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Methods for Identifying the Main Pathogens of Pneumonia and Analytical Assessment of the Importance of Microbiological Analysis

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Abstract

In developed nations, community-acquired pneumonia is the leading cause of infection-related deaths and the third leading cause of death overall. Even though international health programs generally follow recommendations for handling this illness model, new information keeps coming to light that causes dispute or necessitates revising its management. The most crucial aspects of this process are reviewed in this study, including the diagnostic management in various clinical contexts and an aetiologic update utilizing novel molecular platforms or imaging modalities. Additionally, it goes over the requirements for clinical stability to discharge as well as admission to the intensive care unit. Lastly, an overview of the primary immunization and preventative options for immunocompetent and immunocompromised hosts is provided. The most dangerous type of community-acquired pneumonia is severe, which is marked by significant morbidity and fatality rates as well as admission to an intensive care unit. Six remaining debatable elements of severe community-acquired pneumonia are thoroughly covered in this review article: PCR molecular techniques for microbial diagnosis; biomarkers for initial management; duration of treatment, use of macrolides or quinolones in the initial empirical antibiotic therapy; modification of initial empirical therapy based on prediction scores for drug-resistant pathogens; use of high-flow nasal oxygen and noninvasive mechanical ventilation; and corticosteroid use as an adjuvant therapy for severe community-acquired pneumonia. An overview of the microbiological causes, diagnostic techniques, and epidemiology of severe pneumonia will be provided in this paper. The topic of management will next be covered, including the use of adjuvant medicines, antimicrobial therapy, respiratory support, and complication prevention.

Keywords: Community-acquired pneumonia, aetiological diagnosis, antibiotic resistance, microbiological diagnosis, diagnostic technologies, risk-benefit analysis.

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Introduction. Pneumonia was the third leading cause of death in the United States in 1930. Even with the advent of medicines in the 1950s, pneumonia and other respiratory infections continue to rank as the fourth leading cause of mortality globally than a century later. Even while immunization campaigns around the world have decreased the prevalence of pneumonia, particularly in populations that are at risk, the disease still causes a significant burden in terms of morbidity, death, medical expenses, and missed work days. In order to guarantee appropriate antibiotic therapy, which is linked to a decrease in mortality, microbiological diagnosis of pneumonia is essential [1,2,3,4]. But only half of patients receive an aetiological diagnosis, so the first antibiotic course should be determined empirically to prevent the delay in starting the right treatment, which is linked to a high death rate. We will be able to identify the bacteria that cause pneumonia more accurately and quickly if we combine new and old methods. In addition to ensuring that patients receive the best antimicrobial treatment possible, this approach may lessen the need for broad-spectrum antibiotics, which would lower antibiotic resistance. More research is required to thoroughly and methodically assess the performance characteristics of molecular techniques, as well as to ascertain how these new technologies will enhance diagnostic testing for respiratory pathogens and impact patient management when they are eventually incorporated into routine practice [5,6,7,8]. In developed nations, community-acquired pneumonia (CAP) is the leading cause of infection-related mortality. It has an incidence of 1.2 to 2.4 cases per 1000 adults in Europe and the USA, excluding the effects of COVID-19. The greater pneumococcal immunization rate in Europe has been blamed for these discrepancies. The incidence rises at extreme ages. Despite the fact that international health schemes generally follow the guidelines for handling this model of infection, there is variation in the diagnostic-therapeutic management, as evidenced by variations in admission rates, microbiological diagnosis, requests for supplementary studies, antimicrobial regimen selection, and the variety of care provided. Furthermore, new material that sparks debate or necessitates an update in its handling is continually being discovered [9,10,11,12,13]. Reviewing the ten areas that have seen the most advancements in community-acquired pneumonia—such as the use of novel molecular platforms to identify the cause, diagnostic guidelines in various clinical contexts, the suitability of imaging methods, or the requirements for admission to the intensive care unit and clinical stability upon discharge—was the goal of the current study. We therefore provide an update on oxygen, steroid, or antibiotic medication. The approach to therapeutic failure or rescue, the primary causes for readmission, and the out-of-hospital management of CAP necessitating hospitalization are further themes covered in this document. Lastly, we went over the primary vaccine and preventative approaches for both immunocompetent and immunocompromised patients [1,2,7,9,11,12,13]. The diagnosis and identification of the pathogenic organisms, the choice of suitable antibiotics and the determination of the length of therapy, and the avoidance of subsequent pneumonia are the most obstacles in the intensive care management of pneumonia. The epidemiology of severe pneumonia, its aetiology, and how our knowledge of microbial ecology is transforming the idea of infection will all be covered in this review. Before moving on to the management of both antibiotic and non-antibiotic therapy, it will first discuss diagnosis, taking into account current diagnostic techniques and potential future developments in diagnostic technologies. Management emphasizes safe breathing, supportive therapy, and preventing ICU admission problems in addition to antimicrobial therapy. This is because the majority of the studies discussed in this review demonstrate the potential benefits of molecular techniques, such as increased sensitivity and speed in establishing a microbiological diagnosis [14-21].

The main purpose of the presented manuscript is to identify the main pathogens of pneumonia and to analytically assess the importance of microbiological analysis.

Bacteria that cause severe pneumonia. Both the patient's underlying immunological status and the

environmental exposure they had before being infected have an impact on the microbial infections that cause pneumonia. According to the widely recognized pathophysiology of bacterial pneumonia, the organism first colonizes the upper respiratory tract before migrating to the lower respiratory tract and proliferating to cause illness. Although being resistant to colonization with a certain organism does seem to protect against infection from that same organism, it is still unknown why some people develop a colonization with pathogenic organisms but do not develop pneumonia, while others do [1,11,14,17,19]. Although there is a wide range of reactions to viral infection, from resistance to asymptomatic shedding to severe pneumonitis, the acquisition of viral pneumonia is thought to vary from that of bacterial pneumonia in that exposure results in viral infection and growth. It is also clear that severe sickness itself can alter the pulmonary microbiota, leading to a decrease in diversity and a shift toward enteric-type gram-negative microbes. This alteration may occur independently of concurrent antibiotic administration. The balance of lung microbiota is altered by changes in bacterial ingress, growth, and removal during acute sickness. It has been proposed that VAP (and maybe HAP) indicate more "overgrowth" of pathogenic bacteria rather than de-novo acquisition and infection. It has been noted that VAP has a high prevalence of oral commensals such Mycoplasma salivarium, which may further promote immunological suppression and encourage the spread of infection [1,2,5,7,17,19,24,28].

Molecular methods in clinical practice. Rapid diagnostic tests monitor the response to antibiotic therapy, identify a particular pathogen or assist in differentiating between bacterial and viral infections, provide information about antibiotic susceptibility, evaluate prognosis, support antimicrobial stewardship, and provide data for disease surveillance. These technologies can be used with a variety of patient populations, from patients who require intensive care unit therapy to outpatients, enabling safe release. The prompt results (1–2 hours) could be helpful when making decisions about critical patients, particularly when it comes to starting the right antimicrobial therapy right away, which is linked to death. Additionally, prompt patient isolation depends on the quick identification of infections resistant to antibiotics. There are still two significant obstacles to overcome, though. 1) Clinicians still struggle to distinguish between colonization and infection, with the possible exception of S. pneumoniae, and we need sufficient data for any of these methods to make inferences about this. 2) Healthcare systems must weigh the relative costs and results of diagnostic testing when deciding whether to use these quick tests; more research on cost-effectiveness is required[1,2,3,14-18].

The application of molecular methods in sCAP microbiological diagnostics. It is still unclear whether approach is appropriate for defining the microbiological aetiology of sCAP. Viruses and bacteria are among the pathogens that cause sCAP, while combination infections including both bacteria and viruses can also occur. S. pneumoniae is the most commonly isolated bacterium. P. aeruginosa, carbapenem-resistant Enterobacterales, P. aeruginosa, and multidrug-resistant (MDR) S. aureus are examples of "non-core pathogens," which are a small percentage of isolated bacteria that are not typically covered for all CAP patients. Acinetobacter species are rarely seen. The aetiological diagnosis rates using conventional microbiological techniques can reach up to 50% [22,23,24,25]. As with any infectious disease, early and appropriate antibiotic therapy, made possible by an accurate diagnosis, is linked to a better prognosis. The only methods that can yield results quickly are Gram staining and urine antigens. Furthermore, not all patients are intubated, and it might be challenging to collect reliable respiratory samples when taking into account additional diagnostic issues in sCAP. Sputum samples are the only method available to clinicians, and they already have problems with sensitivity and specificity, particularly when there has been previous antibiotic therapy [26,27,28,29]. Viral and bacteriological results can be obtained in less than four hours using rapid molecular techniques like PCR testing. The most common bacteria and viruses that could cause sCAP can be found using PCR platforms for pneumonia. These platforms can also quantify the number of copies of MRSA and identify certain resistance genes in gram-negative bacteria. Because gram-negative bacteria frequently employ many resistance mechanisms at the same time (porin loss, efflux, β-lactamases), it is significantly more difficult to define the phenotype when a gene is detected in MRSA. Single mutations provide distinct spectra even across the many β-lactamase classes [30,31,32].

Biomarkers' function in sCAP. Biomarkers including PCT and C-reactive protein (CRP) are crucial for antimicrobial stewardship in sCAP patients, acting as an adjuvant to shorten the course of antibiotic treatment. They cannot, however, be used to decide whether to begin therapy. There is some attenuation of both biomarker levels if they are evaluated after previous antibiotic therapy. Both biomarkers have been investigated in CAP patients, with PCT being increased early (day 1 after symptom onset) and CRP increasing later (day 3 after symptom onset) [22,23,24,25]. While results for individuals with mixed bacterial and viral infections and those with atypical pathogen infections can be inconclusive, studies have long demonstrated higher PCT levels in patients with bacterial infections but not viral ones. In tissues like the liver, parenchymal cells produce PCT, which can increase up to 100,000 times its normal amount in reaction to bacterial infection. Although they haven't been thoroughly investigated in people with sCAP, other biomarkers might indicate the existence of a viral infection. Additionally, in patients with a combination of viral and bacterial infections, the results might not be definitive [31,32,33,34].

The goal of radiological testing for suspected pneumonia is to show that there is alveolar inflammation, either as diffuse alveolitis or as lobar/sub-lobar consolidation. Given its superior resolution over plain radiographs in identifying and characterizing pulmonary abnormalities, computed tomography (CT) is the gold standard for radiographic evaluation of the lungs. However, a CT scan of the chest necessitates the patient's removal from the intensive care unit, which raises the possibility of complications for both ventilated and non-ventilated patients. As a result, it is not a standard test for patients in the intensive care unit who may have pneumonia. The suggested imaging modality for CAP is plain chest radiography (CXR), which can be done at the patient's bedside [11,14,17,21,22]. Remarkably, despite the fact that almost all clinical studies of HAP/VAP require the presence of radiographic infiltrates as an inclusion criterion and that both the European Center for Disease Control and the US Centers for Disease Control definitions require radiographic demonstration of infiltrates, neither the most recent European nor American guidelines on hospital- and ventilator-acquired pneumonia make recommendations on radiological investigation of pneumonia. At least one-third of intensive care unit (ICU) physicians in the UK believe that radiographic evidence is not necessary to diagnose pneumonia. Although lesions must be relatively shallow inside the lung to be recognized, bedside ultrasonography may be more effective than plain radiography in detecting consolidation. Chest ultrasonography has not yet been approved as a diagnostic technique by guidelines, and no research has shown that using it improves patient outcomes [28,29,30,34,35,36].

Discussion. In industrialized nations, CAP is the leading cause of infection-related mortality. Even though there are international guidelines for diagnosis and therapy, new information has recently surfaced that could help improve its care. The gradual development of syndromic platforms based on real-time PCR techniques, which show that viruses are primarily involved as the etiological agent or at least in coinfection, is starting to alter the etiological perspective. This presents a new challenge for therapeutic management in the field of stewardship as well as for the pathological explanation of the illness. A risk-benefit analysis of each patient is necessary when choosing a treatment for CAP, taking into consideration documented antibiotic allergies, personal risk factors, and local epidemiological data [1,2,3,4,5]. With a period of up to seven days, the combination of a beta-lactam and a macrolide appears to be the most advised initial approach. The risk of an excessive oxygen supply should be considered when treating hypoxemia, and the treatment plan should be modified based on the patient's response and the overall therapeutic approach. Similar to this, steroid treatment needs to be tailored to each patient since, while it has been effective in treating shock and distress, it has not helped all clinical profiles of COVID and may even impair the immune system's ability to control the infection. The most significant problem in HaH units is maintaining continuity of care, particularly for patients whose optimal defervescence cannot be ensured in sequential therapy because of comorbidity or intolerance. To prevent readmission, it is essential to monitor comorbidity instability and administer intravenous medications at the prescribed dosages and frequencies [11[14[17[19]. The presence of resistant microorganisms, insufficient antibiotic concentration in the focus, and the intensity of the pneumonic process, which frequently destabilizes comorbidities, are the most common reasons for treatment failure in CAP. The

most effective way to lower the incidence and mortality of pneumonia in both immunocompetent and immunocompromised people is by vaccination [23-28]. In addition to antibiotic treatment, several adjuvant treatments have been tested for pneumonia; however, none of them have yet to be widely used in clinical settings. While corticosteroids are a risk factor for the development of hospital and ventilator-acquired pneumonia, their role in treating patients with severe community-acquired pneumonia (CAP) in the intensive care unit is yet unknown. Immunostimulation has not yet been used in clinical settings after small-scale clinical trials. Lung protection ventilation is one of the supportive care strategies that has been shown to enhance ARDS outcomes. An overview of the microbiological causes, diagnostic techniques, and epidemiology of severe pneumonia will be provided in this paper. The topic of management will next be covered, including the use of adjuvant medicines, antimicrobial therapy, respiratory support, and complication prevention [29-34].

Conclusion. There are no materials that only address sCAP; instead, specific recommendations for sCAP are part of the CAP general principles. The use of molecular techniques in the microbiological diagnosis of sCAP, the role of biomarkers in the initial diagnosis and the use of antibiotics, the use of macrolides or quinolones as part of the initial empirical therapy of sCAP, the use of prediction scores for the presence of drug-resistant pathogens in sCAP to modify initial empirical therapy, the appropriate use of NIMV and high-flow nasal oxygen (HFNO), the justification for the use of corticosteroids as an adjuvant therapy in sCAP, and the use of these topics are all covered in this review. Since pneumonia is characterized by inflammation of the airways, histopathology analysis is the gold standard for diagnosis. However, in the great majority of instances, post-mortem evaluation is obviously too late to change care, and lung biopsy is neither desirable nor practical in a very sick patient. As a result, clinicians must rely on sometimes questionable surrogate indicators of alveolar inflammation and infection.

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