

Microbial Infection Pathogenesis and Progression: A Critical Review Akhilesh Vats^{*}, Parul Nigam^{*} ACME Research Solutions^{*} Corresponding Email- <u>akhill.anant@gmail.com</u> DOI: 10.5281/zenodo.7002860: Review Article

Abstract: The world is becoming increasingly saturated with microbial infections, and the incidence of these infections will only continue to increase. This article will discuss the key players responsible for microbial infection pathogenesis and progression, as well as some of the most common pathogens that cause infections in humans. By understanding how these organisms cause infection, we can better protect ourselves from these infections in the future. Microbial infection is a global public health problem. One in five people worldwide is infected with a pathogenic microorganism, resulting in millions of deaths annually. Pathogenesis is the process by which a pathogen causes disease, and progression is the sequence of events that lead to disease manifestation. In this review, we will focus on microbial infection pathogenesis and progression, particularly on host-pathogen interactions and the role of inflammation in pathology.

Keywords: Microbial Infection Pathogenesis, Microbial Infection Progression

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1. Overview of Pathogenesis of Infection

Pathogenesis begins with the inoculation of a pathogen into a host organism. Once the pathogen is inside the host, it begins to replicate and cause damage to the host cells. This damage leads to cell death, allowing the pathogen to invade more cells and multiply even further [1]. Eventually, this multiplication results in the development of symptoms or disease. In many cases, however, symptoms may not develop until later stages of infection due to delayed cell death or because other factors (e.g., inflammation) promote the growth and spread of the pathogen [2].

Microbes cause disease by entering and multiplying in host cells. Once microbes reach a critical density, they can trigger the release of harmful toxins that damage host cells and tissues. Infections can progress through four stages: colonization, inflammation, invasion, and termination [3].

The key to preventing infection is recognizing the signs and symptoms of microbial illness, promptly treating the infection with antibiotics if necessary, and monitoring patients for any continuing health problems [4].

1.1.Pathogens that Cause Infection

Bacteria - including streptococcus pneumonia, Staphylococcus aureus, and Escherichia coli [5].

Viruses - such as human immunodeficiency virus (HIV), type 1 diabetes virus, and Epstein-Barr virus [6].

Fungi - including candida Albicans and Aspergillus fumigatus [7].

Protozoa - such as Giardia lamblia and Cryptosporidium parvum [8].

Microbial Cell Wall - Synthesis and Function [9].

The microbial cell wall is a complex structure that constitutes an important part of the cell. It comprises peptides and other polysaccharides and provides structural support to the cell [10].

The cell wall can be classified according to its composition: a core of carbohydrates and proteins, a sheath of mucin, and a surface layer [11].

The role of the cell wall in microbial infection is complex, but it is essential for protecting the cell against invasion by bacteria and other microorganisms [12]. The cell wall's structure can also affect microbes' ability to survive and multiply in vitro. In addition, the cell wall's composition can influence bacteria's acquisition and spread of virulence factors [13].

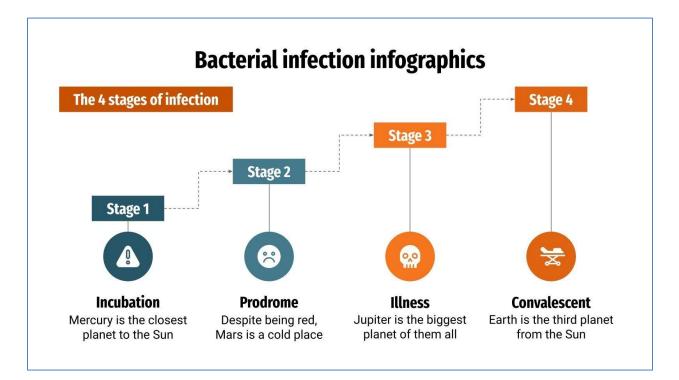


Fig.-1 Infection Stages

The cell wall is synthesized as part of bacteria or other microorganisms' initial response to infection. Initially, cells are surrounded by a layer of the plasma membrane called the external surface membrane (EMS) [14]. This layer is a barrier to outside invaders and helps control entry into and exit from cells. The EMS is also responsible for supplying nutrients to cells through diffusion across the membrane. Cells then begin to produce peptides that form the core of their cell wall [15].

2. Gene Expression in Microbial infection

Pathogenicity is the ability of a pathogen to cause harm or disease in a host. The intricate process by which pathogens cause harm and disease is called pathogenesis. Pathogenesis studies how diseases develop from causes (such as viruses, bacteria, and fungi) in the body. The study of pathogenesis has many applications, including understanding how infections are spread and developing new treatments for infections [16].

Microbial pathogens use various methods to invade cells and disseminate their infection. One of the most common methods is the secretion of virulence factors, proteins that enable pathogens to survive and reproduce inside host cells [17]. Virulence factors can also help pathogens kill host cells or interfere with their function. Virulence factors can be encoded on the surface of bacteria or viruses or encoded within the virus genome [18].

Microbial pathogens also use cellular mechanisms to invade and propagate within host cells. For example, some microbes hijack host cell receptors to gain entry into cells. Other microbes use toxins or enzymes to damage host cell membranes or proteins. Microbes can sometimes hijack cellular signaling pathways to enter and propagate inside host cells [19].

Once inside a host cell, microbial pathogens use the cell's machinery to replicate and spread their infection. Microbial cells use DNA replication and transcription to produce new copies of them [20]. These new copies of the virus or bacteria invade other host cells; spread the infection, and cause harm or disease [21].

Microbial pathogens can also use host cells to produce toxins that can damage or kill other organisms. For example, some bacteria produce toxins that can damage human cells or interfere with the function of important enzymes [22].

The study of microbial pathogenesis has many applications, including developing new treatments for infections and understanding how infections are spread [23].

2.1. Regulation of Cell Motility and Biofilm Formation

Microbial infection is a complex and rapidly progressing process that can cause significant health concerns. In order to understand this process, it is important to understand the

regulation of cell motility and biofilm formation. This review will explore the current understanding of these processes in microbial infection pathogenesis and progression [24].

Cell motility is the ability of cells to move forward or backwards. Biofilm formation is the creation of a lattice of microbial cells that can resist antibacterial agents. Biofilm formation is involved in the acquisition and maintenance of bacterial infections and in the progression of these infections [19].

Cell motility is regulated by various factors, including chemical signals, physical forces, and environmental stressors. Chemical signals are responsible for directing cell movement and are generated by cells and their environment [25]. Physical forces include drag and shear, which can cause cells to move or reorganize. Environmental stressors include fluctuations in temperature, pH, and oxygen levels. All of these factors play a role in regulating cell motility and biofilm formation [26].

A variety of factors also regulate biofilm formation. Physical forces such as drag and shear play an important role in forming biofilms. Environmental stressors such as fluctuations in temperature, pH, and oxygen levels can also affect biofilm formation. The presence of specific nutrients can also promote the growth of biofilms [27].

2.2.Immune Response to Microbial Infection

Pathogenesis of microbial infections begins with recognizing a pathogen by the host's immune system. The host's immune system will then mount an appropriate response to combat the invading microorganism [28]. This response can involve the activation of specific cells and molecules in the immune system, as well as the release of mediators that can damage or kill the pathogen. Microbial infection can progress through several stages, each with risks and complications. Understanding microbial infection signs of progress are crucial for treating patients and preventing further spread of the infection [29].

The initial response of the host's immune system is typically directed against proteins that are unique to the invading microorganism. This response is known as the innate immune response, based on recognizing pathogen-associated patterns of amino acids that are not found in normal body tissues [30]. The innate immune response can be broadly divided into two categories: the acute phase reaction and the chronic phase reaction [31].

The acute phase reaction is initiated within minutes of exposure to a pathogen and involves activating cells known as neutrophils. Neutrophils are important mediators of the acute phase response and are responsible for destroying pathogenic bacteria and viruses [22]. The release of chemicals called cytokines during the acute phase reaction can cause inflammation and tissue damage [23].

The chronic phase reaction begins days or weeks after a person becomes infected with a pathogen and lasts for months or years. It involves activating cells called lymphocytes and macrophages, which play a critical role in protecting the host from future infections by the same or different pathogens [24]. The accumulation of toxins produced by invading microorganisms during the chronic phase reaction can lead to organ failure or death [25].

2.3.Cell-mediated immunity

Microbial infection can cause significant health problems for individuals, and the cells that help protect us are often targeted first. In this blog post, we will discuss how microbial infection progresses and how cell-mediated immunity plays a role in pathology [25]. We will also highlight some key research areas currently being investigated to understand microbial infection pathogenesis and progression better [26].

Microbial infections can cause significant health problems for individuals. Innate immunity, our body's initial response to infection, is designed to recognize and attack specific pathogens [27]. However, in most cases, this response is ineffective against complex microbial infections. Instead, the body relies on help from another type of cell-mediated immunity called adaptive immunity. *Adaptive immunity* is cells trained to recognize and attack specific pathogens [28].

Innate and adaptive immunity work together to protect us from infection. The first line of defense against microbes is the skin barrier. This layer of skin cells protects against environmental contaminants and viruses [29]. The skin barrier also protects the underlying tissues from microbial invasion. The second line of defense is the immune system cells in the

blood and lymphatic systems. These cells are activated when they come into contact with a pathogen. They then travel throughout the body and start attacking the pathogen directly or helping to destroy infected cells [30].

Cell-mediated immunity plays an important role in the pathology of microbial infection. Several studies have shown that impaired cell-mediated immunity is associated with increased susceptibility to various infections, including tuberculosis, pneumonia, and CAP (community-acquired pneumonia) [31]. In addition, cell-mediated immunity is also responsible for the clearance of infected cells from the body. This process is known as phagocytosis. Phagocytosis is important because it helps eliminate infected cells and prevent them from spreading to other body parts [32].

Several research areas are currently being investigated to understand microbial infection pathogenesis and progression better. One area of focus is understanding how adaptive immunity functions in innate immunity [33]. Another area of focus is investigating how microbial infections trigger responses from the cell-mediated immune system. Finally, studies are being conducted to identify novel methods of enhancing cell-mediated immunity in patients with infection. These efforts will help to improve our ability to treat and protect against microbial infections [30].

2.4.Phagocytosis

Phagocytosis is a fundamental process by which cells consume and destroy foreign material. Microbes use various strategies to escape the phagosome, including producing toxins and deploying virulence factors that promote macrophage uptake [31]. Once engulfed, microorganisms are subjected to many processes that can lead to their demise, including cell lysis and oxidative killing. The role of phagocytosis in the progression of microbial infection is complex but essential. By understanding how it works and can be disrupted, we can better protect our patients from serious infections [32].

2.5.Complement-mediated lysis

Microbial infection can result in significant morbidity and mortality. Pathogenesis is a critical review of the various factors contributing to microbial infection progression [33].

This review will focus on complement-mediated lysis, a process essential for pathogenesis in many infectious diseases. Complement activation leads to toxic mediators that can damage host cells. The ensuing inflammation and tissue damage can lead to disease progression [31].

Lysis is a process by which cells are broken down into smaller pieces. In the context of microbial infection, lysis occurs when complement proteins bind to microorganisms and trigger a cascade of events that ultimately destroy the microorganism. Complement-mediated lysis is an important process in pathogenesis because it forms toxic mediators that can damage host cells [34].

Complement activation begins with the binding of complement components to microorganisms. The most common complement protein to bind to microorganisms is C3. C3 binds to microorganisms via its lectin domain, and this domain covalently attaches to small pieces of the microorganism called dsDNA [36]. dsDNA is also known as double-stranded DNA, and it is the genetic material of bacteria and viruses. Once C3 binds to dsDNA, it initiates a series of reactions that lead to the formation of toxic molecules called C5a and C5b [35].

C5a and C5b are two of the most important toxic molecules produced during complementmediated lysis. C5a is a pro-inflammatory molecule that can damage cells lining the respiratory tract. C5b is a destructive molecule that can damage cells throughout the body [36].

Complement-mediated lysis is essential for pathogenesis in many infectious diseases. The formation of C5a and C5b leads to the destruction of the microorganism, resulting in the infection's resolution [37].

3. Conclusion

Microbial infection is a common and serious health problem. This article will review the literature on microbial infection pathogenesis and progression, focusing on how these concepts can be applied to the clinical setting. We will also discuss the current state of knowledge concerning antibiotic resistance, inflammation, and tissue damage in cases of

microbial infection. This information will help us develop better interventions to combat microbial infections and improve patient outcomes.

4. Refrences

- Schaible, U. E., & Kaufmann, S. H. (2004). Iron and microbial infection. Nature Reviews Microbiology, 2(12), 946-953.
- Place, D. E., Lee, S., & Kanneganti, T. D. (2021). PANoptosis in microbial infection. Current opinion in microbiology, 59, 42-49.
- Hauser, A. R., Jain, M., Bar-Meir, M., & McColley, S. A. (2011). Clinical significance of microbial infection and adaptation in cystic fibrosis. Clinical microbiology reviews, 24(1), 29-70.
- Zhu, X., Radovic-Moreno, A. F., Wu, J., Langer, R., & Shi, J. (2014). Nanomedicine in the management of microbial infection–overview and perspectives. Nano today, 9(4), 478-498.
- Kopp, E., & Medzhitov, R. (2003). Recognition of microbial infection by Toll-like receptors. Current opinion in immunology, 15(4), 396-401.
- Doyle, R. J. (2000). Contribution of the hydrophobic effect to microbial infection. Microbes and infection, 2(4), 391-400.
- 7. Ørstavik, D. (2019). Apical periodontitis: microbial infection and host responses. Essential endodontology: prevention and treatment of apical periodontitis, 1-10.
- 8. Schaberg, D. R., Culver, D. H., & Gaynes, R. P. (1991). Major trends in the microbial etiology of nosocomial infection. The American journal of medicine, 91(3), S72-S75.
- Hu, H., Tian, M., Ding, C., & Yu, S. (2019). The C/EBP homologous protein (CHOP) transcription factor functions in endoplasmic reticulum stress-induced apoptosis and microbial infection. Frontiers in immunology, 9, 3083.
- Tan, J., Tay, J., Hedrick, J., & Yang, Y. Y. (2020). Synthetic macromolecules as therapeutics that overcome resistance in cancer and microbial infection. Biomaterials, 252, 120078.
- Zhou, C. B., & Fang, J. Y. (2019). The role of pyroptosis in gastrointestinal cancer and immune responses to intestinal microbial infection. Biochimica et Biophysica Acta (BBA)-Reviews on Cancer, 1872(1), 1-10.

- 12. Zhang, Y., Liu, Y., Tang, Y., Zhang, D., He, H., Wu, J., & Zheng, J. (2021). Antimicrobial α-defensins as multi-target inhibitors against amyloid formation and microbial infection. Chemical Science, 12(26), 9124-9139.
- Culbertson, E. M., Khan, A. A., Muchenditsi, A., Lutsenko, S., Sullivan, D. J., Petris, M. J., ... & Culotta, V. C. (2020). Changes in mammalian copper homeostasis during microbial infection. Metallomics, 12(3), 416-426.
- 14. Van Ngo, H., & Mostowy, S. (2019). Role of septins in microbial infection. Journal of cell science, 132(9), jcs226266.
- 15. Amoah, I. D., Kumari, S., & Bux, F. (2022). A probabilistic assessment of microbial infection risks due to occupational exposure to wastewater in a conventional activated sludge wastewater treatment plant. Science of The Total Environment, 843, 156849.
- Chen, M. Y., Kueneman, J. G., González, A., Humphrey, G., Knight, R., & McKenzie, V. J. (2022). Predicting fungal infection rate and severity with skin-associated microbial communities on amphibians. Molecular Ecology, 31(7), 2140-2156.
- Bhattacharjee, B., Mukherjee, S., Mukherjee, R., & Haldar, J. (2022). Easy Fabrication of a Polymeric Transparent Sheet to Combat Microbial Infection. ACS Applied Bio Materials.
- Moyat, M., Lebon, L., Perdijk, O., Wickramasinghe, L. C., Zaiss, M. M., Mosconi, I., ... & Harris, N. L. (2022). Microbial regulation of intestinal motility provides resistance against helminth infection. Mucosal Immunology, 1-13.
- Wang, Y. H., Chang, M. M., Wang, X. L., Zheng, A. H., & Zou, Z. (2018). The immune strategies of mosquito Aedes aegypti against microbial infection. Developmental & Comparative Immunology, 83, 12-21.
- 20. Baek, K., & Choi, Y. (2018). The microbiology of oral lichen planus: Is microbial infection the cause of oral lichen planus?. Molecular oral microbiology, 33(1), 22-28.
- Goggin, K. P., Gonzalez-Pena, V., Inaba, Y., Allison, K. J., Hong, D. K., Ahmed, A. A., ... & Gawad, C. (2020). Evaluation of plasma microbial cell-free DNA sequencing to predict bloodstream infection in pediatric patients with relapsed or refractory cancer. JAMA oncology, 6(4), 552-556.
- 22. Baishya, J., & Wakeman, C. A. (2019). Selective pressures during chronic infection drive microbial competition and cooperation. npj Biofilms and Microbiomes, 5(1), 1-9.

- Mullish, B. H., McDonald, J. A., Pechlivanis, A., Allegretti, J. R., Kao, D., Barker, G. F., ... & Marchesi, J. R. (2019). Microbial bile salt hydrolases mediate the efficacy of faecal microbiota transplant in the treatment of recurrent Clostridioides difficile infection. Gut, 68(10), 1791-1800.
- Nogueira, M. S. (2020). Biophotonics for pandemic control: large-area infection monitoring and microbial inactivation of COVID-19. Photodiagnosis and Photodynamic Therapy, 31, 101823.
- 25. Hammerbacher, A., Coutinho, T. A., & Gershenzon, J. (2019). Roles of plant volatiles in defence against microbial pathogens and microbial exploitation of volatiles. Plant, Cell & Environment, 42(10), 2827-2843.
- 26. MacGowan, A., Grier, S., Stoddart, M., Reynolds, R., Rogers, C., Pike, K., ... & Wootton, M. (2020). Impact of rapid microbial identification on clinical outcomes in bloodstream infection: the RAPIDO randomized trial. Clinical Microbiology and Infection, 26(10), 1347-1354.
- 27. Hiroyasu, A., DeWitt, D. C., & Goodman, A. G. (2018). Extraction of hemocytes from Drosophila melanogaster larvae for microbial infection and analysis. JoVE (Journal of Visualized Experiments), (135), e57077.
- Mazzitelli, C., Ionescu, A., Josic, U., Brambilla, E., Breschi, L., & Mazzoni, A. (2022). Microbial contamination of resin composites inside their dispensers: An increased risk of cross-infection?. Journal of Dentistry, 116, 103893.
- 29. Lin, J., Xia, X., Yu, X. Q., Shen, J., Li, Y., Lin, H., ... & You, M. (2018). Gene expression profiling provides insights into the immune mechanism of Plutella xylostella midgut to microbial infection. Gene, 647, 21-30.
- 30. Ull, C., Yilmaz, E., Baecker, H., Schildhauer, T. A., Waydhas, C., & Hamsen, U. (2020). Microbial findings and the role of difficult-to-treat pathogens in patients with periprosthetic infection admitted to the intensive care unit. Orthopedic reviews, 12(3).
- 31. Spagnolo, A. M., Sartini, M., & Cristina, M. L. (2020). Microbial contamination of dental unit waterlines and potential risk of infection: a narrative review. Pathogens, 9(8), 651.
- 32. Spagnolo, A. M., Sartini, M., & Cristina, M. L. (2020). Microbial contamination of dental unit waterlines and potential risk of infection: a narrative review. Pathogens, 9(8), 651.



- 33. Rhoades, N., Mendoza, N., Jankeel, A., Sureshchandra, S., Alvarez, A. D., Doratt, B., ...
 & Messaoudi, I. (2019). Altered immunity and microbial dysbiosis in aged individuals with long-term controlled HIV infection. Frontiers in immunology, 10, 463.
- 34. Giron, L. B., Tanes, C. E., Schleimann, M. H., Engen, P. A., Mattei, L. M., Anzurez, A., ... & Abdel-Mohsen, M. (2020). Sialylation and fucosylation modulate inflammasomeactivating eIF2 Signaling and microbial translocation during HIV infection. Mucosal immunology, 13(5), 753-766.