TREATMENT OF LOWER RESPIRATORY TRACT INFECTION

- Knowledge of the current sensitivity of prevalent organisms directs choice of antibiotic.
- Empirical treatment of community acquired LRTI targets *Streptococcus pneumoniae* and *Haemophilus influenzae*.
- Choice of antibiotics should be made on the basis of cost effectiveness as there is little to choose between clinical efficacy but costs varies widely.
- Ampicillin or amoxycillin remain drugs of first choice.

Acute chest infections are common. Identifying the pathogens in lower respiratory tract infection (LRTI) as well as changing patterns of organism susceptibility to antibiotics continue to make definitive treatment a challenge for physicians. However LRTI in the community has been extensively studied and guidelines exist that facilitate the prescriber in their choice of antibiotic particularly if an empirical approach is required. Knowledge of prevalent organisms and their current sensitivity is of great help in choosing an antibiotic. The term LRTI covers a wide spectrum of disease including acute bronchitis, acute exacerbations of COAD and community acquired pneumonia (CAP).

MICROBIOLOGY

The most common causative organism of CAP is *Streptococcus pneumoniae* which should always be covered with antibiotics and amoxycillin or ampicillin is the preferred choice. Some strains of *Streptococcus pneumoniae* with decreased sensitivity to penicillin have been isolated but are not yet common in Ireland.

Patients with COAD frequently develop respiratory tract infections and the most common organism identified in the sputum is *Haemophilus influenzae* of which about one third are resistant to ampicillin. Most are sensitive to co-amoxyclav (Augmentin), the new macrolides (e.g. clarithromycin, azithromycin) and the new third generation oral cephalosporins. Most strains of *Haemophilus influenzae* are resistant to erythromycin and many prescribers do not recommend erythromycin as a first choice except in cases of suspected atypical infection, such as *Mycoplasma pneumoniae*.

Viral pathogens should also be considered as a cause of LRTI and are more likely to be the causative agent in acute bronchitis and in exacerbation of COAD.

ACUTE BRONCHITIS

Acute bronchitis is characterised by a persistent cough and occasionally fever and chest pain. It often follows an upper respiratory tract infection, is self-limiting and typically lasts 7-14 days. In previously healthy patients bacterial infection is uncommon. Routine antibiotic use is not warranted in healthy patients with cough and purulent sputum as this may lead to the development of resistant strains. If the illness is severe or persists longer than seven days, then the bacterial infection secondary to a viral infection can be assumed.
ACUTE EXACERBATION OF CHRONIC BRONCHITIS

Acute exacerbation of chronic bronchitis (AECB) has a multifactorial aetiology including a viral, bacterial, allergic or environmental pollutant as possible causes. Antibiotics are commonly prescribed during AECB but evidence that they appreciably alter outcome is lacking\(^3\). As one quarter of patients return to their GP's with incomplete recovery, antibiotics may only benefit certain sub-groups that are not yet well characterised\(^4\). However studies have shown significant benefit from antibiotics compared with placebo in patients judged to have moderate to severe COAD on the basis of increased dyspnoea, sputum production and sputum purulence. In the same study no benefit from antibiotics was demonstrated for milder exacerbations involving only one of these symptoms\(^5\).

Ideally antibiotic treatment should be based on sputum culture but in practice empirical treatment is necessary. The choice of antibiotics should cover the most common organisms which include \textit{Haemophilus influenzae}, \textit{Streptococcus pneumoniae} and \textit{Moraxella catarrhalis}.

COMMUNITY ACQUIRED PNEUMONIA (CAP)

Most cases of CAP can be treated in the community but there is increased mortality associated with respiratory rate greater than 30 per minute, age over 60 years, confusion, diastolic blood pressure less than 60mmHg, multilobar involvement and atrial fibrillation\(^1\). Antibiotic therapy should be commenced immediately without waiting for culture results and should always cover \textit{Streptococcus pneumoniae}, the most common cause of CAP. \textit{Haemophilus influenzae} and \textit{Moraxella catarrhalis} are the next most prevalent.

Infection with \textit{Mycoplasma pneumoniae} occurs in epidemics of 4-5 year cycles, occurs commonly in children and young adults and if suspected should be treated with erythromycin for 10-14 days\(^6\). \textit{Staphylococcus aureus} should be considered during epidemics of influenza and should be treated with flucloxacillin if suspected.

TREATMENT OF LRTI

The penicillins are still suitable for the empiric treatment of CAP and amoxycillin 250-500mg tid (or ampicillin 250-500mg qid) for seven days is usually sufficient. Clinically severe CAP may require alternative antibiotic therapy. \textit{Some strains of Streptococcus pneumoniae have "intermediate resistance" to penicillin, but studies show that these resistant strains are sensitive to higher doses of penicillin}\(^6,7,8\).

Generally elderly patients with COAD tend to be colonised with \textit{Haemophilus influenzae} and if the exacerbation is severe they should be given co-amoxyclov or the newer macrolides (e.g. clarithromycin, azithromycin) because these antibiotics have greater activity against \textit{Haemophilus influenzae}. In addition these patients tend to reinfect with bacteria that already colonise their respiratory tract and so previous sputum cultures may provide a clue to the possible cause. There are an increasing number of beta-lactamase producing strains of \textit{Haemophilus influenzae} and \textit{Moraxella catarrhalis} and so co-amoxyclov is recommended in cases suspected of these organisms.

The newer oral cephalosporins, cefaclor, cefixime and cefuroxime are all beta-lactamase stable and are alternatives to the penicillins, for beta-lactamase producing strains of \textit{Haemophilus influenzae} and \textit{Moraxella catarrhalis}. These cephalosporins are generally no more active than penicillin in penicillin-sensitive and penicillin-resistant \textit{Streptococcus pneumoniae}. It has been suggested that cephalosporins should not be used to treat most community acquired infections because multiple resistant organisms are unusual and other drugs exist with narrower spectrum of activity\(^9\).

The fluroquinolones, (ciprofloxacin and ofloxacin) have relatively poor activity against \textit{Streptococcus pneumoniae} which is a predominant LRTI pathogen, and so have no place as single agents in blind treatment of LRTI. They are effective against \textit{Haemophilus influenzae} and atypical pathogens such as \textit{Mycoplasma pneumoniae}. Co-trimoxazole, while effective against \textit{Streptococcus}
*pneumoniae* and *Haemophilus influenzae* is associated with several undesirable adverse effects such as blood and generalised skin disorders. It should only be considered for the treatment of community acquired LRTI when there is good bacteriological evidence of sensitivity to co-trimoxazole and a good reason to prefer this combination to a single antibiotic. Tetracycline cannot be recommended for the routine treatment of LRTI.

**RESISTANCE AND ANTIBIOTIC ASSOCIATED COLITIS**

Microbial resistance problems arise as antimicrobial therapy leads to alteration of normal body flora with a resultant increase in the number of resistant organisms. Many organisms are naturally resistant to antibiotics, but resistance may also be acquired. In addition beta-lactamase stable antibiotics, particularly the third generation cephalosporins are more likely to lead to the emergence of resistant strains mainly in the gram negative pathogen spectrum leading to fungal infections and antibiotic associated colitis.

Almost all antibacterial agents have been observed to induce diarrhoea in some patients which if severe may indicate pseudomembranous colitis (PMC). Patients treated with cephalosporins, penicillinase resistant or multiple antibiotic regimes are seen to be at higher risk of PMC. A patient with severe diarrhoea during or within 4-6 weeks of antibiotic treatment should be suspected of antibiotic associated colitis.

**IMPORTANT DRUG INTERACTIONS**

A number of the newer antimicrobials may inhibit liver drug metabolism:

- The anticoagulant effect of warfarin may be enhanced by the macrolides (e.g. erythromycin), ciprofloxacin, ofloxacin.
- Theophylline levels may be increased by the macrolides and ciprofloxacin.
- Hypoglycaemic effect of sulphonylurea is enhanced by ciprofloxacin, ofloxacin and co-trimoxazole.
- Carbamazepine blood levels are elevated by macrolides.

- Broad spectrum antibiotics may reduce the contraceptive efficacy of the combined oral contraceptive pill.

**SAFETY OF ANTIBIOTICS IN PREGNANCY**

- The aminopenicillins (amoxycillin and ampicillin) are generally regarded as safe to use during pregnancy. There is no evidence of teratogenicity due to co-amoxaclav (augmentin), although the manufacturer advises to avoid use unless essential.
- The fluoroquinolones (ciprofloxacin and ofloxacin) are contraindicated during pregnancy due to the risk of arthropathy in animal studies.
- Cephalosporins are not thought to be harmful during pregnancy, yet all manufacturers advise caution and to avoid unless necessary.
- The macrolides are not known to be harmful, but caution is advised so that they are used only when the benefit exceeds the risk.

**CONCLUSION**

As repeat consultations for acute respiratory symptoms are common, general practitioners are under considerable pressure to prescribe a wide variety of new antibacterial drugs as a potential solution to this problem. These treatments will have to be much more effective than current therapy in order to be cost effective and there is little evidence that they are clinically superior to penicillins in the majority of patients.

**COST**
COMPARATIVE COSTS FOR FIVE DAYS ANTIBIOTIC THERAPY IN THE TREATMENT OF LOWER RESPIRATORY TRACT INFECTIONS

Drug costs are based on data from GMS 1996.

REFERENCES