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A comprehensive review on the molecular basis of microbial pathogenesis of viral and bacterial infections

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Abstract
Research on microbial infections determines both the immediate and long-term interactions between specific microorganism and their hosts. Microbial pathogenesis is a complex phenomenon involving the interaction between microbial virulence factors and host cellular responses. These virulence factors include invasins, capsules, siderophores, enzymes, endotoxins, and exotoxins. Though the main problem in the current scenario is the coinfection. Beyond initiating infection, these factors also help the pathogenic microbes survive and thrive within the host's environment. Understanding the molecular mechanisms of microbial infections is essential for developing effective treatments, preventive measures, and vaccines. This review delves into how microbial pathogens invade host cells, evade the immune system, and establish infections. It also covers mechanisms of immune evasion, such as antigenic variation, mimicry, and the manipulation of host signaling pathways, utilizing advanced molecular biology techniques like CRISPR-Cas9 gene editing, transcriptomics, and proteomics. Additionally, it focuses on the key molecular interactions between viral and bacterial pathogen induced infections like respiratory co-infection and secondary bacterial pneumonia in patients with covid-19.

Keywords: Enzyme, host response, microbial virulence factors, molecular mechanism

Introduction
The pathogenesis of coronavirus disease 2019 (COVID-19), which is caused by the coronavirus type-2 (SARS-CoV-2) virus, is still not fully known despite the disease's global expansion. A thorough description has been provided of respiratory infections brought on by multiple viruses (viral co-infection) or by bacteria and viruses together (combined viral and bacterial pneumonia). Secondary bacterial pneumonia may develop during the healing phase of a viral respiratory infection, or it may follow the original phase [1]. The overall incidence of viral co-infection has varied greatly from 0% to 19% in different case series, according to the limited data on SARS-CoV-2. The rates of combined viral and bacterial pneumonia also seem modest [3] [8-10]. Furthermore, little is known about the organisms and risk factors that cause the condition. The most well-studied cases of combined viral and bacterial pneumonia, secondary bacterial pneumonia caused by Staphylococcus aureus and other prevalent community-acquired pneumonia pathogens, and considerable morbidity and mortality are associated with seasonal and pandemic influenza [2, 3]. During the previous pandemic of severe acute respiratory syndrome (SARS), methicillin-resistant S aureus (MRSA) caused 47% of cases of secondary bacterial pneumonia, although there was serious concern about cross-transmission. This pneumonia occurred as ventilator-associated pneumonia in 25% of patients at a single center [7]. The following commentary is based on available clinical data and experience with similar viruses, such as influenza and SARS-CoV, because there isn't a clear pattern or set of guidelines for viral co-infection, combined viral and bacterial pneumonia, or secondary bacterial pneumonia in the context of SARS-CoV-2. Based on our current understanding, a comprehensive approach to COVID-19 would ideally encompass both the entire presentation and the illness trajectory.

Viral Co-Infection
In addition to SARS-CoV-2 testing, polymerase chain reaction (PCR) assays should be used to screen for influenza in all individuals who exhibit symptoms of a respiratory infection. If accessible, PCR assays can also be used to test for additional respiratory viruses.

All patients with co-infection with the influenza A or B viruses should receive treatment with oseltamivir or a different medication, regardless of the severity of their illness [11]. If there is a clear exposure or risk factor, empirical treatment for influenza virus co-infection may be explored while test results are awaited. Therapy alternatives are restricted and only work in certain situations, including immunosuppression or hypogammaglobulinemia, if viral co-infection with another respiratory virus, such as respiratory syncytial virus, is found [12, 13]. It is highly advised to visit an infectious disease specialist to weigh the advantages of this course of treatment against the possibility of aggravating COVID-19-related organ failure and the possible side effects of the prescribed medicine or medications.

Bacterial Pneumonia

A strong index of suspicion is needed to diagnose secondary bacterial pneumonia with COVID-19 or combination viral and bacterial pneumonia. Even while viral and bacterial symptomatology significantly overlap [2-10, 14-29], some aspects of bacterial infection may still be distinguishable. Bacterial pneumonia is characterized by neutrophilicleukocytosis, but COVID-19 patients usually exhibit lymphopenia along with a normal white blood cell count [5, 8, 14, 15].

Mode of Infection

In order to distinguish between the two possible causes of community-acquired pneumonia, procalcitonin is neither sensitive nor specific [11]. But procalcitonin levels in isolated SARS-CoV-2 infection have been regularly reported to be normal (low) in various COVID-19 case series. This has led to its widespread, albeit unvalidated, usage to “rule out” combination viral and bacterial pneumonia, but the precise cutoff is still unknown. This comment emphasizes how important it is to take into account every factor within the framework of the clinical setting. Antibiotics can be safely delayed in patients with mild to moderate respiratory failure consistent with COVID-19 presentation and without clear evidence of bacterial infection. This is because there is little chance of mixed viral and bacterial pneumonia in these individuals. In this instance, the advancement of COVID-19 is more likely to be the cause of the steadily deteriorating respiratory failure during the first week of presentation than the emergence of a newly superimposed secondary bacterial pneumonia. This covers patients who begin receiving supplemental oxygen support in a non-invasive manner before eventually needing invasive mechanical ventilation. Even if respiratory discomfort is getting worse, medicines shouldn't be started if there isn't any sign of bacterial pneumonia. Unless otherwise demonstrated, nosocomial acquisition of secondary bacterial infection—that is, hospital-acquired pneumonia, infection at an extrapulmonary site, or both—is likely if a patient experiences new or sharply worsening respiratory failure, sepsis, or both following an initial period of consistent improvement (considered to be days).

Although COVID-19 can induce acute respiratory decompensation on its own, there is little information on the potential involvement of secondary bacterial pneumonia in this condition. Consequently, until this secondary infection is ruled out, using empiric antibiotics based on guidelines may be prudent. One or more of the following symptoms could indicate secondary bacterial pneumonia: new or recrudescent fever; fresh onset or change in sputum characteristics; fresh neutrophilia or leukocytosis (or both); fresh pertinent imaging results; and fresh or rising oxygen demand. It's crucial to manage these patients appropriately and take into account any additional potential causes of hospital-acquired infections, such as urinary tract or indwelling central venous catheters. Empirical treatment for all potential causes at the outset is crucial for a critically ill patient who has been admitted and is experiencing acute respiratory failure. Because procalcitonin levels in patients with multiorgan failure can be mistakenly increased, this is very crucial [30, 31], therefore it may be difficult to distinguish between concealed bacterial infection consolidation and bilateral infiltrates of acute respiratory distress syndrome using imaging investigations.

Possible Mode of Management

The American Thoracic Society (ATS) and Infectious Diseases Society of America (IDSA) guidelines, host risk factors, and previous microbiologic data should all be taken into consideration when developing an empirical treatment plan for community-acquired pneumonia [19]. For every patient, respiratory samples (tracheal aspirate is preferred over sputum in those on mechanical ventilation) and blood cultures should be submitted, ideally prior to the initiation of medications. All patients who come with severe community-acquired pneumonia should have a test for the urine antigen of streptococcus pneumoniae. Depending on the clinical setting and epidemiology, samples for Legionella pneumophila urine antigen and Mycoplasma pneumoniaeIgM and IgG antibodies may be provided. If there are no symptoms of bacterial pneumonia, a positive respiratory culture may indicate colonization, particularly in those who have already had pneumonia caused by the same organism in the past or have changed airway anatomy. This distinction can be made with the aid of laboratory markers, radiologic characteristics, and quantitative and semiquantitative culture techniques [19]. While the presentation of secondary bacterial pneumonia in a patient receiving invasive mechanical ventilation resembles that of hospital-acquired pneumonia, guidelines dictate the aggressive use of empiric broad-spectrum antibiotics that cover MRSA, Pseudomonas aeruginosa, and potentially other multidrug-resistant organisms [19]. The adverse effects of institutional antibiograms and antibiotics must also be taken into account. In addition to frequently exhibiting lower-grade fevers and higher secretions, patients with ventilator-associated tracheobronchitis may also have low-grade fevers and prove challenging to wean off of ventilator assistance. Only a careful case-based review is necessary because the evidence supporting antibiotic therapy for this clinical entity is weak.

For community-acquired pneumonia [32], antibiotic therapy should be administered for 5 to 7 days; in the case of hospital-acquired pneumonia and ventilator-associated pneumonia [19], it should be administered for 7 days, provided no problems arise. In particular, if side effects are observed, think about reducing the period if patients show symptoms of clinical stability. Based on the procalcitonin level trend over the course of 24 to 48 hours, determining the procalcitonin level at presentation will aid in the de-escalation of antibiotics [33]. It is permissible to stop all antibiotics if, after 48 hours of testing, a microbiological source cannot be found and the procalcitonin level is less

than 0.5 μg/L or drops by 80% or more from peak concentration [19]. Because interleukin 6 (IL-6) inhibitors, such tocilizumab, reduce frequent indications of sepsis, using them for COVID-19-related cytokine activation syndrome poses a special problem. When tocilizumab is used for rheumatologic illnesses, there is a consistently observed increased risk of serious bacterial infections [34, 35, 36, 37]. After using tocilizumab, C-reactive protein and other acute-phase reactants, such as white blood cell count, may not rise in response to a secondary bacterial infection [35, 38, 39]. It's unclear exactly how long this impact lasts after taking one or two doses. Although procalcitonin may be less influenced by IL-6 inhibitors, there is insufficient data to distinguish between bacterial and viral pneumonia in this setting, and more research is needed to make this determination [40-44].

Conclusion

Combining SARS-CoV-2 with a bacterial pathogen (combined viral and bacterial pneumonia) or SARS-CoV-2 with another virus (viral co-infection) can cause respiratory infections in COVID-19. Either during the healing phase or after the initial viral respiratory illness, secondary bacterial pneumonia can develop. Regarding viral co-infection, combined viral and bacterial pneumonia, or subsequent bacterial pneumonia in COVID-19, there isn't a clear pattern or set of recommendations. The management strategy for COVID-19 should, ideally, take into account the overall presentation and the progression of illness based on available clinical data and experience with viruses related to influenza and SARS-CoV. Last but not least, invasive pulmonary aspergillosis is linked to high rates of morbidity and mortality and has been reported in critically ill patients with seasonal and pandemic influenza. Patients with acute respiratory distress syndrome linked with COVID-19 have also been documented to have invasive pulmonary aspergillosis. High-risk patients include those with immunocompromised states, prior or concurrent influenza viral co-infection, clinical worsening despite proper antibiotic treatment, and positive fungal indicators such as galactomannan on culture. These patients should be monitored closely for this consequence. Treatment with a wide antifungal, such as voriconazole, should be started as soon as invasive pulmonary aspergillosis is detected, after consulting with colleagues in infectious diseases.

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Conflict of Interest

All authors declare that there are no conflicts of interest.

Data Availability Statement

No data was used for the research described in the article.

Author's Contribution

ManojitBysack (MB) participated in the conception of the study. RajenDey (RD) and Sanjana Sengupta (SS) participated in literature searches and extraction. MB and SS wrote the manuscript for submission to this journal.

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