

Antibiotics: The Newer the Better?

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A noticeable surge of new antibiotics has entered the market in the last 17 years. These new drugs are higher priced and typically have a broad spectrum of activity. However, for several common and important infections, the older, established antibiotics remain the drugs of choice.

Group A streptococcal infections

A good example of how older antibiotics are still the drugs of choice is the use of penicillin in the treatment of infections caused by Group A β -hemolytic *Streptococcus pyogenes* (GAS). Penicillin remains the treatment of choice for this infection because of its proven efficacy in the prevention of rheumatic fever, safety, narrow spectrum and low cost. To date, there has been no documentation of any penicillin-resistant Group A streptococci.

Hospitalized patients who have severe GAS infections may be treated with penicillin G, two to four million units intravenously (IV), every four to six hours. Clindamycin should only be added if there is a high suspicion of necrotizing fasciitis/myositis (Table 1).

For outpatient therapy of confirmed Group A streptococcal pharyngitis, penicillin V, 600 mg, twice daily, offers a convenient dosing regimen for adults and adolescents. The prevention of acute rheumatic fever is believed to require eradication of the infecting streptococcus from the pharynx,

Jessica's case

- Jessica, 42, presents with diffuse erythema, swelling and pain across her forehead, scalp and malar areas.
- Inflammation began two days prior, after she sustained a small burn on her forehead from a curling iron.
- She has shaking chills, headache, nausea, vomiting and fever (39.2 C).
- The involved area is intensely erythematous, warm and has become increasingly tender in the last 24 hours.
- Localized lymphadenopathy is also noted.
- She has no known drug allergies.
- Admitting lab data are as follows:
 - White blood cell: $21.5 \times 10^9/L$ with a neutrophilia of $17.9 \times 10^9/L$
 - Hemoglobin: 140 G/L
 - Creatinine: Normal



A swab of the burn lesion on the forehead is obtained along with blood cultures. To provide bacterial coverage for streptococci and staphylococci as the usual etiologic organisms, cefazolin, 1 g, intravenously, every eight hours, is initiated.

For more on Jessica, go to page 81.

Cover photograph: Penicillin (Firstlight Images®)

Table 1

Signs of necrotizing fasciitis

- Fever and excruciating pain
- Normal or elevated white blood cell count with a left shift
- Unexplained tachycardia
- Elevated creatine phosphokinase

which has traditionally called for a 10-day course of penicillin therapy.

Cephalexin, a first-generation oral cephalosporin, is an acceptable alternative in the penicillin-allergic patient whose allergy is not of the immediate type.

In true penicillin-allergic patients, erythromycin is the therapy of choice. The newer macrolides (azithromycin, clarithromycin) appear to be effective, but these agents are more expensive than erythromycin. The potential ecologic effects of using broader-spectrum agents to treat such a common bacterial infection are of concern.



Pyelonephritis

Older antibiotics are ideal agents for the treatment of uncomplicated pyelonephritis.

Seriously ill patients, or those with significant nausea and vomiting, require parenteral therapy. Those presenting from the community can be empirically treated with gentamicin, dosed once a day, using 4 mg/kg to 7 mg/kg ideal body weight while awaiting culture results.

Once-daily, intravenous gentamicin therapy provides convenient dosing and maximizes the concen-

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tration-dependent killing effect of the drug. Three to four days of initial treatment with gentamicin is safe without monitoring drug levels in patients with normal renal function [estimated glomerular filtration rate (GFR) > 50 mL/min]. This timeframe allows for pathogen identification to direct the step-down to an appropriate oral agent.

Ampicillin can be added empirically to gentamicin if the patient has complicating factors. For example, Group B streptococci have been implicated in patients with diabetes and in pregnant women.

After a clinical response and defervescence occurs, the results of cultures will provide guidance

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for a step-down to oral therapy to complete a 10- to 14-day course of therapy. Used since the 1970s, trimethoprim-sulfamethoxazole (TMP/SMX), one double-strength tablet, twice daily, remains a drug of choice for oral step-down, if local susceptibility and allergy status allows.



Cellulitis

Cellulitis is an acute spreading infection that involves the epidermis, dermis and upper subcutaneous tissue. Group A streptococcus and *Staphylococcus aureus* (*S. aureus*) are the most common etiologic agents.

The first-generation parenteral cephalosporin cefazolin is a sound empiric choice and has activity versus both of the major associated pathogens. The use of either cloxacillin or penicillin G, if the pathogen is identified, provides focused therapy for moderate cellulitis that requires parenteral therapy.

A switch to oral therapy (*i.e.*, cephalexin) if the

pathogen is not identified, or to cloxacillin or penicillin V if the pathogen is known, may be made after the fever decreases and the erythema begins to resolve. If the cellulitis is mild and no significant co-morbidities are present, initial therapy with oral agents is suitable.

Cellulitis in the setting of a diabetic foot infection may involve a wider spectrum of potential pathogens and warrants broader antimicrobial coverage. Anaerobic coverage is based on clinical suspicion (*i.e.*, the presence of necrotic tissue or a foul odour) and the severity of the infection. The older first—and second—generation cephalosporins are still reliably useful for these infections. For example, mild infections can be treated with cefotetan, 1 g, IV, every 12 hours, or a combination of cefazolin, 1 g, IV, every eight hours, plus metronidazole, 500 mg, orally, twice daily. If renal function permits (*i.e.*, GFR > 50 mL/min), another alternative is gentamicin plus clindamycin, 600 mg, IV, every eight hours. Oral options include TMP/SMX, one

More on Jessica's

By the second day of therapy, the involved area is less erythematous and it is not as warm or tender on exam. The blood cultures are negative, but the swab reveals Group A streptococcus.

With the culture report available, her antibiotic therapy is changed to penicillin G sodium 2 million units, intravenously, every six hours.

By day four, the cellulitis is resolving further and the systemic symptoms are considerably improved. Jessica is discharged on oral penicillin VK, 300 mg, four times a day for seven days to, complete 10 days of total therapy.

Obtaining an antibiotic history for patients with pneumonia is important to agent selection.

to two double-strength tablets, orally, twice daily, or cephalexin, 500 mg, orally, four times daily, plus metronidazole, 500 mg, orally, twice daily.

Osteomyelitis

Osteomyelitis can be hematogenous or contiguous to a soft tissue infection. In hematogenous osteomyelitis, the etiologic organism is typically *S. aureus*, whereas a contiguous infection is usually polymicrobial.

Adults usually have vague symptoms with non-specific pain around the affected site and may have an absence of systemic signs and symptoms. The diagno-

sis of osteomyelitis is first suspected on clinical grounds and confirmed via radiologic and microbiologic tests.

The identification of an etiologic micro-organism is crucial to optimize antibiotic therapy. Organism identification is best accomplished by surgical sampling or by radiologist-guided needle aspiration to obtain tissues for pathology and microbiology.

For patients with osteomyelitis, cefazolin and cloxacillin (IV) are useful empiric choices because of their low toxicity profile and their spectrum of activity against staphylococci and other bacteria that can cause osteomyelitis.

Pneumonia

Guidelines have been developed by the American Thoracic Society, the Infectious Diseases Society of America and the Canadian Infectious Disease Society. For an outpatient who has no modifying factors, such as chronic obstructive lung disease, and for whom no clear distinction between pneumococcal or mycoplasma-chlamydia pneumonia can be made, both types should be covered. Obtaining an antibiotic history for patients with pneumonia is important to agent selection and to avoiding treatment with a specific class (beta-lactam, macrolide) if the patient was previously or repeatedly treated with that class.

Doxycycline is a reasonable and inexpensive choice for some cases of community-acquired pneumonia. Treatment with doxycycline should suffice to cover pneumococci, mycoplasma and chlamydia, the most likely pathogens in low-risk patients who lack specific co-morbidities. Doxycycline remains effective against ampicillin-resistant strains of *Haemophilus influenzae*, as well as against beta-lactamase-producing strains of *Moraxella catarrhalis*.

Clinicians are encouraged to consult regional data on rates of drug-resistant *Streptococcus pneumoniae* to support the role of this antibiotic. In this manner, doxycycline has been named in the list of first-line therapy in some Canadian regions for nursing-home acquired pneumonia.

Because of the long half-life and large volume of distribution of doxycycline, it is important to prescribe a loading dose of 200 mg on day one, followed by 100 mg, orally, daily. Since doxycycline can cause esophagitis, the patient should be instructed to take the drug during the day with a full glass of water.



Community-acquired intra-abdominal sepsis

These infections are typically polymicrobial. At a minimum, an empiric antimicrobial regimen for this type of infection must have activity against *Escherichia coli* and *Bacteroides fragilis*. This is the rationale for using

gentamicin and metronidazole in combination. Etronidazole can be reliably and conveniently dosed twice a day and its

high oral bioavailability makes intravenous use the exception.

Once-daily dosing of gentamicin may be used for gram-negative coverage. It is particularly important to calculate an estimate of renal function (*i.e.*, GFR, creatinine clearance) for older patients; technologic resources have simplified this task. If aminoglycoside treatment is required for more than five days, it is prudent to monitor drug levels and renal function.



Methicillin-resistant Staphylococcus aureus

Increases in community-acquired methicillin-resistant *Staphylococcus aureus* infections are currently being identified in various sub-populations in Canada. As a rule, parenteral vancomycin should be reserved for moderate to severe infections that require parenteral therapy. However, both the older sulfonamide and tetracycline classes of drugs are resurfacing as useful agents for this pathogen.

For example, TMP/SMX or doxycycline may be the only options for patients who may not be suitable candidates for a home parenteral program or hospitalization. Also, these drugs provide convenient therapy for those with mild infections or for those who can be stepped down to oral therapy. These alternative drug classes also relieve the selective pressure of using a glycopeptide in an era of concern regarding vancomycin resistance.



In summary...

Don't retire the older antibiotics just yet—they still work and they are reasonably priced. In many settings, it is not necessary to treat patients with newer, more expensive agents. The older antibiotics have established safety profiles and have proven efficacy in many settings. **Dx**

Additional references and resources available—contact *The Canadian Journal of Diagnosis* at **diagnosis@sta.ca**.