., skin or mucous membranes) and gains entry into an animal, the pathogen must rapidly adapt to the host environment. Pathogens express *virulence factors* capable of facilitating infection by evading or outcompeting host defenses. Segments of pathogen DNA coding for virulence factors are called *pathogenicity islands*; *pathogenicity islands* may be transferred between members of a microbial species in a process called horizontal gene transfer (Schmidt and Hensel 2004). Virulence factors can be *adherence factors* that permit physical attachment of the organism to host, *invasion factors* that facilitate spread to other cells, or *toxins* that negatively alter the metabolism of the host cell (Willey et al. 2017). Not all members of a microbial species produce the same virulence factors. In fact, some members of a microbial species may not produce any virulence factors. For instance, most strains of *Escherichia coli* (*E. coli*) are nonpathogenic and relatively harmless to animal hosts. Nonpathogenic *E.coli* are helpful members of the mammalian intestinal microbiota, where they are known to aid in nutrient metabolism. Pathogenic strains of *E.coli* are responsible for bouts of gastroenteritis (inflammation of stomach and intestines) associated with contaminated food sources; pathogenic *E.coli* express virulence factors that nonpathogenic *E.coli* do not. There are six known pathotypes of *E.coli* with each pathotype of *E.*

coli expressing different virulence factors. For example, the enterotoxic *E.coli* (ETEC) pathotype produces virulence factors called enterotoxins. Heat-stable enterotoxin (ST) and heat-labile enterotoxin (LT) act to increase electrolyte and water content of the intestines, thereby producing symptoms of ETEC gastroenteritis, such as watery diarrhea. The ETEC *E.coli* pathotype is known to cause traveler's diarrhea and is found in contaminated water, as well as raw fruits and vegetables. Conversely, enterohemorrhagic *E.coli* (EHEC) expresses a different toxin, Shiga toxin, which kills vascular endothelial cells and produces severe, bloody diarrhea. EHEC is found in raw or undercooked ground beef and unpasteurized fruit juices (Croxen et al. 2013). The virulence factors that allow pathogens to penetrate, grow, and thrive cause infection or disease in the host.

Establishing Infection: Invasion, Adhesion, and Colonization

Pathogens produce a variety of invasion factors which allow for microbial penetration into the host. The microbial penetration process may be active or passive. Active penetration occurs when a pathogen produces and released lytic substances that alter the host tissue by destroying the host's extracellular matrix or basement membrane underlying epithelial tissue, destroying glycocalyx components, or triggering a rearrangement of the host cell membrane. For example, *Clostridium perfringens* (causative agent in clostridial gas gangrene) produce an invasion factor called collagenase which destroys collagen molecules found in connective tissues (Petit et al. 1999). Destruction of connective tissue by collagenase allows for *C. perfringens* to penetrate and spread into the deep tissues of the body. The invasiveness of pathogens varies, however. Some pathogens utilize passive penetration mechanisms. Passive penetration occurs when the first line of defense is damaged and a pathogen enters the host through a lesion, wound, abrasion, damaged mucous membrane, or otherwise damaged/inflamed tissue (Willey et al. 2017). In passive penetration, the pathogen takes advantage of the weakened host first line of defense.

After a pathogen has gained entry into the host organism, it must adhere to the target cell and colonize. Adherence usually requires the pathogen to have specialized structures, such as *fimbriae* or *pili*, to attach to the host cell. Fimbriae and pili are examples of bacterial adherence virulence factors. Yet, pathogens can express a wide variety of attachment structures; all are well-suited to attach to a designated host cell. For example, influenza virus utilizes a hemagglutinin (HA) spike protein for viral adherence to α-sialic acid on the membranes of host upper respiratory tract cells (Luo 2012). After adhesion is complete, the pathogen will colonize (actively reproduce). Pathogens also possess ways to elude the immune system once established, whether it be by hiding inside a host cell (*Shigella*), attacking immune cells (*Streptococcus pyogenes*), or surviving phagocytosis (*Salmonella*) (Willey et al. 2017).

Damage to Host

Many pathogens enter, adhere, and colonize within a host organism, thereby taking valuable nutrients and resources from the host organism. Yet, there are other ways in which pathogens can inflict damage on a host organism, including the release of toxins. Toxins are substances encoded for by the genetic material of bacteria, fungi, and viruses which change the normal metabolism or activities of a host cell in such a way as to benefit the pathogen while harming the host. The two major classes of toxins are exotoxins and endotoxins. Exotoxins are heat-labile proteins that are released from the microorganism into the surrounding environment; they are inactivated at 60–80 °C. The food-borne disease botulism is caused by products of the bacterium *Clostridium botulinum*; *C. botulinum* produces the exotoxin *botulin* which blocks acetylcholine release at the neuromuscular junction. The botulin toxin prevents neuromuscular communication and produces flaccid muscle paralysis. In the case of food-borne botulism, the individual ingests food contaminated with the heat-stable toxin. Botulism

can occur when low-acidity foods are improperly canned (Nester 2012). Ingestion of the botulin toxin causes the symptoms associated with botulism, not the bacterium itself (except in cases of infant botulism). The *E.coli* enterotoxins (Shiga toxin, ST, LT) discussed in the previous section are also examples of exotoxins. Endotoxins, such as lipopolysaccharide (LPS), are found within the cell walls of Gram-negative bacteria. When the animal immune system destroys the Gram-negative bacterial cell, the endotoxin is released into the blood and produces widespread deleterious effects, such as fever, hypotension, organ failure, and blood coagulation. The net result of LPS activity is often referred to as septic shock (Willey et al.). Fungi are also capable of producing toxins called mycotoxins. *Aspergillus flavus* produces aflatoxins; aflatoxins are known to cause liver disease and liver cancer (Cowan et al.). Viruses are nonliving pathogens capable of utilizing host cell machinery to produce dangerous toxins. Rotaviruses are common causative agents in viral gastroenteritis. Rotaviruses encode an enterotoxin called NSP4 that induces vomiting in a serotonin-dependent mechanism (Hagbom et al. 2011). Thus, the ability of pathogens to produce signs and symptoms associated with infectious disease reaches beyond its ability to invade the body's tissues. Over generations of microevolution, pathogens continue to evolve to become more effective pathogens, whether by finding new ways to elude the host immune system or produce more effective virulence factors.

Cross-References

- Archaea
- Bacteria
- DNA
- Eukaryota
- Fungi
- Immunity
- Immunology
- Parasitism
- Pathogen Load
- RNA
- Woese's Three Domains of Cellular Life

References

Biosafety in Microbiological and Biomedical Laboratories. (2019, 1 Aug 2019). Fifth. Retrieved from https://www.cdc.gov/biosafety/publications/bmbl5/

Cowan, M. K. (2018). *Microbiology: A systems approach* (5 ed.). New York: McGraw-Hill Education.

Croxen, M. A., Law, R. J., Scholz, R., Keeney, K. M., Wlodarska, M., & Finlay, B. B. (2013). Recent advances in understanding enteric pathogenic *Escherichia coli*. *Clinical Microbiology Reviews, 26*(4), 822–880. https://doi.org/10.1128/CMR.00022-13.

Hagbom, M., Istrate, C., Engblom, D., Karlsson, T., Rodriguez-Diaz, J., Buesa, J., … Svensson, L. (2011). Rotavirus stimulates release of serotonin (5-HT) from human enterochromaffin cells and activates brain structures involved in nausea and vomiting. *PLoS Pathog, 7*(7), e1002115. https://doi.org/10.1371/journal.ppat.1002115

Luo, M. (2012). Influenza virus entry. *Advances in Experimental Medicine and Biology, 726*, 201–221. https://doi.org/10.1007/978-1-4614-0980-9_9.

Nester, E. W. (2012). *Microbiology: A human perspective* (7th ed.). New York: McGraw-Hill.

Petit, L., Gibert, M., & Popoff, M. R. (1999). Clostridium perfringens: Toxinotype and genotype. *Trends in Microbiology, 7*(3), 104–110.

Schmidt, H., & Hensel, M. (2004). Pathogenicity islands in bacterial pathogenesis. *Clinical Microbiology Reviews, 17*(1), 14–56.

Talaro, K. P., & Chess, B. (2012). *Foundations in microbiology: Basic principles* (8th ed.). New York: McGraw-Hill.

Willey, J. M., Sherwood, L., & Woolverton, C. J. (2017). *Prescott's microbiology* (10th ed.). New York: McGraw-Hill.