

ANTIBIOTICS IN GENERAL PRACTICE

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I recently reviewed antibiotic prescribing at a Postgraduate Meeting and have been asked to put my thoughts on paper. In this series of articles I shall give a personal view of the main oral antibiotics used outside hospital, starting with the penicillins and cephalosporins. This large and venerable group of agents is highly active microbiologically but often has disappointing pharmacological performance. Chemical modifications have addressed the problem of resistance and improved pharmacological performance, but in the right situation the older agents are still highly effective and very cheap. With improvements in purity the problem of allergy has declined somewhat.

PENICILLIN

PENICILLIN (*phenoxymethyl penicillin, penicillin V*)

These days activity can only really be guaranteed against haemolytic streptococci and meningococci. It is still the drug of choice for sore throats (if an antibiotic is needed). Staphylococci became resistant in the late 1950's and now only 10% of isolates are sensitive, making it an unsuitable empirical choice for soft tissue infections (see under cloxacillin). Increasing resistance among the gonococci and awareness of chlamydia leave it with little place in the management of urethritis. Fortunately, meningococci are still uniformly sensitive and an intravenous injection of benzylpenicillin before transfer to hospital can be lifesaving in cases of fulminant meningococcal infection. Injections of long-acting penicillins are no longer recommended for tetanus prophylaxis in casualties.

AMPICILLIN/AMOXYCILLIN/ MECILLINAM

Simple penicillin has no gram-negative activity and ampicillin was developed to get around this. It has been a very valuable antibiotic for almost 30 years, being the mainstay of treatment for urinary and lower respiratory infections. However, amongst the coliforms, 50-60% of isolates are now resistant and resistance amongst haemophilus is increasing. Most staphylococci are resistant and it is no better than penicillin against streptococci. Thus it is no longer a useful empirical agent for infections of the urinary and respiratory tracts or for skin and soft tissue infections. The sensitisation seen in people with glandular fever should preclude its empirical use in sore throats. It needs a well-earned retirement. Amoxicillin is a pharmacologically superior ampicillin with some microbiological differences which have little relevance in practice. It is undoubtedly tolerated better

than ampicillin, but my comments about ampicillin apply equally here, as they do to the prodrug esters, talampicillin, bacampicillin, and pivmecillinam.

CLOXACILLIN AND FLUCLOXACILLIN

These were developed in response to the increasing problem of resistance among the staphylococci and have been the mainstay of antistaphylococcal therapy for many years. Resistance has been described (the dreaded MRSA) but is very rare this far north. I have just examined an unselected series of swabs from infected wounds in casualty patients and from general practice. Of 100, 96 were due to *Staphylococcus aureus* with another two being due to group A streptococci. Flucloxacillin will cover both these and it is the best empirical agent for simple soft-tissue infections in the community. The addition of ampicillin achieves little, so the least said of combinations the better. If the wound infection follows an animal bite, the microbiological possibilities are somewhat greater and the addition of ampicillin or the use of Augmentin might be justified. The differences between flucloxacillin and cloxacillin are minor and of little practical relevance. Nowadays flucloxacillin is the more widely available.

AUGMENTIN

Most resistance to penicillins is mediated by bacterial enzymes that break down the antibiotics. Augmentin (it has no generic name yet) addresses this problem by combining amoxicillin with an enzyme inhibitor, clavulanic acid. Whatever microbiological purists might think of this, the effect is to broaden the spectrum of amoxicillin to include staphylococci, a greater range of coliforms, haemophilus and anaerobes. Very broad spectrum agents avoid the need to consider the microbiological possibilities and encourage lazy medicine and resistance problems. Augmentin can be a useful general purpose antibiotic. Patients with glandular fever will still be hypersensitive.

CEPHALOSPORINS

These agents are very similar to the penicillins, and were developed to avoid the problems of narrow spectrum and poor oral absorption of simple penicillin. Only 6% of penicillin-allergic patients will react to a cephalosporin, so they can be used with care if it is clinically important. They are more popular than penicillins in many parts of the world and the potential market has stimulated the development of a

mind-numbing range of similar agents. My current textbook discusses 35 cephalosporins in 260 pages. Fortunately, many are not available in this country or can only be given parenterally, so the task here is simplified. The customary classification into three generations is based on their chemistry. This is of limited use in practice, but coincides reasonably well with their microbiological properties, so it is a variant of this which I use here. I will limit myself to the first and second generation cephalosporins. The third generation agents are injectable, broad spectrum antibiotics for hospital use.

FIRST GENERATION CEPHALOSPORINS

These are reasonably broad-spectrum antibiotics covering about 80% of coliforms and most staphylococci. They are effective, but unnecessarily broad-spectrum, for soft-tissue infections and are good empirical urinary antibiotics. Their main weakness is low activity against *Haemophilus influenzae*, which makes them poor empirical agents for community-acquired respiratory infections. Of this group, Cephadrine (Velosef) is a standard drug for hospital use, but only because it is cheap and there is an injectable

formulation. In general practice, Cephalexin (Ceporex, Keflex) is cheaper and slightly more active. Cefadroxil (Baxan) can be given less frequently and this could improve compliance.

SECOND GENERATION CEPHALOSPORINS

These have been modified to give even greater activity against coliforms and to improve their activity against *Haemophilus influenzae*. They are a better choice for chest infections but like all the Beta lactams have no activity against mycoplasma. Depending on the year and season these organisms are significant and are really only covered by erythromycin or tetracycline. Cefaclor (Distaclor) is quite widely used though most of the time offers little more than first generation cephalosporins. Cefuroxime axetil (Zinnat) is an oral ester of cefuroxime. It is a second generation cephalosporin and has a product licence.

In the next article, I will go on to consider erythromycin, tetracycline, sulphonamides, quinolones and the urinary antibiotics. The last article will attempt to bring things together in a suggested formulary.

QUIZ



1. What is the study?
2. What does it show?

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