

# Hospital management of community-acquired pneumonia in Malta

Roberta Callus, Josef Micallef, Jonathan Mamo, Stephen Montefort

## Abstract

Community-acquired pneumonia (CAP) remains a common diagnosis requiring hospital admission and a leading cause of death worldwide. No local guideline is currently available for the management of CAP. Our aim was to evaluate current practices in the management of CAP at Mater Dei Hospital, Malta. In this prospective study we looked at all adult patients admitted with CAP in winter and summer (105 consecutive days for both seasons). Data collected and analysed included: basic patient demographics; symptoms at presentation; antibiotics prescribed and time of administration; co-morbidities; CURB65; blood oxygenation levels; admission plan; length of stay and follow-up; length of stay, follow-up chest radiography and death within 30 days from hospital admission. Of note the average time to first dose antibiotic was 7 hours 48 minutes (range 2 hours 13 minutes – 14 hours 17 minutes). A total of 178 patients (50.1%) were admitted with CURB65 scores of 0 ( $n=99$ ) and 1 ( $n=86$ ). Most of these could have been discharged and managed in the community with significant impact on hospital bed occupancy. Eventual standardisation of acute management of CAP by the set-up of a local guideline will improve outcome and reduce hospital bed occupancy.

## Keywords

Pneumonia, mortality, management audit

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## Introduction

Community-acquired pneumonia (CAP) is a common and potentially life threatening infectious disease with significant impact on patient morbidity and mortality as well as hospital resources. According to population based studies, the annual incidence rate of radiologically proven CAP in adults varies between 2.6 to 13.4 per 1000 inhabitants, with an increased incidence in males and at the extreme ages of life.<sup>1</sup> Up to 50% are reported to require hospital admission. In 2007, 1.2 million people in the USA. were hospitalised with pneumonia.<sup>2</sup> Critical care admissions with CAP vary from 5% in the British Thoracic Society (BTS) multicentre study<sup>3</sup> to 10% in a Spanish study.<sup>4</sup>

Globally, pneumonia causes more deaths than any other infectious disease. In 2007 more than 52,000 people died from the disease in the USA.<sup>2</sup> Mortality rates in hospitalised patients ranges from 5-15% in various developed countries.<sup>1</sup> Patients requiring intensive care have a mortality of up to 55%.<sup>5</sup> Mortality increases with age and in the presence of co-morbidities.<sup>6</sup> The CURB65 score (confusion; urea >7mmol/L; respiratory rate  $\geq$  30 breaths/min; blood pressure <90 mmHg systolic or  $\leq$  60mmHg diastolic; aged >65 years old) is a verified mortality prediction tool adopted by the BTS to assess the severity of CAP.

The management of CAP may vary both within and in between countries for a number of reasons including different lung pathogens, in or out-patient management, caring physician, antibiotic availability and different health-care systems.<sup>7</sup> For this reason several guidelines have been published by various international societies to ensure standardisation in management.

The aim of this study was to evaluate current practices in the management of CAP in the Accident and Emergency and Internal Medicine departments at Mater Dei Hospital, Malta.

## Methods

CAP was defined as an acute respiratory illness acquired outside hospital with characteristic symptoms and signs associated with the appearance of new radiographic infiltrates on chest radiography. Patients from nursing homes and those with a diagnosis of aspiration pneumonia, tuberculosis or doubtful initial radiographic appearances were excluded. All adult patients (above 16 years) with CAP admitted to Mater Dei Hospital, Malta were included in a prospective study. The two periods studied were: December 1, 2008 to March 15, 2009 (winter) and June 1, 2009 to September 13, 2009 (summer).

The picture archiving and communication systems (PACS) system was used to review radiological findings.

Admission and clinical data were collected from the patients' medical case notes. The data collected included: symptoms at presentation; antibiotics prescribed and time of administration; co-morbidities; CURB65; blood oxygenation levels (oxygen saturation and/or arterial partial pressure of oxygen); admission plan; length of stay (LOS), follow-up chest radiography and death within 30 days from hospital admission.

The CURB65 score was used to assess severity on admission.<sup>8</sup> A co-morbidity score was devised to include the following risk factors: smoking, diabetes mellitus, chronic kidney disease, cardiovascular disease, respiratory disease and immunosuppression (malignancy, HIV, patients on long-term steroids or immunosuppressants). Each co-morbidity was given a score of 1. The total score ranged from 0 to a maximum of 6. Ethical approval was obtained from the Malta University Research Ethics Committee after all consultants in the department of medicine gave their written consent.

### Statistical analysis

The data were analysed using Statistical Package for Social Sciences (SPSS) version 16.0. We used chi-square to analyse associations between categorical variables and t-test for continuous variables.

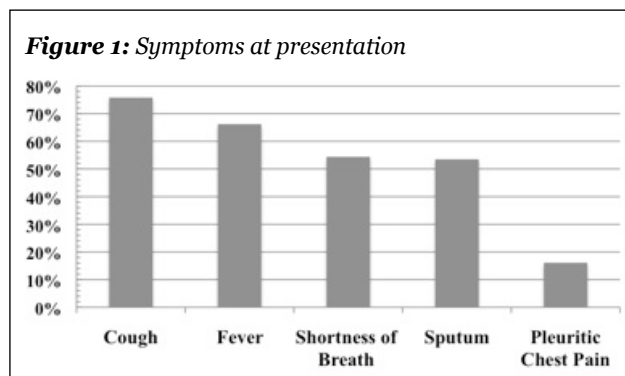
## Results

### Incidence and demography

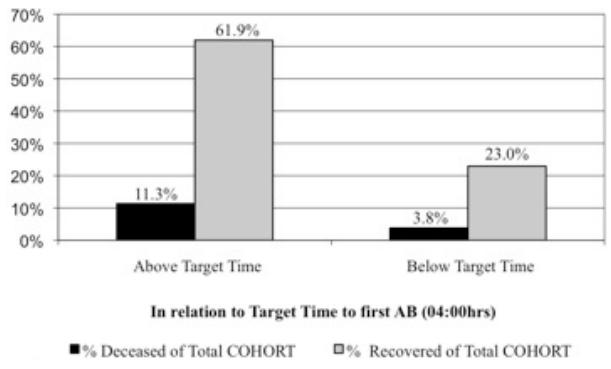
A total of 355 patients with CAP were included during the study periods: 193 and 162 patients during winter and summer respectively. This gives an annual inpatient incidence rate of 1.62 cases per 1,000 inhabitants (95%CI 1.42 to 1.82). The mean daily number of general medical admissions was 46, of which 1.7 were admitted with CAP. The mean age was 65 (range 16-95). Sex distribution was 182 males and 173 females. Twenty patients (5.6%) required ICU care and 24 (6.8%) were admitted to a high dependency medical ward.

### Symptoms at presentation

The two main presenting symptoms were cough (75.8%) and fever (66.2%), followed by shortness of breath (54.4%) and sputum expectoration (53.5%). Pleuritic chest pain was present in only 16.1%. Most patients had more than one symptom at presentation (Figure 1).



**Figure 2: Percentage of recovered vs deceased in relation to target time to antibiotic administration**



### Antibiotic use

Thirty one percent of admitted patients ( $n=110$ ) had received at least one dose of antibiotic at home prior to hospitalisation. The main antibiotic combination prescribed in hospital was intravenous cefuroxime and oral clarithromycin (38.6%,  $n=137$ ), followed by intravenous co-amoxiclav and oral clarithromycin (13.5%,  $n=48$ ). Monotherapy with co-amoxiclav, cefuroxime or clarithromycin was prescribed in 6.8% ( $n=24$ ). Fluoroquinolone monotherapy was prescribed in 10.3% ( $n=37$ ). More potent antibiotics were prescribed in 30.8% ( $n=109$ ), of whom 26.1% ( $n=29$ ) had no co-morbidities. There was a change in the original antibiotic prescription in 57.2% throughout the admission ( $n=203$ ).

The average time to first dose antibiotic was 7 hours 48 minutes (range 2 hours 13 minutes – 14 hours 17 minutes). There was 73.2% ( $n = 260$ ) of the whole cohort who received antibiotics outside the four-hour target. From the deceased patients, 75% ( $n = 39$ ) had received their first antibiotic dose after four hours (Figure 2). The average total antibiotic treatment duration was 7.2 days.

### Co-morbidity score

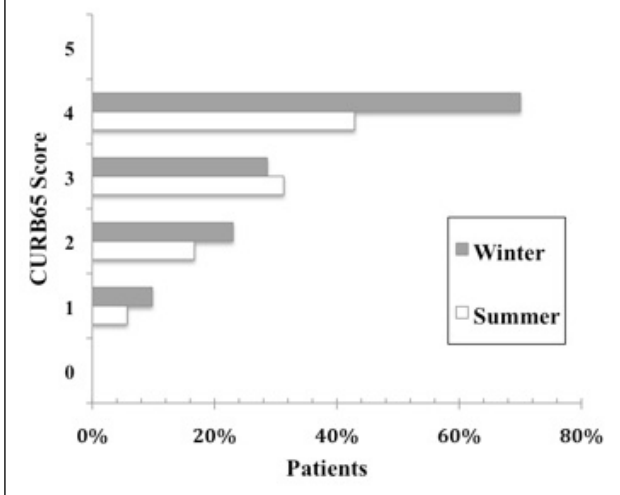
The mean co-morbidity score was 1.8. This increased to 2.4 in the deceased patients ( $p = 0.049$ ).

### CURB65

The CURB65 score was used to assess severity on admission. In the study population 52% ( $n=184$ ) of admissions scored CURB65 of 0 (28%,  $n=99$ ) or 1 (24%,  $n=85$ ). The most common CURB65 score at presentation was 2 with 110 (31%) patients. Twelve percent ( $n=43$ ) and 5% ( $n=18$ ) had a CURB65 score of 3 and 4 respectively.

Increasing CURB65 scores showed positive correlation with 30-day mortality in both seasons. Patients admitted during the winter period with a CURB65 score of 1, 2 and 4, had a 1.7, 1.4 and 1.6 increased risk of death within 30 days respectively, despite similar co-morbidities (Figure 3).

**Figure 3:** Seasonal 30-day mortality in relation to CURB65 +



### Oxygen prescription

Oxygen saturations were assessed with pulse oximetry and/or arterial blood gas sampling. Oxygen saturation on air was measured in 85.1% ( $n=302$ ) patients and on oxygen in 39.4% ( $n=140$ ). Oxygen was prescribed with a  $\text{PaO}_2$  of  $\leq 60$ mmHg in 52.4% ( $n=186$ ).

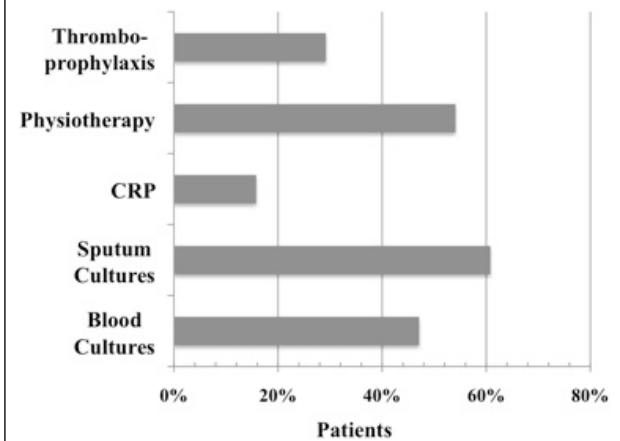
### Further management

Blood cultures and sputum cultures were requested in 47.1% ( $n=167$ ) and 60.8% ( $n=216$ ) respectively. C-reactive protein (CRP) was taken in 15.8% ( $n=56$ ). Chest physiotherapy was requested in 54.1% ( $n=192$ ). Thrombo-prophylaxis was prescribed in 29.2% ( $n=104$ ) (Figure 4).

### Follow up chest radiography

A chest radiograph was repeated during admission in 16.3% ( $n=58$ ) and after discharge in 19.2% ( $n=68$ ). This was repeated in 8.7% ( $n=31$ ) both during admission and upon discharge. No follow-up chest radiograph was done in 67.3% ( $n=204$ ).

**Figure 4:** Further management



### Outcome: 30-day mortality

The average 30-day mortality for the whole population under study was 14.6% ( $n=52$ ). There was a difference between the winter and summer cohorts: 17.6% ( $n=34$ ) versus 11.1% ( $n=18$ ) respectively ( $p=0.085$ ). The mean age of the deceased was 78 years (range 51-95). Patients admitted to ICU had 15% mortality ( $n=3$ ) and all died in winter. High dependency medical ward admissions had 25% mortality: 36.4% ( $n=4$ ) winter, 15.4% ( $n=2$ ) summer.

### Respiratory/Infectious Disease firms versus General Medical firms

General medical firms admitted 56.3% ( $n=200$ ) of patients and respiratory and infectious disease firms admitted 43.7% ( $n=155$ ). An independent-sample t-test was conducted to compare length of hospital stays (LOS) between General Medical firms and Respiratory firms. There was no significant difference for General Medical ( $M = 7.96$ ,  $SD = 6.79$ ) and Respiratory and Infectious Disease firms ( $M = 7.40$ ,  $SD = 5.89$ ;  $t(354) = 0.83$ ,  $p=0.408$ , two-tailed). The magnitude of the differences in the means (mean difference = 0.56, 95% CI: -0.77 to 1.89) was very small ( $\eta^2 = 0.0006$ ). General medical firms had a 30-day mortality of 15.5% whilst respiratory and infectious disease firms had 13.6%.

### Discussion

CAP remains a common presentation in the A&E department of every hospital. Decisions whether hospital or outpatient management is most appropriate are important in determining outcome, hospital stay and bed occupancy.<sup>9</sup> In May 2005 the European Respiratory Society in collaboration with the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) published new guidelines for the management of adult lower respiratory tract infections.<sup>10</sup>

The incidence of CAP is very variable in most European countries ranging from 11 per 1000 in Finland<sup>11</sup> to 1.6 per 1000 in Spain and Italy.<sup>12</sup> For the period under study, the incidence rate was 1.62 per 1000 which is similar to neighboring Mediterranean countries. This excludes patients managed in the community by general practitioners.

In the USA there were 17.3 deaths per 100,000 with an in-patient mortality of 5.4% in 2006.<sup>2</sup> The local 30-day mortality of 14.6% was relatively high when compared to other European countries, however in a recent study the 30-day mortality in a UK GP cohort was 18.5% in the community.<sup>13</sup> The most widely studied scoring systems are the CURB65 and the Pneumonia Severity Index (PSI). Each has its advantages and limitations with the CURB65 easily identifying more severely ill patients and the PSI identifying low mortality risk patients. The limitation of these prognostic tools includes their variable utility in stratifying risk in the elderly, associated co-morbidities and social factors. The use of such scoring systems, combined with clinical judgement is crucial for determining the need for hospitalisation.<sup>10</sup> This was clearly demonstrated in this study. Mortality remains high in CURB65 score of 2 or more. These patients will require hospitalisation, intensive treatment and

monitoring. A total of 178 patients (50.1%) were admitted with CURB65 scores of 0 ( $n=99$ ) and 1 ( $n=86$ ). Most could have been discharged and managed in the community with significant impact on hospital bed occupancy. This study shows a 1.7-fold increased risk of 30-day mortality in winter. This may be due to: more aggressive pathogens, later presentation, longer waiting times, time to effective treatment and inpatient care in a busy hospital. It is difficult to say which is the most important contributing factor, but all could play a role.

The antibiotic choice should be guided by illness severity, patient age, co-morbidities, clinical presentation, epidemiology, previous antibiotic exposure and local antibiotic resistance.<sup>14</sup> Antibiotic choice and time to first dose of administration remain issues of discussion.<sup>15</sup> International guidelines currently aim for administration within four to six hours of admission, which was not achieved in our hospital. This was due to long waiting times and lack of antibiotic access within our A&E department, which were then administered on the wards. Blood cultures and waiting for the next scheduled drug round also delayed administration. The most commonly prescribed combination was cefuroxime and clarithromycin. Respiratory fluoroquinolones were prescribed mostly in patients with penicillin allergy. Locally almost 30% of *Streptococcus pneumoniae* strains are resistant to macrolides,<sup>16</sup> however these antibiotics cover atypical organisms. Appropriate and judicious antibiotic use should be guided by local sensitivity and resistance patterns keeping in mind tolerability and toxicity in each individual patient. Treatment directed towards particular pathogens suspected clinically is highly commendable.

The duration of antibiotic treatment is usually 7 to 10 days, except for intracellular pathogens (*Legionella* sp.) where more prolonged treatment is necessary.<sup>17</sup> The current trend is to further shorten antibiotic treatment.<sup>18</sup> Switching from intravenous to oral treatment depends on clinical resolution and ability to tolerate oral intake. This allows earlier hospital discharge reducing costs and risk of hospital-acquired infections.

There is considerable variability in LOS between hospitals reflecting variations in clinical practice preferences, hospital characteristics and patient characteristics and attitudes.<sup>19</sup> The mean LOS varies in many countries from 7 days in the USA<sup>20</sup> to 11.7 days in Spain.<sup>1</sup> Our local mean LOS was 7.7 days.

The BTS states that all patients should receive appropriate oxygen therapy with the aim of maintaining  $\text{PaO}_2 >8$  kPa and  $\text{SaO}_2 >92\%$ . Oxygenation levels should be assessed by pulse oximetry, followed by arterial blood gas analysis if oxygen saturation is  $<92\%$  and in patients with chronic obstructive lung disease. Only half of the patients in this study were prescribed appropriate oxygen therapy. Oxygen therapy should be clearly prescribed in the treatment chart including flow rate, concentration and mask type.

A number of studies have questioned the clinical value and cost-effectiveness of routine blood cultures.<sup>21</sup> Many clinicians agree that these are important in severely ill patients (CURB65  $\geq 2$  or PSI IV, V) and if a specific risk factor for pathogens resistant to empirical therapy is present.

Sputum cultures are another controversial laboratory tool. In our study these were requested in 60.8%, however the actual number reaching the laboratory was much less and most were after first antibiotic administration. Samples should be sent to the laboratory in moderate to severe CAP and in those failing to improve clinically. The Infectious Disease Society of America (IDSA) and the Canadian Infectious Disease Society/Canadian Thoracic Society (CIDS/CTS) recommend routine sputum analysis for all inpatients with CAP, while the American Thoracic Society (ATS) recommends this only if a drug-resistant pathogen or an organism not covered by usual empiric therapy is suspected.

CRP whose initial description was based on pneumonia patients is useful for establishing the severity of CAP.<sup>22</sup> Seppa *et al.* reported that a CRP level  $>100$  mg/L is a marker independently associated with higher risk of death.<sup>23</sup> A Scandinavian study observed that patients with higher CRP levels had longer fever duration, longer hospital stays and fewer patients had recovered clinically or radiographically at 8 weeks follow-up.<sup>24</sup> Failure of CRP to fall by 50% or more at day 4, independent of admission CRP level, was shown to be associated with increased 30-day mortality and need for mechanical ventilation and/or inotropic support and complicated pneumonia.<sup>25</sup> In our study CRP was only taken in 15.8% mostly on the day after admission. Another biomarker gaining interest is procalcitonin (PCT). PCT rises in response to systemic inflammation associated with infection and correlates well with pneumonia severity.<sup>26,27</sup> A low PCT ( $<0.228$  ng/ml) has a high negative predictive value for mortality from CAP when compared with the CURB65 score.<sup>26</sup>

Chest physiotherapy has been widely used as a routine adjunctive therapy for pneumonia. A review of six randomised controlled trials concluded that chest physiotherapy has no benefit in reducing LOS, and mortality during the acute phase of CAP.<sup>28</sup>

Guidelines for prevention of venous thromboembolism recognise pneumonia as a risk factor causing significant morbidity and mortality. Decreased mobility, dehydration and co-morbidities increase this risk further. This study reflects local inadequacy in prescribing thromboprophylaxis.

According to the BTS, the chest radiograph need not be repeated prior to hospital discharge in those with a satisfactory clinical recovery. A chest radiograph should be arranged after about 6 weeks for patients with persistence of symptoms or physical signs or those at higher risk of malignancy (smokers and age  $>50$  years). Our study shows that most of the discharged patients ( $n=204$ ) were not followed up with a chest radiograph.

## Conclusion

Standardisation of acute management of CAP will improve outcome and reduce hospital bed occupancy. A clear delineation of hospital admission criteria on basis of severity scores is essential as a significant number of patients may be managed in the community with the establishment of a general practitioner/nurse-led home treatment programme. Timely and appropriate antibiotics, supportive treatment and laboratory tools may optimise inpatient management. Admission under respiratory



or infectious disease firms may also improve outcome. Clinical improvement together with radiology and laboratory tools reflect resolution of CAP and hence decision on discharge. Follow up with a chest radiograph in six weeks is often necessary. The set up of a local guideline on the management of CAP is pivotal for providing excellence in clinical care of these patients.

## References

- Almirall J, Bolibar I, Vidal J, Sauca G, Coll P, Niklasson B et al. Epidemiology of community-acquired pneumonia in adults: a population-based study. *Eur Respir J*. 2000;15:757-63.
- Centers for Disease Control and Prevention - Pneumonia. [Accessed Dec 22 2010]. Available from: <http://www.cdc.gov/features/pneumonia>.
- British Thoracic Society Research Committee and Public Health Laboratory Service. The aetiology, management and outcome of severe community-acquired pneumonia on the intensive care unit. *Respir Med*. 1992;86:7-13.
- Torres A, Serra-Batllés J, Ferrer A, Jiménez P, Celis R, Cobo E, et al. Severe community-acquired pneumonia. Epidemiology and prognostic factors. *Am Rev Respir Dis*. 1991;144:312-8.
- Lee JH, Ryu YJ, Chun EM, Chang JH. Outcomes and prognostic factors for severe community-acquired pneumonia that requires mechanical ventilation. *Korean J Intern Med*. 2007;22:157-63.
- Waterer GW, Kessler LA, Wunderink RG. Medium-term survival after hospitalization with community-acquired pneumonia. *Am J Respir Crit Care Med*. 2004;169(8):910-4.
- Woodhead M. Community-acquired pneumonia guidelines – an international comparison: a view from Europe. *Chest*. 1998;113(3):183S-7S.
- Lim W, van der Eerden MM, Laing R, Boersma WG, Karalus N, Town GI, Lewis SA, and Macfarlane JT. Defining community-acquired pneumonia severity on presentation to hospital. *Thorax*. 2003;58(5):377-82.
- Fine MJ, Hough LJ, Medsger AR, Li WH, Ricci EM, Singer DE. The hospital admission decision for patients with community-acquired pneumonia. *Arch Intern Med*. 1997;157:36-44.
- Woodhead M, Blasi F, Ewig S, Huchon G, Ieven M, Ortqvist A, et al; European Respiratory Society; European Society of Clinical Microbiology and Infectious Diseases. Guidelines for the management of adult lower respiratory infections. *Eur Respir J*. 2005;26:1138-80.
- Jokinen C, Heiskanen L, Juvonen H, Kallinen S, Karkola K, Korppi M, et al. Incidence of community-acquired pneumonia in the population of four municipalities in Eastern Finland. *Am J Epidemiol*. 1993;137:14-8.
- Almirall J, Morató I, Riera F, Verdaguer A, Priu R, Coll P, et al. Incidence of community-acquired pneumonia and Chlamydia pneumoniae infection. *Eur Respir J*. 1993;6:14-8.
- Myles PR, Hubbard RB, Gibson JE, Pogson Z, Smith CJ, McKeever TM. Pneumonia mortality in a UK general practice population cohort. *Eur J Public Health*. 2009 Oct;19(5):521-6.
- Mandell LA, Bartlett JG, Dowell SF, File JM, Musher DM, Whitney C. Infectious Disease Society of America update of practice guidelines for the management of community-acquired pneumonia in immunocompetent adults. *Clin Infect Dis*. 2003;37:1403-33.
- Pines JM, Isserman JA, Hinfey PB. The measurement of time to first antibiotic dose for pneumonia in the emergency department: A white paper and position statement prepared for the American Academy of Emergency Medicine. *J Emerg Med*. 2009 Oct;37(3):335-40.
- National Antibiotic Committee Malta. Antibiotic resistance – facts and figures. Nov 2010.
- Mandell LA, Bergeron MG, Gribble MJ, Jewesson PJ, Low DE, Marrie TJ, et al. Sequential antibiotic therapy: effective cost management and patient care. *Can J Infect Dis*. 1995;6:306.
- el Moussaoui R, de Borgie CA, van den Broek P, Hustinx WN, Bresser P, van den Berk GE, et al. Effectiveness of discontinuing antibiotic treatment after 3 days versus 8 days in mild to moderate-severe CAP: randomised, double blind study. *BMJ*. 2006;332:1355-61.
- Menendez R, Cremdes MJ, Martinez-Moragon E, Soler JJ, Reyes S, Perpina M. Duration of length of stay in pneumonia: influence of clinical factors and hospital type. *Eur Respir J*. 2003 Oct;22(4):643-8.
- Fine MJ, Medsger AR, Stone RA, Marrie TJ, Coley CM, Singer DE, et al. The hospital discharge decision for patients with community-acquired pneumonia. *Arch Intern Med*. 1997;157:47-56.
- Campbell SG, Marrie TJ, Anstey R, Dickinson G, Ackroyd-Stolarz S. The contribution of blood cultures to the clinical management of adult patients admitted to the hospital with community-acquired pneumonia. *Chest*. 2003;123:1142-50.
- Luna CM. C-reactive protein in pneumonia: let me try again. *Chest*. 2004;125(4):1192-5.
- Seppä Y, Bloigu A, Honkanen PO, Miettinen L, Syrjälä H.. Severity assessment of lower respiratory tract infection in elderly patients in primary care. *Arch Intern Med*. 2001;161:2709-13.
- Hedlund J. Diagnostic and prognostic value of interleukin-6 and C-reactive protein in community-acquired pneumonia. *Scand J Infect Dis*. 1995;27(5):457-62.
- Chalmers JD, Singanayagam A, Hill AT. C-reactive protein is an independent predictor of severity in community-acquired pneumonia. *Am J Med*. 2008;121:219-25.
- Christ-Crain M, Stolz D, Bingisser R, Müller C, Miedinger D, Huber PR, et al. Procalcitonin guidance of antibiotic therapy in community-acquired pneumonia: a randomised trial. *Am J Respir Crit Care Med*. 2006;174:84-93.
- Masiá M, Gutiérrez F, Shum C, Padilla S, Navarro JC, Flores E, et al. Usefulness of procalcitonin levels in community-acquired pneumonia according to the patients outcome research team pneumonia severity index. *Chest*. 2005;128:2223.
- Yang M, Yuping Y, Yin X, Wang BY, Wu T, Liu GJ, et al. Chest physiotherapy for pneumonia in adults. *Cochrane Database Syst Rev*. 2010;2:CD006338.