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Community-Acquired Pneumonia

Norbert Suttorp
Tobias Welte
Reinhard Marre
Editors

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Community-Acquired Pneumonia

Edited by N. Suttorp, T. Welte and R. Marre

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Preface

Community-acquired pneumonia is a disease of high morbidity and mortality. Demographic changes in industrialised countries with a growing population of elderly persons will add to its significance. In the last years much progress in the field of community-acquired pneumonia has been achieved. Vaccination programs against influenza and *Streptococcus pneumoniae* have been established. Risk-adjusted management of patients with community-acquired pneumonia allows to identify patients in need of hospitalisation and intensive care and helps to choose an effective antibiotic therapy. "New" pathogens such as *C. pneumoniae*, *Legionella pneumophila*, *Chlamydia*-like organisms, the human coronavirus or the avian influenza virus have been detected. In spite of all progress, clinical diagnosis of community-acquired pneumonia is by no means trivial; detection of respiratory pathogens often fails or gives inconclusive results and duration and choice of antibiotics still is a matter of debate.

Moreover, many patients progress from uncomplicated pneumonia to severe pneumonia and even to pneumonia-related septic shock despite adequate antibiotic therapy. Therefore, besides new antibiotics we definitely need a non-antibiotic approach and a better understanding of what determines individual immune responses to pneumonia is crucial. Fundamental molecular and cellular pathologic characteristics of disease must be linked with clinical aspects of infection.

The present book is intended to bridge the gap between basic science, clinical research and patient management and to crosslink patient care with biology and microbiology. It gives a state of the art information on different aspects of community-acquired pneumonia and allows the reader to get data on recent developments in community-acquired pneumonia. The editors Norbert Suttorp, Tobias Welte and Reinhard Marre themselves, representing clinical medicine, clinical research, microbiology as well as cell biology, hope that this book will help to manage patients with community-acquired pneumonia and to identify promising areas of research.

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Community-Acquired Pneumonia
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Diagnosis and treatment of community acquired pneumonia – the German perspective

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Abstract

Current concepts of diagnosis and treatment of CAP are risk stratified and adapted to the national resistances of important pathogens. Thorough surveillance systems have to be implemented in all countries.

The risk of patients can be assessed reliably with a limited number of clinical data (CRB-65 score). Extended microbiological and laboratory diagnosis is recommended for hospitaliszed patients only. Outpatient treatment can be performed with classic antibiotics like amoxicillin or doxycyclin. Macrolides are only an alternative in these patients. In the hospital, treatment has to be adapted to the severity of the disease. Further studies concerning the duration of treatment and advantageous combinations are necessary.

Recommendations for treatment of CAP have to be adapted to the quickly changing epidemiology and have to be updated every 2 to 3 years.

Introduction

Pneumonia is a worldwide, serious threat to health, and an enormous socio-economic burden for healthcare systems. According to recent WHO data, each year three to four million patients die from pneumonia, a large proportion of whom are children or elderly people. Pneumonia is the third most common cause of death among infectious diseases in the world [1].

Detailed epidemiological data is available from the USA, where two to three million cases of CAP occur each year, leading to around 10 million doctor-patient contacts [2]. If an estimated proportion of 20 % (half a million) of these patients were hospitalised, the incidence is 258 hospital admissions per 100,000 inhabitants. The requirement for hospitalization depends on age, with the highest rates observed for patients over age 65, among whom the necessity for hospital admissions rises by a factor of four to around 1000 per 100,000 inhabitants [3]. In total, it is estimated that the costs for pneumonia treatment reach 8 billion dollars annually in the USA.

The largest proportion of this amount is spent on elderly and hospitalized patients.

Community Acquired Pneumonia (CAP) results in high mortality (mean about 8%). In the US, CAP is the sixth most frequent reason for dying, and there is an increase of 0.5 to 1% per year [2]. The increase is caused by the growing life expectancy, by aging of the population, and by a better treatment of chronic diseases. Elderly people with concomitant diseases are more susceptible to infectious diseases [4], and have typically a spectrum of pathogens (gram negative enterobacteriaceae, staphylococci, legionella, bacteriaemic pneumococci), which is associated with higher mortality [5, 6]. While the mortality of CAP is low in outpatients (1%), it can rise to up to 12% in hospitalized patients [2].

Definition

Pneumonia is an infection of the alveolar space, with accumulation of inflammatory cells and secretions in the alveoli, resulting in impaired gas exchange [8]. Each pneumonia acquired outside of a hospital is defined as community acquired pneumonia [4], while nosocomial pneumonia is caused during a stay in the hospital and up to one week after discharge. A subgroup of CAP is the ”healthcare associated pneumonia” of patients with frequent contact with the healthcare system (haemodialysis patients, patients in nursing homes) [9]. Although it is community acquired, this form is treated similar to a nosocomial infection.

The approach of scientific communities to CAP is very different. A proof of the disease is the pathologic result, combined with a positive microbiologic specimen of the tissue. In the clinical routine, biopsies of the lungs cannot be obtained. The typical signs on the chest radiograph can be delayed, even with the best technical equipment. Initial diagnostics often shows no pulmonary infiltration [10]. All other signs which are typical for pneumonia, such as the typical sounds on auscultation, fever, cough and sputum expectoration, dispnoea, chest pain and serological markers of inflammation are not pathognomic, and are nearly not always present in all patients. In the English-speaking countries, the appearance of a new or progressive infiltration is absolutely necessary for a diagnosis of pneumonia. All other criteria are of minor importance for the diagnosis [11]. The European Respiratory Society (ERS) defines pneumonia not *via* a chest radiograph finding, since many outpatients do not receive this diagnostic and therefore chest x-ray cannot be the major criterion. The ERS defines a “lower respiratory tract infection”, according to the clinical presentation. This includes tracheo-bronchitis, influenza infection, exacerbation of COPD, and pneumonia [12]. The recommendations of the ERS are much broader and cannot been compared with the narrowly focused American recommendations for CAP.

Aetiology

The spectrum of pathogens and resistances varies widely between continents and countries. Universal guidelines for diagnosing and treatment are for rough orientation only; the treatment must be adapted to the specific local situation.

Even under optimal diagnostic conditions, sufficient sputum specimen can be obtained in only 50% of patients [13]. In the early phase of the infection, sputum production may still be normal. In about one-third of all cases, the specimen do not meet international quality standards, which require a high proportion of leukocytes and a low proportion of squamous cells (Bartlett-criteria [4]). Depending on the patient group (all patients, all patients with positive results in the specimen, all patients who were able to expectorate sputum, all patients who produced purulent sputum), very different distributions of pathogens has been reported. According to results from the German competence network for CAP (CAPNETZ [14]), a reliable microbiologic diagnosis can be established in only 20% of all cases [15]. Worldwide, the most important pathogen is *Streptococcus pneumoniae*, followed by *Haemophilus influenzae* and *Mycoplasma pneumoniae*. *Legionella* is rare with a frequency of 4%, but associated with an excessive mortality. This underlines the importance of the very sensitive urinary-antigen testing in cases with clinically suspected infection with legionella (Tab. 1). Infections with enterobacteriaceae are most common in patients from nursing homes, elderly patients and multi-morbid patients (cardiac and kidney diseases, neurologic disorders and chronic obstructive pulmonary disease, CODP). The mortality of these patients is much higher than in patients who are living in the normal community [16]. In the USA, *Pseudomonas aeruginosa* is also a typical pathogen in CAP [6], but *Pseudomonas* is not important in middle and northern Europe.

Some studies from Italy and Spain [17] report a high prevalence of *Chlamydia pneumoniae* (> 10%). These results come from serologic test-

Table 1. Clinical findings in patients with legionella infection

Fever	100%
Chills	73%
Cough	83%
Purulent sputum	50%
Chest pain	30%
Abdominal symptoms	30%
Polymyositis	78%
Neurological symptoms	23%

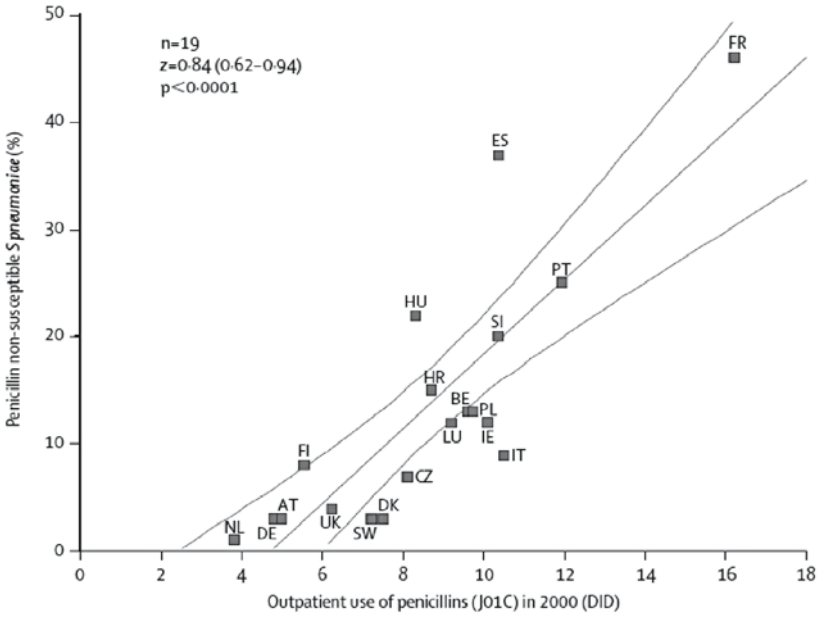

Figure 1. Association of the consumption of penicillins and the prevalence of penicillin resistant pneumococci in Europe (modified according to [22]).
AT, Austria; BE, Belgium; HR, Croatia; CZ, Czech Republic; DK, Denmark; FI, Finland; FR, France; DE, Germany; HU, Hungary; IE, Ireland; IT, Italy; LU, Luxembourg; NL, The Netherlands; PL, Poland; PT, Portugal; SI, Slovenia; ES, Spain; UK, England only.

ing. Studies using polymerase chain reaction (PCR) show in less than 3% a positive finding [15]. The titres of IgA and IgM may remain elevated, even after previous or oligosymptomatic infections. The use of serologic testing seem not to be sensible in an acute infection. *Chlamydia pneumoniae* might be very prevalent is special outbreaks, but presently, the importance of *C. pneumoniae* for CAP seems to be low.

Viruses had been found in a number of studies (with or without PCR) in 10 to 1 % of all CAP cases [5, 15, 18]. The question of whether viruses are the responsible pathogen for CAP, or if the virus induced damage of the bronchial epithelia is the precursor of bacterial infection, is still open. In winter, influenza viruses are most important (70% of all viruses), underlining the importance of influenza vaccination in the elderly because of the prevalence and severity of pneumonia. Large trials revealed that vaccination results in lower rates of pneumonia [19]. Similar results could not be obtained for the vaccination against *S. pneumoniae*, since the vaccinate did not cover all serotypes of this pathogen. Bacteriaemic infections could be prevented, but there is no local protection [14]. American studies revealed

that vaccination of children reduced the incidence of severe pneumonia in adults, albeit different serotypes play the dominant role [20].

Resistances

Problems with resistances of the most important pathogens, especially pneumococci, vary widely between different countries [21]. The main reasons are differences in the consumption of antibiotics. There is a direct correlation between the use of antibiotics and resistances in many countries (Fig. 1) [22].

The significance of pathogen resistances for the outcome of a patient is controversially discussed. Increasing resistances of pneumococci against penicillin did not affect the mortality, even when treatment with penicillin was continued. On the other hand, resistances against Cefuroxim had been found to worsen mortality of pneumonia patients [23].

Pneumococci resistant against makrolides seem to be associated with higher rates of bacteriaemia [24], but the impact on mortality in unclear. If peumococci are resistant against fluorochinolones (there has been one epidemic in Hong Kong), treatment with fluorochinolons had worsened the prognosis of some individual patients [25].

An improvement of resistances can be achieved – as documented in Scandinavia – by temporary reduction of the use of the respective classes of antibiotics [26].

Risk stratification

The risk factors for an increased CAP mortality are age, the number of concomitant diseases, and the place of residence before admission to the hospital (patients from nursing homes had an eight-fold higher risk for dying than patients coming from "regular" homes) [7].

Different scores for the estimation of the prognosis of patients with CAP had been evaluated to substantiate the decision for hospital admission and the decision of where to treat the patient (regular ward, intermediate care unit, intensive care unit). Many scores designed for hospital patients (Pneumonia Severity Index, PSI [27], CURB Score [28]) have the disadvantage that they need laboratory testing, what is not available in the outpatient setting. Recent data revealed that a simple clinical score (CRB-65; C: Confusion, R: respiratory rate > 30/min, B: blood pressure < 90 mmHg, 65: age > 65 years) allows to stratify patients into a low, moderate, or high mortality risk group [29, 30].

The risk within the hospital can be best assessed with the modified ATS Score [31]. If one major criterion (septic shock requiring vasopressor therapy or mechanical ventilation) or two minor criteria (acute respiratory