

SEVERE COMMUNITY-ACQUIRED AND NOSOCOMIAL PNEUMONIA — A COMMENTARY

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In the March/April 1996 issue of *Intensive Care Monitor*, Mark Smithies,¹ in an editorial entitled 'How close is the post-antibiotic era?', wrote that patients in intensive care units (ICUs) are under constant threat from hospital infections acquired within the ICU itself, where susceptible patients are concentrated in a high antibiotic usage environment and where transfer of resistant bacterial pathogens is increased. The emergence of resistant bacteria is, however, a global problem affecting not only nosocomial but also community-acquired infections. To some extent these are matters over which workers in the ICU have little control except to limit antimicrobial use and enforce infection control procedures in the critically ill individual. Within the wider community the difficulties with this approach are reflected by a report from the Centers for Disease Control (Atlanta) which suggested some new strategies that could (or should) be employed to try to curb these increasing problems. They stressed that although existing infection control guidelines are rational, they have failed to change people's behaviour.

CLASSIFICATIONS AND DEFINITIONS

The classification of pneumonia into community-acquired and nosocomial (hospital-acquired) does not imply that one form is more severe than the other or that community-acquired pneumonia (CAP) is necessarily Gram-positive and hospital-acquired pneumonia (HAP) Gram-negative. CAP ranges from a mild illness that can be treated with oral antibiotics to a more severe form where patients require ICU and possibly ventilation. Both forms may involve Gram-positive or Gram-negative organisms.

Community-acquired pneumonia

CAP is defined as pneumonia arising within the community. This excludes those who contract the infection while in old-age homes, as patients in these institutions frequently have comorbid disease and are exposed to a resistant population of organisms.

Therapy in CAP is based upon its initial classification. The South African Pulmonology Society recognises four categories:

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- Ambulant non-hospitalised
- Hospitalised age < 60 years
- Hospitalised age > 60 years, or with comorbid disease, or with two poor prognosticating features
- Severe pneumonia: three or more poor prognosticating features.

The features of severity are recognised in numerous references as the following:

- Hypoxaemia: partial pressure of oxygen (PaO₂)/fractional inspired oxygen concentration (FiO₂) < 200 or requirement for mechanical ventilation
- Hypotension — systolic < 90 mmHg, diastolic < 60 mmHg
- Tachypnoea > 30/min
- Bilateral or rapidly progressive pulmonary infiltrates
- Urea > 7.0 mmol/l
- White cell count < 4 000 or > 30 000
- Confusion.

The above classification also includes certain risk factors which may predispose to specific infections, e.g. aspiration (anaerobes, *Staphylococcus*) and steroids (*Pseudomonas*, *Staphylococcus*). This classification is useful in that it allows a rational approach to management according to the likelihood of the organism and mandates an assessment of severity.

In 1998 the European Respiratory Society (ERS) published the updated guidelines on the management of adult community-acquired lower respiratory tract infections. They refer to:

- Acute bronchitis, defined as an acute viral/bacterial infection of the bronchi
- Pneumonia, defined as infection of the lung parenchyma
- Super-infection of chronic bronchitis
- Influenza.

Although less severe forms of these illnesses may be difficult to distinguish one from the other, those who are more ill will have a chest radiograph from which the diagnosis of CAP can be made confidently.

MANAGEMENT OF SEVERE CAP

Management of this category of infection depends first on the identification of severity. Frequently death occurs as a consequence of inadequate initial assessment. Therapy should consist of supportive therapy, rehydration, inotropes and oxygenation (which might include ventilation) as well as antibiotics.

Although antibiotics are essential, there is nevertheless a category of patients who may die early regardless of antimicrobial agents or the sensitivity of the organism.

The CAP guidelines are still appropriate to the South African situation. These guidelines suggest that the following are adequate for severe infection:

- Cefuroxime or amoxicillin/clavulanate
- Plus gentamicin
- Plus a macrolide.

These agents are given intravenously and cover all the likely organisms. Severe pneumonia is most often due to *Streptococcus pneumoniae*, but *Klebsiella* and *Legionella* are also possible causes which would be covered by such a regimen. The penicillin-resistant pneumococcus in South Africa most frequently manifests with intermediate resistance. This means that the administration of high-dose penicillin achieves the minimal inhibitory concentrations (MICs) necessary to eradicate pulmonary pneumococci. This does not apply to meningitis or otitis media, where a third-generation cephalosporin is essential.

There is little indication for third- or fourth-generation cephalosporins regardless of the severity of the pneumonia, as there is little increase in spectrum with regard to community-acquired organisms. If cefuroxime is used and anaerobes are suspected, metronidazole is an effective addition. However, in this setting replacement of the cefuroxime with amoxicillin/clavulanate would be equally efficacious. Clindamycin may be a useful alternative anaerobic agent if the patient is allergic to penicillin.

Staphylococcus is more important as a nosocomial pathogen. However, most studies in South Africa have found a prevalence in the region of 5%, particularly following influenza epidemics. Community-acquired staphylococcus is still usually sensitive to cefuroxime or amoxicillin/clavulanate; however, sputum Gram staining and blood cultures would rapidly identify this organism. If this patient is not responding to therapy, addition of a glycopeptide pending availability of sensitivity could be considered. This should be stopped if sensitivity to another anti-staphylococcal agent is confirmed.

South Africa appears to have a particularly high prevalence of CAP caused by *Klebsiella*, most of which are still sensitive to at least one of the initial empiric antibiotics. This does not appear to be the case in Europe or America, and it is currently uncertain why this difference should exist.

The quinolones have been used in management of CAP. Ciprofloxacin and ofloxacin are inappropriate, as they are relatively inactive against Gram-positive organisms. The new generation of quinolones, such as moxifloxacin, clinafloxacin, levofloxacin and grepafloxacin, offer a rational choice for first-line therapy for CAP. This has been suggested by the European Respiratory Society, particularly in view of the possibility of penicillin-resistant pneumococci. There is evidence, however, that two agents may be preferable in *Klebsiella* infections, and it is uncertain whether they should be used alone in severe CAP. In addition there are also early reports of quinolone-resistant pneumococci in Canada, where quinolones have frequently been used for infections in the community. I would suggest that these agents be reserved for

cases confirmed to be resistant to penicillin, and when they are used for severe CAP another Gram-negative agent should be added.

Whether or not to cover for atypical infections is controversial. The prevalence of *Legionella* in this country is probably low, and it has been well established that the mortality rates for *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* are low even if no antibiotics are given. If any suspicion of *Legionella* exists, however, a macrolide should be given intravenously. All studies have shown *M. tuberculosis* to cause CAP, and non-resolving pneumonia should raise the suspicion of this pathogen.

Clinical deterioration after the initiation of guideline-directed empiric antibiotics is seldom due to worsening infection, but rather to a florid systemic inflammatory response syndrome with organ dysfunction, including adult respiratory distress syndrome (ARDS). Hypotension and disseminated intravascular coagulopathy (DIC) may complicate any severe pneumonia and may mimic all the features of worsening sepsis.

HOSPITAL-ACQUIRED PNEUMONIA

HAP is defined as a pneumonia occurring at least 48 hours after admission to hospital. Although it is possible that the infection was incubating within the preceding 48 hours, guidelines such as those of the American Thoracic Society recognise that HAP is not one entity. If empiric therapy is to be applied, a classification must be devised in which the most likely organisms will be covered. This depends upon the length of stay in the hospital and the presence of risk factors.

1. Less than 5 days in hospital:
 - without risks: less resistant enteric Gram-negative organisms, hemophilus or *S. pneumoniae*
 - plus coma, head injury, influenza, intravenous drug abuse, renal failure or diabetes: consider additionally *Staphylococcus aureus*
 - plus previous antibiotics, steroids or structural lung disease: consider *Pseudomonas*, *Legionella*
 - witnessed aspiration or thoraco-abdominal surgery: anaerobes or *S. aureus*.
2. More than 5 days, or not severe: resistant enteric Gram-negative organisms.
3. More than 5 days or less than 5 days but severe, or ventilator-associated pneumonia: *Pseudomonas*, *Acinetobacter*.

Considerable diagnostic difficulty is associated with ventilation-associated pneumonia. This is discussed in detail elsewhere in this issue of the journal. Because the mortality is considerable emphasis should be on prevention and appropriate initial antibiotic therapy once the diagnosis is made. Kollef has recently published a review of preventive interventions, the most important of these being hand washing. This seemingly simple manoeuvre is extremely poorly adhered

to. Bartzokas *et al.*³ observed that senior doctors only washed their hands twice during 21 hours of ward rounds. Doctors are mobile and have numerous transient contacts with patients, yet neglect this basic necessity. It is clear that health care workers fail to understand the importance of hand washing. There should be no contact with any ICU patient without hand washing before and after contact. This should be enforced to the extent that health care workers shown not to do so should be held accountable in the event of hospital-acquired infections. Gowns and gloves reduce infection with certain specific organisms such as vancomycin-resistant enterococci. This is not necessary routinely.

Patients should be nursed at a minimum of 15° to prevent aspiration and in addition avoid gastric overdistension by feeding continuously or into the jejunum. Avoid nasogastric intubation, which increases the incidence of sinusitis and ventilator-associated pneumonia (VAP). Rigorous exclusion and treatment of maxillary sinusitis in this setting reduces morbidity and mortality.

Ventilation circuits should be replaced only once a week unless there is overt soilage such as with vomit or blood. Continuous subglottic aspiration of secretions above the cuff decreases the incidence of VAP and also allows identification of the type and sensitivity of colonising organisms. Do not let the cuff down when checking pressures.

Closed suction catheter systems decrease environmental contamination and may be an option in open-plan ICUs. The risk of pneumonia is not reduced by either type of catheter. Stress ulcer prophylaxis should not reduce gastric acidity. Sucralfate is as efficacious as H₂-receptor antagonists and antacids and should be used in preference.

Combinations of antibiotics should be limited to specific circumstances such as pseudomonal infections or infections with multiple organisms. Monotherapy has not been shown to be associated with more rapid acquisition of resistance. Antibiotic prophylaxis is not recommended in the ICU, and selective digestive tract decontamination is not of value. Aerosolised antibiotics are ineffective as therapy or prophylaxis.

The use of immune-enhancing diets containing glutamine, omega-3 fatty acids, arginine and nucleotides has been shown to reduce infections in the ICU. Similarly, it is recommended that early enteral feeding be employed routinely, particularly for patients with potential for intraperitoneal sepsis.

Appropriate initial antibiotic therapy has a significant impact on outcome. Wherever possible therapy should be surveillance-guided and the routine use of both Gram-positive and Gram-negative cover should be avoided.

A clear distinction must be made between colonisation and infection, particularly where routine non-directed bronchiolar alveolar lavage surveillance is employed. Finding an organism should not lead to therapy until signs of systemic sepsis ensue.

Empiric therapy should be based on the microbial profile of infections within the unit, the duration of admission, the insult

sustained and the presence or absence of immunosuppression. Reasonable initial regimens for VAP would be:

- Fourth-generation cephalosporin or tazobactam/piperacillin plus aminoglycoside or quinolone
- Quinolone or carbapenem plus aminoglycoside
- Carbapenem monotherapy.

Potential additions to each regimen could be metronidazole/clindamycin if the patient is not on tazobactam/piperacillin or a carbapenem. This should be given if there has been a witnessed or potential aspiration. Vancomycin or teicoplanin should not be used routinely. They should be strongly considered in patients with coma or head injury, or those who have recently had steroids. Perhaps the most important indication would be profuse Gram-positive cocci on a Gram stain.

Frequently forgotten is the potential problem of fungi. *Candida* species and less often *Aspergillus* are now seen frequently in the ICU, particularly in patients on steroids, those with burns or who have received broad-spectrum antibiotics, those who have required prolonged ventilation, or those with abdominal sepsis or pancreatitis. Amphotericin B is still the agent of choice until sensitivity is confirmed. Routine prophylaxis with fluconazole is associated with colonisation of the unit with fluconazole-resistant *Candida* species.

Third-generation cephalosporins should be avoided, as there is a link between their use and colonisation of the unit with stably depressed β -lactamase-producing organisms and the development of extended-spectrum plasmid-mediated β -lactamases. In addition, their lack of activity against enterococci could cause overgrowth of these organisms with an increased potential for resistance.

It must be realised that after only 50 years we are nearing the end of the antibiotic era. Continued misuse of this precious resource will only hasten their demise.

References

1. Smithies M. How close is the post-antibiotic era? (Editorial). *Intensive Care Monitor* 1996; **111** (2): 21.
2. Kollef MH. Current concepts: The prevention of ventilator associated pneumonia. *N Engl J Med* 1999; **340**: 627-634.
3. Bartzokas CA, Williams EE, Slade PDA. A psychological approach to hospital acquired infections. In: *Studies in Health and Human Sciences*. London: Edward Mellen, 1995.

Suggested reading

- American Thoracic Society. Hospital acquired pneumonia in adults: diagnosis, assessment of severity, initial anti-microbial therapy and preventative strategies: a consensus statement. *Am J Respir Crit Care Med* 1995; **153**: 1711-1725.
- Beale R. Immunonutrition in the ICU. *International Journal of Intensive Care* 1999; Spring: 12-17.
- Bruchhaus JD, McEachern R, Campbell GD. Hospital acquired pneumonia: recent advances in diagnosis, microbiology and treatment. *Curr Opin Pulm Med* 1998; **4**(3): 180-184.
- Chen D, McGeer A, De Azavedo J, Low D. Decreased susceptibility of *Streptococcus pneumoniae* to fluoroquinolones in Canada. *N Engl J Med* 1999; **341**: 233-239.
- Community-acquired pneumonia guidelines. *S Afr Med J* 1996; **86**: 1152-1155.
- Davey PG, Bax RP, Newey J, *et al.* Growth in the use of antibiotics in the community in England and Holland in 1980-93. *BMJ* (SA Edition) 1996; **4**: 820.
- Dominguez MA, Pallares R. Antibiotic resistance in respiratory pathogens. *Curr Opin Pulm Med* 1998; **4**(3): 173-179.
- Handwashing Liaison Group. *BMJ* 1999; **318**: 686.
- Huchon G, Woodhead M, eds. Management of adult community acquired lower respiratory tract infections. *Eur Respir Rev* 1998; **8**(61).
- Maartens G. Controversies in the management of community acquired pneumonia in adults. *Specialist Medicine* 1997; Aug: 76-80.
- Richards GA. Hospital acquired pneumonia. *Specialist Medicine* 1997; Nov: 20-28.