

**Manuscript type: Invited review**

**DOI: 10.5152/etd.2018.01288**

**Title: Community-acquired pneumonia in adults:**

**What's new focusing on epidemiology, microorganisms and diagnosis?**

**Running title: Community-acquired pneumonia in adults.**

**Authors: Sofía Tejada\*<sup>1,2</sup> BSc, MSc, Anabel Romero<sup>1,2</sup> BSc, PhD and Jordi Rello<sup>1,2</sup> MD PhD**

1- CIBER de Enfermedades Respiratorias, CIBERES, Barcelona, Spain.

2- Vall d'Hebron Institut of Research (VHIR), Barcelona, Spain.

Conflicts of interest: J.R. has received honoraria for consulting from Paratek, KaloBios, LASCO and MedImmune.

\*Corresponding author.

Sofía Tejada

CIBERES - Vall d'Hebron Institut de Recerca

**Clinical Research/epidemiology In Pneumonia & Sepsis (CRIPS)**

Ps Vall d'Hebron 119 14th floor

08035 Barcelona, Spain

Email address: stmagraner@gmail.com

**Cite this article as:** Tejada S, Romero A, Rello J. Community-acquired pneumonia in adults: What's new focusing on epidemiology, microorganisms and diagnosis? Erciyes Med J 2018; DOI: 10.5152/etd.2018.01288

## **Abstract**

Community-acquired pneumonia (CAP) is one of the most leading causes of hospital admissions and death worldwide..The incidence and mortality of CAP are associated to presence of comorbidities and increasing age. *Streptococcus pneumoniae* is the most

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as: Tejada S, Romero A, Rello J. Community-acquired pneumonia in adults: What's new focusing on epidemiology, microorganisms and diagnosis? Erciyes Med J 2018; DOI: 10.5152/etd.2018.01288

©Copyright 2018 by Erciyes University Faculty of Medicine - Available online at [www.erciyesmedj.com](http://www.erciyesmedj.com)

frequently microorganism causative of CAP, although in many patients with CAP, the causative microorganism remains unidentified. Currently, antimicrobial resistance is increasing, so the accurate diagnosis and determining the causative microorganism are even more important. This is a key point in reducing both morbidity and mortality from CAP, and appropriate antimicrobial stewardship which is now a worldwide priority. This review summarizes on epidemiology, microbiological etiology and diagnosis of CAP in adults.

**Keywords: Community-acquired pneumonia (CAP), Comorbidity, *Streptococcus pneumoniae*, epidemiology, adults, microbiological diagnosis, immunological biomarkers.**

#### Key messages

- It is expected that CAP will continue as an outstanding public health problem worldwide, with some differences in its epidemiology across undeveloped and developed countries.
- Co-morbidities have an important role in determining the risk for pneumonia and disease severity.
- *S. pneumoniae* is the most common microorganism identified in CAP patients; although in many patients, microbiological diagnosis is not achieved.
- CAP diagnosis depends on patient history, risk factors, clinical findings and microbiologic tests.

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as: Tejada S, Romero A, Rello J. Community-acquired pneumonia in adults: What's new focusing on epidemiology, microorganisms and diagnosis? *Erciyes Med J* 2018; DOI: 10.5152/etd.2018.01288

©Copyright 2018 by Erciyes University Faculty of Medicine - Available online at [www.erciyesmedj.com](http://www.erciyesmedj.com)

## Introduction

Worldwide, general worsening of health is related to aging of the population. The high proportion of elderly people (> 65 years) suffering from one or several comorbidities, and the increase in the ineffectiveness of the immune system are responsible for the increase of the infectious diseases in the elderly and it is associated with an higher risk of mortality (1). Pneumonia is an inflammatory disease of the lung caused by infectious microorganisms in the lower respiratory tract.. It's a serious and progressive infection that affect between 5 and 11 people per 1,000 of the adult population each year (2). CAP is considered the most infectious cause of sepsis in the world (1) and approximately 50% of admissions caused by CAP in intensive care units (ICUs) are associated with septic shock (3).

CAP can be caused by many microorganisms including fungi, viruses and bacteria, so it's essential to know the pathogenic microorganism that causes the infection to provide an adequate clinical diagnosis (4). The most common pathogen causing CAP is *S. pneumoniae*, but nearly 50% of patients with CAP still have unidentified organisms (5). The objective of this review was to describe the epidemiology, the microbiological etiology and diagnosis of CAP worldwide.

The bibliographic search was performed through ISI Web of Knowledge and PubMed (reports from 2004 onwards) using a comprehensive search strategy. We searched terms relating to community-acquired pneumonia AND microorganisms AND diagnosis. All search results were limited to human adults and exclusion criteria were age under 18 years old, cystic fibrosis, neutropenia, nursing home or transplant recipient. The search lasted approximately three weeks since 1st July 2018 until 19th July 2018, English was the language to use and a total of 36 studies were considered.

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as: Tejada S, Romero A, Rello J. Community-acquired pneumonia in adults: What's new focusing on epidemiology, microorganisms and diagnosis? *Erciyes Med J* 2018; DOI: 10.5152/etd.2018.01288

UNCORRECTED

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as: Tejada S, Romero A, Rello J. Community-acquired pneumonia in adults: What's new focusing on epidemiology, microorganisms and diagnosis? *Erciyes Med J* 2018; DOI: 10.5152/etd.2018.01288

©Copyright 2018 by Erciyes University Faculty of Medicine - Available online at [www.erciyesmedj.com](http://www.erciyesmedj.com)

## **CAP epidemiology**

CAP is the main cause of infectious disease related mortality across the world, and is responsible for approximately one million of hospital admissions with a great impact on health care resources. Its incidence and mortality are related to the increase in age and the presence of comorbidities (4). Given that population is aging, it is expected that CAP will continue increasing as an outstanding public health problem (6).

CAP epidemiology can show differences according to geographical areas, healthcare setting and population of study. According to a report by the National Center for Health Statistics, in 2014 influenza and pneumonia together were the eighth cause of mortality in the USA. Also in the USA, in 2013 CAP incidence reported in adults over 65 years ranged from 63 cases per 10,000, to 164.3 cases per 10,000 in adults over 80 years old (7). For the same period, 2013, CAP incidence ranged from 76 to 140 cases per 10,000 adults in patients over 65 years in Europe (1). In Turkey, lower respiratory tract infections (including pneumonia) rank fifth among main causes of death (8). Few articles on CAP epidemiology in Turkey have been found. The article by Koulenti *et al.* (9) carried out in 9 European countries, including Turkey, deals with nosocomial pneumonia, which is out of scope of this review.

In developed countries, older age is the main risk factor for CAP. In a population-based surveillance study by Jain *et al.* (7) performed in five hospitals in Chicago and Nashville (USA) from January 2010 through June 2012, they found that incidence of hospitalized CAP increased with older age. They reported an overall annual incidence of pneumonia of 24.8 cases per 10,000 adults. By age groups, those adults between 65 and 79 years of age showed a rate of 63.0 cases per 10,000 adults, while the group with 80 years of age or older showed the highest

**This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as: Tejada S, Romero A, Rello J. Community-acquired pneumonia in adults: What's new focusing on epidemiology, microorganisms and diagnosis? Erciyes Med J 2018; DOI: 10.5152/etd.2018.01288**

rate: 164.3 cases per 10,000 adults. ). In the study by Torres *et al.* (10) performed in Europe – not including Turkey - the overall incidence rates for CAP were 68–7,000 per 100,000.

In countries in development, few data can be found about population-level pneumonia incidence. Using hospital data, pneumonia is one of the most frequent cause of hospitalization in adults. While in developed countries, the main burden of patients hospitalized with CAP is in older patients, with comorbidity; in many in development countries the main burden of hospitalized CAP patients is among adults in working-age. World Health Organization (WHO) reported that the average number of deaths related to CAP was approximately 700,000 deaths per year in developing countries. Moreover, the contracting-risk CAP is also strongly linked to the prevalence of the disease in the environment, which is the case of populations with poor access to primary health care services (4).

#### ***Risk factors for CAP***

Quickly identify patients at risk for severe CAP are important to pneumonia prevention and management. The etiology has been related to age and variations in less representative pathogens. The patient's age and comorbidities play an important role in determining the risk and disease severity of pneumonia. Thereby, patients with other diseases such as diabetes, cancer, chronic heart failure, Chronic Obstructive Pulmonary Disease (COPD), Alzheimer, coronary artery disease, cystic fibrosis, renal insufficiency/dialysis,, diabetes mellitus (DM), malignancy, chronic neurologic disease, or chronic liver disease, have a higher incidence of pneumonia. Besides co-morbidities, toxic habits such as smoking, or alcoholism have been also reported as risks factors for CAP. In elderly( $\leq 60$  years), the risk increases in the presence of asthma, alcoholism, or immunosuppression (11). Other important factors are male sex, and the development of acute respiratory failure (ARF), severe sepsis and bacteremia (3).

**This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as: Tejada S, Romero A, Rello J. Community-acquired pneumonia in adults: What's new focusing on epidemiology, microorganisms and diagnosis? Erciyes Med J 2018; DOI: 10.5152/etd.2018.01288**

Regarding mortality, a study conducted between 2011 and 2013 by Akyil *et al.* (12) studied the reasons and factors that underlie the patients' lower survival. According to this study, the risk factors that must be considered are: advanced age, male sex, black race, pneumonia associated with medical care and chronic comorbid diseases. In general, 82% of patients were diagnosed with at least one of the following diseases: asthma, COPD, coronary heart disease (CHD), chronic kidney disease (CRD), congestive heart failure (CHF), malignancy diabetes mellitus (DM), among others. During follow-up, it was observed that malignancy, COPD, cardiovascular diseases and neurodegenerative disorders increased mortality (Table 1.).

### **Causative microorganisms**

Knowledge of the most common causes of CAP is important to initial empirical antibiotic prescription. Globally, *S. pneumoniae* caused more than 90% of cases of pneumonia in adults (13). On the other hand, atypical pneumonia is caused by fastidious organisms, enclosing *Mycoplasma pneumoniae*, *Legionella pneumophila*, *Coxiella burnetti*, *Chlamydomphila pneumoniae* and *Chlamydomphila psittaci*, among others (14), representing up to 22% of all cases. In immunocompromised patients with CAP Enterobacteriaceae spp, *P. aeruginosa*, methicillin-resistant *S. aureus* (MRSA) and extended-spectrum beta-lactamase (ESBL+) are more frequent (15). The study by Gunduz *et al.* (16) conducted in Turkey between 2009 and 2013 observed that the causative bacteria isolated most frequently in patients with CAP were *S. pneumoniae*, *P. aeruginosa*, *E. coli*, *H. influenzae*, *S. aureus*, *K pneumoniae*, *Streptococcus* spp. (others) and *Moraxella catarrhalis*. Another study (17) conducted between 2002 and 2009 highlighted that 0.5% to 10% of CAP cases were attributed to *Legionella*, being, the most common species *L. pneumophila*.

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as: Tejada S, Romero A, Rello J. Community-acquired pneumonia in adults: What's new focusing on epidemiology, microorganisms and diagnosis? Erciyes Med J 2018; DOI: 10.5152/etd.2018.01288

A more useful approach in clinical practice is to classify organisms and episodes based on degree of severity. Scores such as CURB-65 or PIRO-CAP among others help to stratify in severity, being acute respiratory failure and shock, most important causing of ICU admission (3, 18, 19).

As mentioned above, *S. pneumoniae* is the main bacterial agent that causes CAP. This is consistent with studies conducted in the last 10 years in Europe, Asia and the USA, showing that the most common worldwide bacteria are *S. pneumoniae*, *P. aeruginosa*, *S. aureus* and *H. influenzae* (Table 1).

## **Diagnosis**

Pneumonia is the main cause of sepsis. As a consequence, personalized medicine is an important approach in current management strategies. A detailed review on biomarkers and molecular diagnostic tests is far away of the purposes of this study. We refer the interested reader to the recent ESCMID position paper Towards a Personalized medicine approach in Sepsis (20).

## **Clinical**

An important part of the diagnosis of CAP is a thorough evaluation of a patient's condition. Before making a diagnosis, patient's history must be acquired, physical examination and microbiological tests such as Gram stain and blood cultures must be performed. It's very important to follow the proposed guidelines of national and international clinical practice guidelines for the correct microbiological diagnosis of pneumonia (11). According to these guides, for severe CAP, it is recommended to perform blood cultures, cultures and sputum staining, and the urinary antigen test for Legionella and Pneumococcus. For example, sputum culture and urinary antigen test for *L. pneumophila* and *S. pneumoniae* are used for outpatients with failure of antibiotic therapy; sputum and blood culture are used for hospitalized patients with positive urinary antigen test for Pneumococcus and cavitary infiltrates; sputum, blood culture, urinary antigen test for *L. pneumophila* and *S. pneumoniae*, tracheal aspirate or bronchoalveolar lavage culture and viral studies also need to be performed

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as: Tejada S, Romero A, Rello J. Community-acquired pneumonia in adults: What's new focusing on epidemiology, microorganisms and diagnosis? Erciyes Med J 2018; DOI: 10.5152/etd.2018.01288

are used for severe CAP admitted to ICU; urinary antigen test for Legionella serotype 1 and influenza test during influenza season are used for epidemiological factor or specific risk factors suggesting pathogen. The low performance, the long time for a response and the previous antibiotic exposure are the main problems of these diagnostic methods (21).

### ***Conventional Microbiological Diagnosis***

Microbiological techniques allow the identification and characterization of the etiological agent of CAP. However, due to the low sensitivity of microbiological studies, the difficulty in obtaining an adequate sample and the low cost/benefit ratio, it is not recommended to carry out routine microbiological tests (11). For this, the following techniques are available:

1. Blood and pleural cultures: Blood cultures are still the reference technique used for the microbiological diagnosis of infections that occur in the bloodstream. Nevertheless, these methods have limitations, such as false-negatives and long time to positivity. On the one hand, it has inconvenient bacteria, such as the possible presence of non-culturable pathogens and the low number of microorganisms (11). On the other hand, blood cultures are relatively cheap, use widely available / accepted technologies and facilitate the evaluation of the antimicrobial susceptibility of the pathogen (20).
2. Thoracocentesis is an invasive technique that is based on the surgical puncture to evacuate the pleural fluid from the chest wall, for cytochemical study and bacteriological examination. Pleural or molecular technical samples are recommended for the detection of pneumococcal antigen (22).
3. Sputum stain and culture: It is important to perform sputum sample collection before starting antimicrobial therapy. Sputum cannot be processed for the cultivation of anaerobes

**This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as: Tejada S, Romero A, Rello J. Community-acquired pneumonia in adults: What's new focusing on epidemiology, microorganisms and diagnosis? Erciyes Med J 2018; DOI: 10.5152/etd.2018.01288**

because it is contaminated when passing through the oral cavity so it is recommended that the sample be collected and transported to increase the diagnostic accuracy. A good quality sample is considered when the sputum sample contains less than 10 epithelial cells and more than 25 lymphocyte cells (22). When a pathogen is isolated from sputum culture, a presumptive diagnosis is considered (23).

4. Antigen detection: They are usually performed in hospitalized patients. The bacterial pneumococcal and *Legionella* serotype 1 can be detected. The use of previous antibiotics does not affect the detection of antigens. The detection of pneumococcus has sensitivity between 50% and 80% with a specificity of 70% to 90%. The most common serogroup detected is *Legionella* serogroup 1, with sensitivity between 70% and 90% and 99% of specificity (24).

#### ***Immunological biomarkers***

The biomarkers are used for a quick diagnosis of the disease and to reduce the time of antibiotics administration. Therefore, the biomarkers can help with the correct choice of antibiotics and help measure the treatment response (25). In view of the complexity of the pneumonia response, it is unlikely that a single ideal biomarker will ever be found. A combination of several biomarkers may be more effective, but this requires further evaluation (20). The role of some interleukins (IL-6, IL-8, L-10), C-reactive protein (CRP), lipopolysaccharide binding protein, soluble trigger receptor expressed in myeloid cells (TREM-1) and the soluble urokinase plasminogen activator receptor (suPAR) has been evaluated in recent studies. No one of the biomarkers mentioned is enough specific to be used alone. One of the biomarkers most studied today is procalcitonin (PCT). PCT is a calcitonin propeptide that is released in response to existing endotoxins in the walls of bacterial cells, cytokines and chemokines. It's a biomarker that is usually used to know the dose and duration of treatment

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as: Tejada S, Romero A, Rello J. Community-acquired pneumonia in adults: What's new focusing on epidemiology, microorganisms and diagnosis? *Erciyes Med J* 2018; DOI: 10.5152/etd.2018.01288

with antibiotics for patients with sepsis (26). The arrays of biomarkers available have improved both diagnosis and prognosis and aid a personalized approach for pneumonia treatment (20).

### ***Molecular Diagnosis***

Molecular techniques are faster and precise for the detection of respiratory pathogens (27). In addition, they provide information on susceptibility to antibiotics and help control the response to therapy, among others. Currently, the PCR technique is widely used for the identification of pathogen from positive blood cultures (sensitivity and specificity > 90%).

Another technique to evaluate antimicrobial susceptibility is matrix-assisted laser desorption / ionization mass spectrometry (MALDI-TOF) for the detection of beta-lactam resistance, which can be used in positive blood cultures (28). However, a novel technique is the Accelerate Pheno system (Accelerate Diagnostics), which identifies microorganisms by fluorescent in situ hybridization (FISH) and evaluates phenotypic antimicrobial susceptibility (AST) in positive blood cultures (29). On the one hand, the new techniques allow detecting resistance to antimicrobials, and on the other hand, they are not able to quantify the degree of antibiotics susceptibility. A recent study (30) found that in a sample of the lower respiratory tract, molecular techniques detected pathogens in 87% of cases with pneumonia and culture-based techniques detected pathogens in 39% of cases. The most frequent detected pathogens were *H. influenzae* and *S. pneumoniae*. That is, molecular techniques improve the detection of pathogens in CAP, even in cases in which patients have been previously treated with antibiotics.

The best strategy for the correct identification of pathogens is through the direct detection of DNA from the blood, but it may be false positive results due to bacterial DNA contamination, the presence of PCR inhibitors, reagents and the detection of circulating microbial DNA. Another problem with molecular techniques is that they usually provide little information about susceptibility to antimicrobials, especially Gram-negative bacteria (28). In conclusion,

**This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as: Tejada S, Romero A, Rello J. Community-acquired pneumonia in adults: What's new focusing on epidemiology, microorganisms and diagnosis? *Erciyes Med J* 2018; DOI: 10.5152/etd.2018.01288**

these techniques can be very useful for the diagnosis of pneumonia, but should be complemented with conventional microbiological diagnosis.

UNCORRECTED

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as: Tejada S, Romero A, Rello J. Community-acquired pneumonia in adults: What's new focusing on epidemiology, microorganisms and diagnosis? *Erciyes Med J* 2018; DOI: 10.5152/etd.2018.01288

©Copyright 2018 by Erciyes University Faculty of Medicine - Available online at [www.erciyesmedj.com](http://www.erciyesmedj.com)

## Conclusion

In this review, CAP has been emphasized as the most frequent cause of morbidity and mortality worldwide. The main trends in the determination of the etiological agents in pneumonia include the continuous identified of *S. pneumoniae* as the most frequently bacterial pathogen, especially in patients with risk factors or comorbidities; a higher frequency of pneumococcus in Europe, detection of other important pathogens such as *P. aeruginosa*, *H. influenzae* in greater proportion and atypical pathogens such as *Mycoplasma* and *Legionella* and, perhaps most importantly, the impossibility of establishing an etiological diagnosis in more than 50% of the patients. Therefore, it is important to combine the microbiological and molecular techniques, together with the immunological biomarkers, to help identify the etiology of CAP in patients and provide guidance on the most appropriate treatment. Main research priorities are summarized in Table 2.

## Acknowledgements

The authors take full responsibility for the content of this article and supported by funding from CIBERES, Instituto de Salud Carlos III, Madrid, Spain.

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as: Tejada S, Romero A, Rello J. Community-acquired pneumonia in adults: What's new focusing on epidemiology, microorganisms and diagnosis? Erciyes Med J 2018; DOI: 10.5152/etd.2018.01288

©Copyright 2018 by Erciyes University Faculty of Medicine - Available online at [www.erciyesmedj.com](http://www.erciyesmedj.com)

## References

1. Cillóniz C, Rodríguez-Hurtado D, Torres A. Characteristics and Management of Community-Acquired Pneumonia in the Era of Global Aging. *Med Sci* 2018; 6(2): 35.
2. Walden AP, Clarke GM, McKechnie S, Hutton P, Gordon AC, Rello J, et al. Patients with community acquired pneumonia admitted to European intensive care units: an epidemiological survey of the GenOSept cohort. *Crit Care* 2014; 18(2): R58.
3. Rello J. Demographics, guidelines, and clinical experience in severe community-acquired pneumonia. *Crit Care* 2008; 12(6): S2.
4. El-Emshaty W, Mashaly M, Moawad A, ELGamal M, Hewidy A. Diagnostic value of neutrophil lymphocyte ratio versus C-reactive protein in discrimination between different pathogens causing community-acquired pneumonia. *Comp Clin Path* 2017; 26(4): 757-765.
5. Leoni D, Rello J. Severe community-acquired pneumonia: optimal management. *Curr Opin Pulm Med* 2017; 30(2): 240-247.
6. World Population Prospects: The 2017 Revision | Multimedia Library - United Nations Department of Economic and Social Affairs. Available online: <https://www.un.org/development/desa/publications/world-population-prospects-the-2017-revision.html> (accessed on 12 September 2018).
7. Jain S, Self WH, Wunderink RG, Fakhran S, Balk R, Bramley AM, et al. Community-Acquired pneumonia requiring hospitalization among U.S. adults. *N Eng J Med* 2015; 373: 415–427.
8. Soylar ÖK, Kılınç O, Ellidokuz H. Comparison of Patients with Community-Acquired Pneumonia Who Did and Did not Receive Treatment in Accordance with the 2009 Pneumonia Guideline of Turkish Thoracic Society. *Turk Thorac J* 2015; 16(2): 64.
9. Koulenti D, Tsigou E, Rello J. Nosocomial pneumonia in 27 ICUs in Europe: perspectives from the EU-VAP/CAP study. *Eur J Clin Microbiol Infect Dis* 2017; 36(11): 1999-2006.
10. Torres A, Cillóniz C, Blasi F, Chalmers JD, Gaillat J, Dartois N. Burden of pneumococcal community-acquired pneumonia in adults across Europe: A literature review. *Respir Med* 2018.
11. Mandell LA, Wunderink RG, Anzueto A, Bartlett JG, Campbell GD, Dean NC, et al. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. *Clin Infect Dis* 2007; 44: S27–S72
12. Akyil FT, Yalcinsoy M, Hazar A, Cilli A, Celenk B, Kilic O, et al. Prognosis of hospitalized patients with community-acquired pneumonia. *Pulmonology* 2018; 24(3): 164-169.
13. Musher DM, Abers MS, Bartlett JG. Evolving understanding of the causes of pneumonia in adults, with special attention to the role of pneumococcus. *Clin Infect Dis* 2017; 65(10): 1736-1744.
14. Torres A, Blasi F, Peetermans WE, Viegi G, Welte T. The aetiology and antibiotic management of community-acquired pneumonia in adults in Europe: a literature review. *Eur J Clin Microbiol Infect Dis* 2014; 33(7): 1065-1079.

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as: Tejada S, Romero A, Rello J. Community-acquired pneumonia in adults: What's new focusing on epidemiology, microorganisms and diagnosis? *Erciyes Med J* 2018; DOI: 10.5152/etd.2018.01288

15. Prina E, Ranzani OT, Polverino E, Cillóniz C, Ferrer M, Fernandez L, et al. Risk factors associated with potentially antibiotic-resistant pathogens in community-acquired pneumonia. *Ann Am Thorac Soc* 2015; 12(2): 153-160.
16. Gündüz C, Taşbakan MS, Sayiner A, Cilli A, Kılıncı O, Şakar AC. Clinical characteristics and outcome of healthcare associated pneumonia in Turkey. *Tuberk Toraks* 2016; 64(3): 185-190.
17. Erdogan H, Erdogan A, Lakamdayali H, Yilmaz A, Arslan H. Travel-associated Legionnaires disease: clinical features of 17 cases and a review of the literature. *Diagn Microbiol Infect Dis* 2010; 68(3): 297-303.
18. Rello J, Lisboa T, Wunderink R. Severe community-acquired pneumonia and PIRO: A new paradigm of management. *Curr Infect Dis Rep* 2009; 11(5): 343-348.
19. Rello J, Perez, A. Precision medicine for the treatment of severe pneumonia in intensive care. *Expert Rev Respir Med* 2016; 10(3): 297-316.
20. Rello J, van Engelen TSR, Alp E, Calandra T, Cattoir V, Kern WV, et al. Towards precision medicine in sepsis: a position paper from the European Society of Clinical Microbiology and Infectious Diseases. *Clin Microbiol Infect* 2018.
21. Liu YF, Gao Y, Chen MF, Cao B, Yang XH, Wei L. Etiological analysis and predictive diagnostic model building of community-acquired pneumonia in adult outpatients in Beijing, China. *BMC Infect Dis* 2013, 13(1): 309.
22. Michelow IC, Olsen K, Lozano J, Rollins NK, Duffy LB, Ziegler T, et al. Epidemiology and clinical characteristics of community-acquired pneumonia in hospitalized children. *Pediatrics* 2004; 113(4): 701-707.
23. Shimoda M, Saraya T, Yonetani S, Araki K, Takizawa H. The significance of bacterial engulfment in Gram-stained sputum in patients with respiratory infections. *Med* 2018; 97(14)
24. Saukkoriipi A, Pascal TM, Palmu AA. Evaluation of the BinaxNOW(R) Streptococcus pneumoniae antigen test on fresh, frozen and concentrated urine samples in elderly patients with and without community-acquired pneumonia. *J. Microbiol Methods* 2016; 121: 24–26
25. van der Poll T, van de Veerdonk FL, Scicluna BP, Netea MG. The immunopathology of sepsis and potential therapeutic targets. *Nat Rev Immunol* 2017; 17: 407e20
26. Mazo C, Borgatta B, Pont T, Sandiumenge A, Moyano S, Roman A, et al. Procalcitonin accurately predicts lung transplant adults with low risk of pulmonary graft dysfunction and intensive care mortality. *J Crit Care* 2018; 44: 142-147.
27. Mok JH, Eom JS, Jo EJ, Kim MH, Lee K, Kim KU, et al. Clinical utility of rapid pathogen identification using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry in ventilated patients with pneumonia: A pilot study. *Respirology* 2016; 21: 321–328
28. Singhal N, Kumar M, Kanaujia PK, Viridi JS. MALDI-TOF mass spectrometry: an emerging technology for microbial identification and diagnosis. *Front Microbiol* 2015; 6:791.
29. Charnot-Katsikas A, Tesic V, Love N, Hill B, Bethel C, Boonlayangoor S, et al. Use of the accelerate pheno system for identification and antimicrobial susceptibility testing of

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as: Tejada S, Romero A, Rello J. Community-acquired pneumonia in adults: What's new focusing on epidemiology, microorganisms and diagnosis? *Erciyes Med J* 2018; DOI: 10.5152/etd.2018.01288

Citation	Country	Study period	Age ([mean± SD])	Number of patients (Incidence of CAP)	Inclusion criteria	Risk factors	Prevalence of microorganisms (%) **
----------	---------	--------------	------------------	---------------------------------------	--------------------	--------------	-------------------------------------

pathogens in positive blood cultures and impact on time to results and workflow. *J Clin Microbiol* 2018; 56.

30. Gadsby NJ, Russell CD, McHugh MP, Mark H, Conway MA, Laurenson IF, et al. Comprehensive Molecular Testing for Respiratory Pathogens in Community-Acquired Pneumonia. *Clin Infect Dis* 2016; 62: 817–823
31. Erdem H, Inan A, Altindis S, Carevic B, Askarian M, Cottle L, et al. Surveillance, control and management of infections in intensive care units in Southern Europe, Turkey and Iran – A prospective multicenter point prevalence study. *J Infect* 2014; 68(2): 131–140.
32. Turktan M, Ak O, Erdem H, Ozcengiz D, Hargreaves S, Kaya S, et al. Community acquired infections among refugees leading to Intensive Care Unit admissions in Turkey. *International J Infect Dis* 2017; 58: 111-114.
33. Menéndez R, Montull B, Reyes S, Amara-Elori I, Zalacain R, Capelastegui A, et al. Pneumonia presenting with organ dysfunctions: Causative microorganisms, host factors and outcome. *J Infect* 2016; 73(5): 419-426.
34. Gattarello S, Lagunes L, Vidaur L, Solé-Violán J, Zaragoza R, Vallés J, et al. Improvement of antibiotic therapy and ICU survival in severe non-pneumococcal community-acquired pneumonia: a matched case–control study. *Crit Care* 2015; 19(1): 335.
35. Ieven M, Coenen S, Loens K, Lammens C, Coenjaerts F, Vanderstraeten A, et al. Aetiology of lower respiratory tract infection in adults in primary care: a prospective study in 11 European countries. *Clin Microb Infect* 2018.
36. Serin DÇ, Pullukçu H, Çiçek C, Sipahi OR, Taşbakan S, Atalay, S. Bacterial and viral etiology in hospitalized community acquired pneumonia with molecular methods and clinical evaluation. *J Infect Dev Ctries* 2014; 8(04): 510-518.

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as: Tejada S, Romero A, Rello J. Community-acquired pneumonia in adults: What's new focusing on epidemiology, microorganisms and diagnosis? *Erciyes Med J* 2018; DOI: 10.5152/etd.2018.01288

Jain et al. 2015 [7]	USA (Chicago, Nashville)	2010 - 2012	57 (46-71)*	N= 2488 (93.25%)	Evidence of acute infection, acute respiratory illness and pneumonia as assessed by means of chest radiography.	CLD, CHD, DM, immunosuppression	S. pneumoniae (8%) S. aureus (5%) Enterobacteriaceae (3%)
Erdem et al. 2014 [31]	Southeast Europe, Turkey, and Iran	June - July 2012	56.5 ± 19.5	N=305 (22.62%)	All patients admitted to ICU with infection.	COPD, DM, CVD, burn, hematological malignancy, acute renal failure, solid organ tumor, CRF, peptic ulcer, chronic liver disease, bronchiectasis, asplenia, immunosuppression	Enteric Gram-negatives (28.8%) Acinetobacter spp. (21.9%) P. aeruginosa (13.5%) S. aureus (8%)
Ieven et al. 2018 [35]	Europe (Belgium, UK, Spain, Poland, Italy, Slovakia, Germany, France, Sweden, Netherlands)	2007-2010	49.8 ± 16.8	N= 3,104 (4.54%)	>18 years, with acute cough, or any clinical presentation.	Risk factors not reported	H. influenzae (14.2%) S. pneumoniae (9.2%) C. pneumoniae (5%)
Turkta n et al. 2017 [32]	Turkey	2010 - 2015	45.92 ± 20.16	N= 37 (49%)	Adult refugee admitted in ICU with CAP.	COPD, DM, trauma history, CeVD, CAD, CHF, CRF, hematologic malignancy	M. tuberculosis (33.3%) E. coli (16.6%) S. aureus (16.6%) H. influenzae

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as: Tejada S, Romero A, Rello J. Community-acquired pneumonia in adults: What's new focusing on epidemiology, microorganisms and diagnosis? *Erciyes Med J* 2018; DOI: 10.5152/etd.2018.01288

							(16.6%)
Gündüz et al. 2016 [16]	Turkey	2009 - 2013	64.9 ± 16.6	N= 785 (73.63 %)	Nonimmunocompromised > 18 years with radiographic infiltrate and two clinical symptoms.	COPD, cerebrovascular accident, CRF, immunosuppression	S. pneumoniae (3.8%) P. aeruginosa (2.1%) S. aureus (1.6%)
Serin et al., 2014 [36]	Turkey	February - December 2010	57.4 ± 18.9	N= 55 (90.91 %)	>18 years, respiratory sample with leukocytes > 25 and squamous epithelial cells < 10 per low-power field with acute lower respiratory tract infection.	CeVD, COPD Malignancy, Bronchiectasis, DM, CHF, CRF, Liver disease	H. influenzae (22%) S. pneumoniae (20%)
Menendez et al. 2016 [33]	Spain	2005-2007	74.6 ± 7.5	N= 4070 (11.30 %)	All individuals who were 65 years or older.	DM, CLD, Heart disease, CRF, Neurological disorder, COPD, Neoplasia	S. pneumoniae (27.2%) S. aureus (1.3%) L. pneumophila (2.8%) P. aeruginosa (1.3%) H. influenzae (1.3%)
Gattarello et al. 2015 [34]	Spain	2000–2002 2008-2014	63.0 (47.5–75)* 62.0 (53–72)*	N= 529 (13.61 %) N= 616 (11.68 %)	All patients admitted to ICU with CAP.	COPD, DM, immunosuppression, IMV, ICU, mortality, smoker, alcohol, spread, overweight,	S. aureus (22.1%) L. pneumophila (20.7%) H. influenzae (20.7%)

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as: Tejada S, Romero A, Rello J. Community-acquired pneumonia in adults: What's new focusing on epidemiology, microorganisms and diagnosis? *Erciyes Med J* 2018; DOI: 10.5152/etd.2018.01288

						AKI, cardiomyopathy, cerebral vascular disease, shock, ,bacteremia, malignancy, rapid radiographic
--	--	--	--	--	--	----------------------------------------------------------------------------------------------------------------------------

Table 1. Risk factors and prevalence of microorganisms for patients diagnosed with CAP

AKI: Acute Kidney Injury; CAD: Coronary Artery Disease; CeVD: Cerebrovascular Disease; CHD: Chronic Heart Disease; CHF: Congestive Heart Failure; CLD: Chronic Lung Disease; COPD: Chronic obstructive pulmonary disease; CRF: Chronic Renal Failure; CVD: Cardiovascular Disease; DM: Diabetes Mellitus.

\*Median of age and interquartil range; \*\* Prevalence of the most frequent microorganisms detected. No pathogens detected in all patients.

#### Future Research Priority / Recommendations

The main challenges for the future seem to be:

- Obtain a balance between conventional diagnostic techniques such as sputum, blood culture and antigen detection; and new diagnostic techniques, such as molecular techniques or the use of biomarkers.
- Identify an etiological agent in half of the cases that are now undiagnosed.
- Further investigate the role of immunological biomarkers such as procalcitonin.

All these factors should be considered as a guide for the management of community-acquired pneumonia.

Table 2. Future Research Priority recommendations.

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as: Tejada S, Romero A, Rello J. Community-acquired pneumonia in adults: What's new focusing on epidemiology, microorganisms and diagnosis? *Erciyes Med J* 2018; DOI: 10.5152/etd.2018.01288

UNCORRECTED

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as: Tejada S, Romero A, Rello J. Community-acquired pneumonia in adults: What's new focusing on epidemiology, microorganisms and diagnosis? Erciyes Med J 2018; DOI: 10.5152/etd.2018.01288

©Copyright 2018 by Erciyes University Faculty of Medicine - Available online at [www.erciyesmedj.com](http://www.erciyesmedj.com)