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Inside this Issue

What will the 2001/02 influenza season bring?

Allison McGeer, MD, FRCPC

For the three influenza seasons from 1997/8 to 1999/2000, a particularly virulent strain of influenza known as A/H3N2/Sydney/05/97 was the most common cause of influenza in Canada. As expected, this strain burnt itself out, and, in the 2000/1 season, infections were due predominantly to A/H1N1/NewCaledonia and B/Yamanashi. These viruses are less virulent than A/H3N2 viruses, and there was less influenza and less severe influenza across Canada last year. The relatively quiet influenza year made it difficult to assess the impact of Ontario's universal vaccination program. There is, however, evidence that the program was successful.

Preliminary data suggest that nearly 45% of Ontario residents were vaccinated. Indicative of a quiet flu season, the number of nursing home outbreaks in BC decreased from 47 in the 99/00 season, to 16 in the 00/01 season. In Ontario, by contrast, the number of all institutional outbreaks decreased from 341 in 99/00 to 9 in 00/01. In addition, Ontario had a nearly two-fold margin decrease in reported viral isolates: for the last several years, Ontario laboratories contributed about 40% of isolates to the national surveillance system: last year, we contributed only 20%.

Predicting influenza seasons is a dangerous occupation. The threat of pandemic influenza is always present, and the pandemic may occur at any time. However, the indications so far this year are that influenza will be primarily due to A/Panama/2007/99(H3N2) or to influenza B. The good news is that all of the viruses identified so far are highly related to vaccine strains, so the vaccine should provide good protection. However, A/Panama is related to A/Sydney, so that this year's season may not be quite as quiet as last year's. There is no indication yet that the season has started, so it is not too late to be encouraging patients to be vaccinated.

Failures of Levofloxacin Treatment for Pneumococcal Pneumonia

Donald E. Low, MD, FRCPC

The emergence of *S. pneumoniae* resistant to the ß-lactam and macrolide antimicrobials has raised concerns regarding the use of these agents for the empiric treatment of community-acquired pneumonia (CAP)[1]. Fluoroquinolones, with increased activity against *S. pneumoniae,* such as levofloxacin, moxifloxacin, and gatifloxacin, are now being recommended and used for the treatment of patients with CAP who are at risk for infection due to multidrug-resistant strains[1-6]. However, there has been relatively little experience with the use of these agents as monotherapy for CAP as compared to the ß-lactam and macrolide antibiotics. We report four cases of pneumococcal pneumonia, treated empirically with oral levofloxacin, that failed therapy. All cases were associated with the isolation of an organism that was either resistant to levofloxacin prior to therapy or which had acquired resistance during therapy.

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So What's a Family Physician to Do?

Practical Strategies for Minimizing Unnecessary Antibiotic Use In the Management of Coughs, Colds and Sore Throats

Warren McIsaac, MD, CCFP

With winter fast approaching, most family doctors are bracing for the increased number of office visits from persons suffering with coughs, colds and sore throats. For the average adult, the worried parent and the physician the question is frequently the same - is an antibiotic needed?

Pharyngitis, bronchitis and upper respiratory tract infections (URI) account for 30 - 32% of all antibiotic prescriptions to children and adults[1,2].

Condition	Prescribing Rate
URI	46% - 53%
Acute Bronchitis	66% - 72%
Pharyngitis	71% - 76%

One of the reasons that prescribing rates are at this level is diagnostic uncertainty as to which patients have conditions requiring antibiotic treatment such as a strep throat or pneumonia. Is there any new evidence-based information to help guide family physicians in clinical decision making about the need for antibiotics?

A. Pharyngitis and URI with Sore Throat :

Two recent studies completed in family practice settings in Ontario[3,4] have validated a method termed the *Sore Throat Score Approach* for decisions about antibiotics in children and adults with a sore throat. In such patients, ask yourself:

1. Is this an uncomplicated infection?

Complete your normal clinical assessment to rule out serious, but thankfully rare, complications like epiglottitis or retropharyngeal abscess. Most times you will conclude the situation is uncomplicated.

2. Treat as appropriate if sinusitis, adenitis or otitis media

[See Additional Readings]:

However, many patients will not have these conditions and you will be left with a person who has a *sore throat* and various accompanying respiratory tract symptoms. The only indication for antibiotics in these other patients is a group A streptococcal throat infection.

Before making your decision about antibiotics for the rest, see where they fit in the following *Sore Throat Score* in terms of their risk for a group A streptococcal infection :

Only 10 – 20% of patients with a complaint of sore throat in Family Practice are found to have group A streptococcal infection. A recent study found prescribing rates remain stubbornly high at 73%[5].

The 'Sore Throat Score' has been shown to be accurate and reliable in family practice offices.

Criteria	Points
Temperature > 38° C	1
No cough	1
Tender, anterior cervical notes	1
Tonsil swelling or exudate	1
Age < 15	1
Age 45 or older	-1

Score Total	Chance of 'Strep' Infection in General Practice (%)	Suggested Management
0 or less	0 - 3%	No culture or antibiotic
1	4 – 10%	Required
2	10 – 19%	Culture all; treat only if
3	24 – 40%	culture positive
4 or more	43 - 60%	Treat with penicillin on clinical grounds*

** If patient has high fever or clinically unwell and early in disease course. Otherwise a culture is appropriate. Use erythromycin if penicillin allergy.*

Following this approach could reduce unnecessary antibiotic use by more than 60% in the management of patients with a sore throat [4].

B. Lower Respiratory Tract Infections and Acute Bronchitis:

1. Is there any evidence for pneumonia?

Only about 5% of adults presenting to physicians with a lower respiratory tract infection have pneumonia, but it can be difficult to predict using history and physical.[6] Clinical criteria that increase the likelihood of pneumonia include more than 1 of compatible symptoms, abnormal vital signs, and focal lung findings[6]. However, physician judgement that an x-ray is not warranted was the most accurate in ruling out pneumonia in 1 study. Only 2% of patients will have pneumonia when physicians feel an x-ray is not warranted. If there is evidence of pneumonia, consider an x-ray and treat as appropriate. If NOT, the patient has an uncomplicated lower respiratory tract infection or acute bronchitis .

2. Do antibiotics improve outcomes in 'Acute Bronchitis'?

Meta-analyses of randomized studies of the effectiveness of antibiotics in acute bronchitis find minimal benefit[7]. While some people were less likely to feel better after a week when they were not prescribed antibiotics, 85% of patients treated with placebo reported they felt well by 7 days.

We recently collected information from the offices of family physicians from across Canada in 407 cases of adults with cough or acute bronchitis:

- *in 58% of cases, an antibiotic was prescribed, but this increased to 79% when the physician diagnosis was acute bronchitis.*

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- *76% of patients reported they felt well within 7 days of seeing their doctor if they received antibiotics. 79% of the group not receiving antibiotics also felt well.*
- *90-95% of such patients not treated with antibiotics reported they had returned to work or their normal activities.*
- *it didn't matter if adults were less than 65 years old or older, or how long they had been sick, the findings were the same.*
- *patients who reported pain in their chest when they coughed were less likely to feel well by 7 days, but this was not improved with antibiotics.*

But people expect an antibiotic, right? Well actually, research shows that while many patients wonder if they need antibiotics, they also visit the doctor to make sure there is nothing seriously wrong, and don't necessarily expect an antibiotic.

WHAT CAN WE CONCLUDE FROM THE ABOVE?

- if your clinical assessment suggests pneumonia is unlikely, the chance of pneumonia is low. *If uncertain,* order an x-ray.
- For acute bronchitis, antibiotic prescribing rates are higher than is warranted given their limited benefit. In a large American study, there was no increase in subsequent office visits when physicians decreased their prescribing rate from 74% to 48%.
- Consider NOT prescribing to adults with normal vital signs and clear chests. You can confidently tell them 3/4 of people are feeling better within a week.

Conclusion:

Limiting antibiotic resistance means that a decrease in unnecessary antibiotic use is needed, but antibiotics remain a highly effective and necessary part of modern medical therapy. The above strategies may be helpful to you in talking to your patients about antibiotic treatment decisions in the coming winter.

References:

1. Nyquist AC et al. *JAMA* 1998; 279:875-877.
2. Gonzales R et al. *JAMA* 1997; 278:901-904.
3. McIsaac WJ et al. *CMAJ* 1998; 158:75-83.
4. McIsaac WJ et al. *CMAJ* 2000; 163:811-5.
5. Linder JA et al. *JAMA* 2001; 286:1181-1186.
6. Metlay JP et al. *JAMA* 1997; 278:1440-1445.
7. Smucny JJ et al. *J Fam Prac* 1998; 47:453-460.
8. Gonzales R et al. *JAMA* 1999; 281:1512-1519.

Additional Reading:

1. Canadian Paediatric Society Clinical Practice Guideline. Antibiotic management of acute otitis media. *Paediatr Child Health* 1998; 3:265-267.
2. Low DE, et al. A practical guide for the diagnosis and treatment of acute sinusitis. *Can Med Assoc J* 1997; (156 (suppl):S1-14.
3. Jadavji T et al. A practical guide for the diagnosis and treatment of pediatric pneumonia.*Can Med Assoc J* 1997; 156(suppl): S703-11.◆

Bioterrorism - Anthrax

Karen Green RN, CIC

There are numerous biological agents that could potentially be used as terrorist weapons including *Bacillus anthracis* (anthrax), smallpox, *Francisella tularensis* (tularemia), *Yersinia pestis* (plague) and botulinum toxin from *Clostridium botulinum.* Of these, anthrax is felt to be the most likely organism to be used for such purposes. Despite recent events in the US, anthrax remains difficult to weaponize.

Anthrax is a serious bacterial infection that occurs when *B. anthracis* spores enter the body through abrasions in the skin or by inhalation or ingestion. Most mammals, especially plant eating animals that graze for food (eg. cattle, goats, sheep, camels), can develop infection. Human infections result from contact with contaminated animals or animal products, and there are no known cases of human-to-human transmission. Human anthrax is not common. Prior to the intentional release of anthrax in the US, only 18 cases of inhalation anthrax had been reported in North America in the last century, the last case being in 1976. Cutaneous anthrax remains the most common form, is usually related to contact with contaminated animals or animal products and is usually curable when treated with antibiotics. Systemic infection resulting from inhalation of the organism (inhalation or pulmonary anthrax) has a high mortality rate, with death usually occurring within a few days after the onset of symptoms. When initiated early during the incubation period, antibiotics are very effective in treating anthrax. The rapid course of the disease once symptoms appear make early treatment an absolute necessity.

Symptoms of anthrax infection vary depending on the type of exposure to the spores and usually occur within 7 days of exposure.

Cutaneous anthrax: Most (about 95%) anthrax infections occur when the bacterium enters a cut or abrasion on the skin, such as when handling contaminated wool, hides, leather or hair products of infected animals. Skin infection begins as a raised itchy bump that resembles an insect bite but within 1-2 days develops into a vesicle and then a painless ulcer, usually 1-3 cm in diameter, with a characteristic black necrotic area in the center. Lymph glands close to the area may become swollen and painful. Death from cutaneous anthrax is rare when treated with appropriate antibiotics.

Inhalation anthrax: Initial symptoms may resemble a common cold. After an incubation period of up to six days, inhalation anthrax initially begins with the onset of muscle aches, malaise, fatigue, nonproductive cough, and fever. This phase lasts an average of four days. The second stage, lasting 24 hours and often culminating in death, develops suddenly with the onset of acute respiratory distress. Up to 50 per cent of cases develop meningitis. After several days, the symptoms may progress to severe breathing problems and shock. Inhalation anthrax is often fatal.

Intestinal anthrax: The intestinal disease form of anthrax may follow the ingestion of contaminated meat and is characterized by an acute inflammation of the intestinal tract. Initial signs of nausea, loss of appetite, vomiting, fever are followed by abdominal pain, vomiting of blood, and severe diarrhea. Intestinal anthrax causes death in 25% to 60% of cases.

References:

1. Anthrax as a Biological Weapon. *JAMA*. 1999;281:1735-1745
2. Anthrax, NEJM 1999; 34(ii);815-26

Websites with information on bioterrorism

www.bt.cdc.gov Centers for Disease Control and Prevention, Public Emergency Preparedness and Response Site

http://www.cdc.gov/ncidod/dbmd/diseaseinfo/anthrax_g.htm Centers for Disease Control and Prevention, General Disease information on Anthrax.

http://www.hc-sc.gc.ca/english/media/releases/2001/anthrax_info.htm
Information for the public on anthrax and suspicious mail

CASE REPORTS

PATIENT A. A 64-year-old male with no history of quinolone use. Clinical findings were compatible with a right-sided pneumonia. A sputum specimen showed gram-positive diplococci on Gram's stain and grew *S. pneumoniae* susceptible to levofloxacin. He was treated for CAP with oral levofloxacin 500 mg daily for 10 days. On the day following his last dose he developed signs and symptoms consistent with recurrent pneumonia. Sputum culture again grew *S. pneumoniae* that was now resistant to levofloxacin.

PATIENT B. A 37-year-old female with no history of quinolone use. A CXR revealed consolidation in the right middle lobe. A sputum specimen showed gram-positive diplococci on Gram's stain and grew *S. pneumoniae* susceptible to levofloxacin. She was treated with oral levofloxacin 500 mg daily. On day three of her treatment, she had not improved clinically and a repeat CXR demonstrated progression of her infiltrates. A repeat sputum specimen showed gram-positive diplococci on Gram's stain and grew *S. pneumoniae* that was now resistant to levofloxacin.

PATIENT C. A 66-year-old woman had a history of chronic obstructive lung disease and penicillin allergy. Eight days before admission she was started on ciprofloxacin 500 mg twice daily because of her respiratory symptoms. At admission she deteriorated clinically and was found to have pneumonia. Blood cultures grew *S. pneumoniae*. She was given oral levofloxacin 500 mg daily. Pleural fluid cultures obtained on the fourth hospital day grew *S. pneumoniae*. On the fifth hospital day, septic shock developed. She was intubated and transferred to the intensive care unit. She died the following day. Fluoroquinolone susceptibility testing was not performed at the time of admission since it was not part of the routine testing panel. Subsequent testing found the initial isolate to be resistant to levofloxacin.

PATIENT D. An 80-year-old woman with history of COPD presented to her doctor with signs and symptoms of an acute exacerbation of chronic bronchitis. She received ciprofloxacin 500 mg twice daily. After 6 days of therapy her symptoms had not improved. A CXR was compatible with pneumonia and she was put on oral levofloxacin 500 mg daily. After eight days of therapy she had not improved and was switched to a macrolide antibiotic. Sputum cultures grew *S. pneumoniae* that was resistant to levofloxacin.

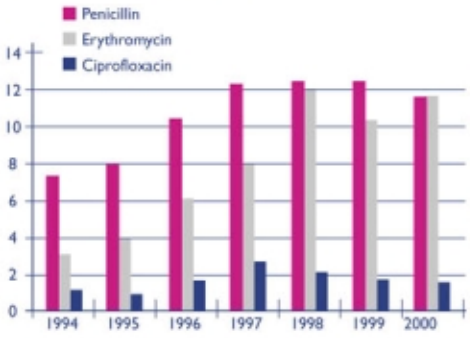
The isolates from each patient had the same pulse field gel electrophoresis pattern and serotype, but was different from the isolates from the other patients. All isolates were susceptible to penicillin and erythromycin.

These findings highlight several important issues regarding the use of fluoroquinolones with enhanced pneumococcal activity for the treatment of pneumococcal pneumonia. Unlike the ß-lactam, tetracycline, and macrolide antibiotics, in which pneumococcal resistance is usually the result of the acquisition of a resistance gene prior to therapy, reduced susceptibility or resistance to the fluoroquinolones may develop while on therapy. Consequently, this could adversely affect the pharmacodynamics of the drug. As the prevalence of pneumococci with first-step and second-step mutations increases, so does the likelihood that clinical failures could occur if susceptibility testing is not performed. A history of recent fluoroquinolone use should be a contraindication for the use of another quinolone for the empiric treatment of CAP. Finally, as the prevalence of fluoroquinolone resistance increases in pneumococci, other risk factors for infection with a resistant strain may have to be taken into consideration before prescribing one of these agents.[7]

References:

1. Bartlett JG et al. Clin Infect Dis 2000; 31(2):347-382.
2. Niederman MS et al. AM J Respir Crit Care Med 2001; 163(7):1730-1754.
3. Mandell LA et al. Clin Infect Dis 2000; 31(2):383-421.
4. Heffelfinger JD et al. Arch Intern Med 2000; 160(10):1399-1408.
5. File TM et al. Antimicrob Agents Chemother 1997: 41(9):1965-1972.
6. Petitpretz P et al. Chest 2001; 119(1):185-195.
7. Ho Pl et al. Clin Infect Dis 2001; 32(5): 701-7. ◆

Percentage of non-susceptible isolates of *S. pneumoniae*, Ontario, 1994-2000



Canadian Bacterial Surveillance Network

Other useful website links

http://www.gov.on.ca/health/english/program/pubhealth/flu_bul/flubul_mn.html

Ontario Ministry of Health weekly Influenza bulletins

http://www.hc-sc.gc.ca/pphb-dgspsp/fluwatch/

Health Canada's website for influenza surveillance

http://microbiology.mtsinai.on.ca

Antimicrobial resistance data, infectious disease topics and research, anthrax information at the Toronto Medical Laboratories/Mount Sinai Hospital Department of Microbiology website.

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