Updates for your practice… January 2014, Volume 3, Issue 1.

TLALETSO

UPDATES FOR YOUR PRACTICE

Principles of Antimicrobial Therapy

Responsible prescribing that benefits both the patient and the community

There is increasing evidence across southern Africa that antibiotic resistance is increasing. The widespread and often inappropriate use of antimicrobial agents is the single most important cause of the emergence of drug resistance, both in the community and hospital settings.

Clearly the emergence of antimicrobial resistance can be delayed or prevented through judicious prescribing, which can be characterized as follows: avoidance of antibiotics for community acquired, mostly viral, upper respiratory infections, use of narrow spectrum antibiotics when possible, and use of antibiotics for the shortest duration that is effective for the treatment of a particular clinical syndrome.

In this issue of Tlaleletso we review some of the key strategies that clinicians should employ to minimize the development of drug resistant pathogens as well as discuss some of the most important principles of antimicrobial therapy, including when to use empiric rather than specific therapy, how different antibiotics should be described differently and how long should patients be treated with antibiotics for.

MAKING THE RIGHT DIAGNOSIS

In order to select the best antibiotic regimen it is essential that the right diagnosis is made. This involves determining the site of infection, defining the host (e.g. HIV, advanced age, diabetic), and establishing when possible a microbiological diagnosis. It is critical to isolate the specific pathogen in many serious life threatening infections, especially for situations that are likely to require prolonged therapy. Similarly when a patient does not benefit from antimicrobial therapy chosen on the basis of clinical presentation, additional investigations maybe needed to determine the causative organism or to exclude a noninfectious diagnosis.

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When to use empiric and when to use definitive therapy.
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Using combinations
Single agent antimicrobial therapy is preferred but combination therapy is recommended in some scenarios
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When is it clearly inappropriate to use antibiotics. We discuss some typical scenarios
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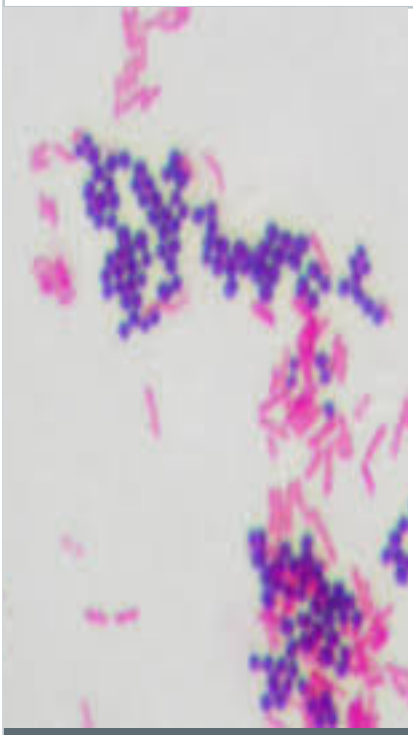

Oral or IV?

Patients hospitalized with infections are often treated with intravenous antibiotics because their administration is often prompted by the severity of infection.

However, patients with mild to moderate infections who have normal GI function are candidates for treatment with oral antibiotics.

Patients initially treated with IV therapy can be safely switched to oral antibiotics when they become clinically stable . When using oral therapy for invasive infections (such as pneumonia or pyelonephritis) clinicians are advised to select an agent that has good penetration. For this reason, a switch to oral therapy is not recommended in patients on IV treatment for meningitis.

EMPIRIC OR DEFINITIVE ANTIMICROBIAL THERAPY?

Because microbiological results to no become available for 24 to 72 hours initial therapy for infection is often empiric and guided by clinical presentation. When patients are critically ill, starting therapy as soon as possible can save lives. Therefore a common approach is to use broad spectrum antibiotics as initial empiric therapy.

For example, in the HIV-negative patient with suspected bacterial meningitis the most likely pathogens would be *Streptococcus pneumonia, Hemophilus Influenze* and *Mycoplasma pneumonia* and thus a combination of amoxicillin and doxycycline would be recommended as empiric therapy, the latter organism being used to cover the atypicals (such as *Mycoplasma).*

In selecting empiric therapy for infections, clinicians should consider the following: (1) Site of infection and organism likely to be colonizing that site, (2) Prior knowledge of bacteria known to colonize a given patient; and (3) The local bacterial resistance patterns or antibiograms that are available for important pathogens (which is available at Princes Marina Hospital).

USING COMBINATIONS OF ANTIBIOTICS

Although single agent therapy is generally preferred a combination of 2 or more antimicrobial agents is recommended in a few scenarios.

1. Synergistic Activity: Synergy between antibiotics means that the combined effect of two drugs is greater that the sum of their independent activities. For example, the combination of pencillins and aminoglycosides exhibits synergistic activity against a variety of gram positive and gram negative bacteria. For example, when treating strep viridans endocarditis, 2 weeks of gentamicin and penicillin or cetriaxone is as effective as 4 weeks of penicillin or ceftriaxone alone.

2. To extend antimicrobial spectrum beyond that achieved by a single agent. As already mentioned, antibiotic combinations are used in empiric therapy when more than one organism might be causing the infection. For example, most intra-abdominal infections are usually caused by a multiple organisms. Antimicrobial combinations, such as ceftriaxone and metronidazole provide reasonable coverage for many of the organisms that may be pathogenic in such cases.

3. When critically ill patients require empiric therapy before the causative organism has been determined. For example when a patient has been hospitalized for several weeks develops septic shock it may be appropriate to broaden coverage to include nosocomial pathogens, such as *P. Aeruginosa*

Host factors to be considered when selecting antibiotics

Although it is helpful for clinicians to gain familiarity with a few specific antbiotics, a one size fits all approach is not always appropriate in choosing the right antibiotic. Factors to bear in mind include the following:

1. Renal and hepatic function – in most cases clinicians have to reduce the dose of antibiotics to prevent accumulation and toxicity in patients with reduced renal or hepatic function. Its worth remembering that sometimes other drugs also effect renal elimination or hepatic metabolism (rifampicin or phenytoin) and it may be necessary to increase the dose.

2. Age – patients at both extremes of age handle drugs differently. In geriatric patients the serum creatinine level alone is not completely reflective of kidney function and the creatinine clearance should be estimated by factoring in age and weight for these patients.

3. Pregnancy and lactation - Special consideration for the use of antibiotics in pregnancy relate to both the mother and the fetus. In the case of the moth, increases in plasma volume and renal blood flow especially by the third trimester can result in more rapid clearance and lower serum levels of certain drugs. In the case of the developing fetus many antibiotics can be teratogenic or otherwise toxic to the fetus. Penicillins, cephalosporins and macrolides like erythromycin, have historically been the most commonly used antimicrobial agents considered safe in pregnancy. Tetracyclines and chloramphenicol have well described fetal and neonatal adverse effects and should be avoided,

4. Allergy or Intolerance - A history of antibiotic intolerance or allergy should be routinely obtained in the evaluation and management of infection.

5. Genetic Variation – Genetic susceptibility to the adverse effects of antimicrobial agents is occasionally significant enough to warrant testing for such variability. One relevant example is glucose-6-phosphate dehydrogenase (G6PD) deficiency which can result in hemolysis in individuals when exposed to certain antibiotics, such as nitrofurantoin.

BOTSWANA-UPENN PARTNERSHIP

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Common Mistakes to avoid!

Here are some examples of where antibiotics might be contraindicated…

1. Prolonged empiric antibiotic therapy without clear evidence of infection: one of the commonest mistakes is to add or switch antibiotics when a patient is not responding to therapy, even though there is no clear evidence of infection. Many noninfectious inflammatory or neoplastic syndromes can mimic infectious diseases. However, TB can also present with fevers and will not respond to standard antibiotics. In HIV patients always consider TB!
2. Treatment of a positive clinical culture in the absence of disease: colonization with potentially pathogenic organisms without any manifestations of disease occurs frequently (e.g, colonization of the urinary tract of women of advanced age) and is not an indication for therapy
3. Failure to narrow antibiotic therapy when the causative organism has been identified.
4. Prolonged prophylactic therapy – while there is an important role for prophylactic antibiotics (presurgery). Prolonged antibiotics in this situation sets the stage for antimicrobial resistance.
5. Excessive use of certain antimicrobials. The frequent use of certain antibiotics can result in selection of organisms resistant to a particular antibiotic. For example the increased use of fluoroquinolones in many settings is thought to be responsible for the epidemic of fluoroquinolone resistant *C. Difficile* which is the most common cause of nosocomial diarrhea in north America. In Botswana, there is a significant amount of E. Coli resistant to amoxicillin and cotrimoxazole. This should have a bearing on how we manage suspected UTI in our setting

OUTREACH IN THE COMING MONTHS

Tsabong
(1st Tues of Month)
Jan None
Feb 4th
Mar 4th
Apr 8th

Hukunsti
(2nd Tues of Month)
Jan None
Feb 11th
Mar 11th
Apr 15th

Ghanzi
(3rd Tues of the month)
Jan 21th
Feb 18th
Mar 18th
Apr 22th

***BLH**
(1/2 Thurs of the month)
Jan 9th
Feb 13th
Mar 6th
Apr 3rd

***Mochudi**
(2/3 Weds of the month)
Jan 14th
Feb 12th
Mar 26th
Apr 23rd

***Thamaga**
(3/4)Thurs of the month)
Jan 15th
Feb 20th
Mar 27th
Apr 24th

Kanye 1 (1st Fri of the month)
Jan 10th
Feb 14th
Mar 7th
Apr 4th

***Kanye 2** (3/4 Fri of the month)
Jan 17th
Feb 21th
Mar 28th
Apr 25th

***Good Hope**
(1st Wed of the month)
Jan 8th
Feb 5th
Mar 5th
Apr 2nd

***Mahalapye**

Jan 14th
Feb 18th
Mar 19th
Apr TBC

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