AMERICAN COLLEGE OF EMERGENCY PHYSICIANS
SCIENTIFIC ASSEMBLY
1999

Recent Updates: Infectious Disease Literature Review

How will the current literature related to infectious diseases affect your practice? The lecturer will critically review literature that addresses the most recent advances in the management of infectious diseases.

- Identify the most current trends and changes in the management of infectious diseases.
- Discuss the impact this will have on the practice of emergency medicine.

WE-131
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9:00 AM - 9:55 AM
Room # N250
Las Vegas Convention Center

FACULTY

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Recent Update: Infectious Disease Literature Review

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I. Course Description

A. The outcome for infected patients depends on a complex interaction between the patient, the environment, and the health care system. Patients suffer because they are exposed to infectious agents to which they are susceptible, causing a disease state which has both immediate and, perhaps, long term sequelae. The ultimate outcome can be impacted by the health care system through education to limit exposure, measures to decrease patient susceptibility, timely diagnosis of disease, and treatment (including antibiotic therapy). New knowledge of each component of this process can increase the emergency physician's ability to improve patient outcome.

B. Recent literature will be reviewed that can impact emergency medical care. Recently published information regarding the following topics will be discussed:

1. **Emerging infections**
2. **New exposure patterns**
3. **New patient susceptibilities**
4. **New diagnostic modalities**
5. **New antibiotics**
6. **New treatment considerations**
7. **New understandings of long term sequelae**
8. **New role of the patient**

II. Objectives

At the conclusion of this course, the participant will be able to: Describe emerging infections, new exposure patterns, changes in patient susceptibility, newly developed diagnostic modalities, new antibiotics, evolving insights into long term sequelae of specific infections and the increasing role of the patient in planning care. The participant will be able to apply this new information to the clinical practice of emergency medicine.

III. Course Outline

A. Emerging infections

1. E coli 0157:H7

This virulent strain of E coli produces a Shiga-like toxin and has led to many outbreaks including serious, and sometimes fatal, cases of

hemolytic-uremic syndrome (HUS). Spread can be via water supply, public pools, food, or personal contact. Antibiotics may be contraindicated in that they may lead to increased release of toxin from bacteria as they are destroyed. Treatment is supportive, including hemodialysis when indicated.

References

Gouveia S, Proctor ME, Lee MS, et al: Genomic comparisons and Shiga toxin production among *Escherichia coli* 0157:H7 isolates from a day care center outbreak and sporadic cases in southeastern Wisconsin, *Journal of Clinical Microbiology*, 1998;36:727-733.

Yukioka H, Kurita S: *Escherichia coli* 0157 infection disaster in Japan, 1996. European Journal of Emergency Medicine. 1997, 4:165.

Mahan BE, Griffin PM, Mead PS, Tauxe RV: Hemolytic uremic syndrome surveillance to monitor trends in infection with *Escherichia coli* 0157:H7 and other Shiga toxin-producing E. coli. *Emerging Infectious Diseases*.

2. Antibiotic resistant organisms

The extensive use of antibiotics, especially for outpatient treatment, has come under increasing scrutiny due, in part, to the increasing emergence of multi-drug resistant organisms.

a. ***Staphylococcus aureus*** resistant to methicillin and even, now, vancomycin.

Reference

Smith TL, et al: Emergence of Vancomycin resistance in staphylococcus aureus, *N Engl. J Med*, 1999; 340:493-501.

Herold BC, et al: Community-Acquired Methicillin-resistant staphylococcus aureus I children with no identified predisposing risk, *JAMA*, 1998;278:593-598.

Staphylococcus aureus with reduced susceptibility to vancomycin-United States. MMWR *Morb Mortal Wkly Rep* 1997; 46:851.

Hiramatsu K, et al: Dissemination in Japanese hospitals of strains of staphylococcus aureus heterogeneously resistant to vancomycin. *Lancet*, 1997;340: 1670-1673.

b. Enterococci resistant to vancomycin (VRE)

Reference

McDonald LC, et al: Vancomycin resistant Enterococci outside the health care setting: prevalence sources, and public health implications, *Emerging Infectious Diseases*, 1998;3(3).

c. ***Campylobacter jejuni*** resistant to quinolones previously reported after foreign travel now being identified in the United States and thought to be caused by the use of fluoroquinolones in poultry.

Reference

Smith KE, et al: Quinolone-resistant campylobacter Jejuni infections in Minnesota, 1992-1998, *N Engl. J Med* 1999;340:1525-1532.

d. ***Streptococcus pneumoniae*** resistant to beta-lactams, macrolides, chloramphenicol and sulfonamides. Flouroquinolone resistance still rare.

Reference

Thornsberry C, Ogilvie PT, Holley HP Jr. Sahm DF In vitro activity of grepafloxacin and 25 other antimicrobial agents against Streptococcus pneumoniae: correlation with penicillin resistance. *Clinical Therapeutics.* 20(6): 1179-90, 1998 Nov-Dec.

Thornsberry C, Ogilvie P, Kahn J, Mauriz Y. Surveillance of antimicrobial resistance in Streptococcus pneumoniae, Haemophilus influenzae, and Moraxella catarrhalis in the United States in 1996-1997 respiratory season. The Laboratory Investigator Group. *Diagnostic Microbiology & Infectious Disease*. 29(4)249-57, 1997 Dec.

Thornsberry C, Burton PH, Vanderhoof BH. Activity of penicillin and three third-generation cephalosporins against US isolates of Streptococcus pneumoniae: a 1995 surveillance study. *Diagnostic Microbiology & Infectious Disease*. 25(2): 89-95, 1996 Jun.

Breiman RF, Butler JC, Tenover FC, Elliott JA, Facklam RR. Emergence of drug-resistant pneumococcal infections in the United States. *JAMA* 1994;271:1831-1835.

B. New Exposure Patterns

1. Behavior

a. Wine

Wine, and, to a lesser extent, other alcohol, can decrease the incidence of *helicobacter pylori* and other gastroenteric infections.

Reference

Brenner H, Rothenbacher D, Bode G, Adler G. Inverse graded relation between alcohol consumption and active infection with *Helicobacter pylori*. American Journal of Epidemiology. 149(6):571-6, 1999 Mar 15.

b. Travel leading to **hepatitis E**

Recently there has been an increase in the reported cases among US travelers and among expatriates from developed countries. Pregnant patients are particularly prone to fulminant hepatitis which is frequently fatal. There is no vaccine available and avoidance of contaminated water is the only known means of prevention.

References

Worm HC, et al: Sporadic Hepatitis E in Austria, N Engl J Med, 1998; 339, 1554-1555.

c. Animal Bites

1) Rabies

New recommendation for rabies prevention include "if anatomically feasible, the full dose of RIG should be thoroughly infiltrated in the area around and into the wounds." Also "post exposure prophylaxis can be considered for persons who were in the same room as the bat and who might be unaware that a bite or direct contact had occurred (e.g. a sleeping person awakens to find a bat in the room or an adult witnesses a bat in the room with a previously unattended child, mentally disabled person, or intoxicated person) and rabies can not be ruled out by testing the bat". Now, healthy domestic ferrets that bite people may be confined and observed for 10 days (instead of euthanized, as previously recommended).

References

Wilde H. Failure of Postexposure Treatment of Rabies in Children, *Clinical Infectious Diseases*, 1996;22:228-32.

Human Rabies Prevention, United States, 1999, January 8, 1999, 48:RR1. MMWR, *Morbidity and Mortality Weekly Report*.

John Pape W, et al: Risk for rabies transmission from encounters with bats, Colorado, 1977-1996, *Emerging Infectious Disease*, 5:3, May-June 1999.

Niezgoda M, Briggs DJ, Shaddock J, et al: Viral excretion in domestic ferrets (*Mustela putorius furo*) inoculated with a rabies isolate of raccoon origin. *Am J Vet Res*, 1998; 59:1-4.

2) Dog bites

While dog bites were thought, previously, to seldom be infected by pasteurella multocida (much more common in cats) recent data indicate that pasteurella species are present in up to 50% of infected dog bites.

Reference

Talan DA, et al: Bacteriologic analysis of infected dog and cat bites, N Engl J Med, 1999; 340, 85-92.

3) Macaque monkey exposure leading to **B-virus**
(*Herpes virus simiae, Cercopithecine herpesvirus 1*)

Increasing contact with macaque monkeys (especially rhesus monkeys used in HIV research) has led to an increase in exposure to this virulent organism that can cause fatal meningoencephalitis. All exposures need to be monitored closely, and strong consideration should be given to IV acyclovir for high risk exposures.

References

Anonymous: Fatal *Cercopithecine herpesvirus 1*(B virus) infection following a mucocutaneous exposure and interim recommendations for worker protection, *MMWR* 1998, 47:1073-1083.

Ostrorwski SR, et al: B-virus from pet macaque monkeys: an emerging threat in the United States? *Emerging Infectious Disease*, 1998, 4:117-21.

d. Body piercing

"Non-mainstream body modification" is associated with the transmission of both viral (including hepatitis B, hepatitis C, tetanus and, perhaps, HIV) as well as bacterial infection. In addition to Staphylococcus aureus and group A beta hemolytic streptococci, *pseudomonas aeruginosa* has resulted in several cases of disfiguring chondritis caused by piercing the upper pinna.

References

Tweeten SSM, Rickman LS, Infectious complications of body piercing, *Clinical Infectious Diseases*, 1998;26, 735-739.

Cetta F et al: Piercing and tattooing in patients with congenital heart disease: patient and physician perspectives. *Journal of Adolescent Health* 1999;24:160-62.

e. Biological warfare

Anthrax could potentially cause sufficient disease and death to cripple a city or region. While anthrax can present as a cutaneous or gastrointestinal disease, the method of spread in warfare is generally inhalational. Inhalational anthrax could lead to the sudden appearance of multiple cases of severe flu-like illness with a fulminant course and high mortality. Hemmorhagic mediastinitis and hemmorhagic thoracic lymphadnitis lead to a widened mediastinum on chest x-ray. Peripheral blood smear can reveal gram positive bacilli in the unspun specimen. Definitive diagnosis requires blood culture and thus may be delayed. Clinical diagnosis is likely to be made by alert emergency physicians who treat multiple, similar cases. Penicillin remains the drug of choice while ciprofloxicin and doxycycline are acceptable alternatives.

Reference

Inglesby TV: Anthrax as a biological weapon, *JAMA*, 1999; 281, 1735-1745.

2. Physician as vector

There has been increasing evidence in the medical as well as the lay press that physicians can serve as vectors in the spread of disease.

Reference

Dorsey ST, Cydulka RK, Emerman CL, Is handwashing teachable?: failure to improve handwashing behavior in an urban emergency department. *Academic Emerg Med*,1996;3(4),360-365.

Hannigan P, Shields JW: Handwashing and use of examination gloves, *Lancet*, 1998;351-571.

C. New patient susceptibility

1. Hepatitis A vaccine

Safe and effective

Reference

Lemon SM, Thomas DL: Vaccines to prevent viral hepatitis, *N Engl J Med*, 1997;336;196-204.

2. Lyme disease vaccine

Administered at time 0, 1 month and 12 months. Efficacy during the first season is 49% and during the second season is 76%.

References

SigalLH et al. A vaccine consisting of recombinant *Borrelia burgdorferi* outer-surface protein A to prevent Lyme disease. *N Engl J Med* 1998:339(8):571.

Steere AC, et al. Vaccination against Lyme disease with recombinant *Borrelia burgdorferi* outer-surface lipoprotein A with adjuvant. *N Engl J Med* 1998:339(4);209-215.

Grabenstein JD. Lyme disease: geography predicts risk. *Journal of the American Pharmaceutical Association*. 39(1): 86-91, 1999 Jan-Feb.

3. Pneumococcal vaccine

New heptavalent vaccine tested on 37,000 children. Efficacy 100% (CI 75.7-100%).

Reference

Black et al: Northern California Keisser Permanente Efficacy Trial, ICAAC, Sept 24-27, 1998.

D. New diagnostic modalities

Polymerase chain reaction (PCR) is a potentially rapid, specific and very sensitive test for viruses (including herpes virus, hepatitis C virus, HIV and rabies) as well as bacteria and parasites (including *Chlamydia trachomatis, Clostridium difficile, Mycobacterium tuberculosis, Mycoplasma pneumonia, Borrelia burgdorferi, Trichomonas vaginalis, and Pneumocystis carinii*).

Reference

Ronai Z, Yakubovskaya M: PCR in clinical diagnosis, *Journal of Clinical Laboratory Analysis*, 1995; 9:269-283.

E. New antimicrobials

1. General principles

New antibiotics replace established treatment when an improved "PPD" (prescription resistance, patient resistance, drug resistance) profile is

demonstrated.

Reference

Bosker G, Antibiotic update 1998: outcome-effective treatment guidelines from bacterial infections managed in the primary care and emergency department settings, *Emergency Medicine Reports*, 1997;18;257-280.

2. Specific drugs

a. Carbapenems

1) Meropenem

This new carbapenem has enhanced gram-negative activity relative to imipenem-cilastatin and is often active against strains resistant to both third generation cephalosporins and imipenem-cilastatin. It may be useful for seriously ill patients with intra-abdominal central nervous system, lower respiratory tract, skin and soft tissue, urinary tract, and febrile neutropenic infections. Seizures are less likely than with imipenem/cilastatin.

Reference

Fish DN et al: Meropenem, a new carbapenem antibiotic, Pharmacotherapy, 1997; 17: 644-669**.**

2) L-796, 392

New variation of carbapenem that was well tolerated in animal safety studies and has significant invitro and invivo activities against methicillin and vancomycin resistant staphylococci and vancomycin resistant enterococci. Not yet available.

Reference

Rosen H, et al: Reduced Immunotoxicity and preservation of antibacterial activity in a releasable side-chain carbapenem antibiotic, *Science*, 1999;283:703-706.

b. Macrolides

Azithromycin and clarithromycin have largely replace erythromycin because of decreased gastrointestinal side effects and less frequent dosing (leading to better compliance) and enhanced activity against *H. influenzae*. Azithromycin offers the advantage of less frequent dosing, fewer drug-interactions, and availability in an IV preparation.

Reference

Piscitelli SC. Et at: Clarithromycin and azithromycin: new macrolide antibiotics, *Clin Pharm*, 1992; 11:137-152.

c. Fluoroquinolones

The new, extended spectrum, quinolones include levofloxacin, grepafloxacin and sparfloxacin. These have improved activity against gram-positive organism including *S. pneumoniae.*

Sparfloxacin has been associated with significant risk of phototoxicity and moderate prolongation of the QT interval. Trovafloxicin has been associated with liver damage and should be used only when the benefits of it's broader spectrum outweigh the risks.

References

Vincent J, et al: The pharmacokinetic effects of coadministration of morphine and trovafloxacin in healthy subjects. *Am J Surg*, 1998;176 (Suppl 6A):32S-38S.

Alghasham AA, Nahata MC. Trovafloxacin: a new fluoroquinolone. *Ann Pharm* 1999; 33:48-60.

Bosker G, Antibiotic update 1998: outcome effective treatment guidelines for bacterial infections managed in the primary care and emergency department settings, *Emergency Medicine Reports*, 1997; 18:257-280.

d. Streptogramins

Increasing drug resistance of gram positive organisms to antibiotics such as methicillin and vancomycin are kindling interest in the streptogramins.

References

Rubinstein, Keller: Future prospects and therapeutic potential of streptogramins. *Drugs* 1996;51(suppl. 1): 38-42.

Finch RG: Antibacterial activity of quinupristin/dalfopristin. *Drugs* 1996;51 (suppl 1): 31-37.

Jones ME, Visser MR, Klootwijk M, Heisig P, Verhoef J, Schmitz FJ. Comparative activities of clinafloxacin, grepafloxacin, levofloxacin, moxifloxacn, ofloxacin, sparfloxacin, and trovafloxacin and nonquinolones linozelid, quinupristin-dalfopristin, gentamicin, and vancomycin against clinical isolates of ciprofloxacin-resistant and susceptible. Staphylococcus aureus strains. *Antimicrobial Agents & Chemotherapy*. 43(2);421-3, 1999 Feb.

Messick CR. Woodward J, Pendland SL: Invitro activity of RPR 106972 alone and in combination with vancomycin, ampicillin, and gentamicin against multidrug-resistant enterococci. Diagnostic Microbiology & Infectious Disease. 32(2):95-9, 1998 Oct

F. New treatment considerations

1. Out patient management of pyelonephritis

Several infections that were once routinely treated in the hospital are now being treated in the outpatient setting. This is in an attempt to increase patient satisfaction, and decrease health care costs while assuring comparable medical outcome. Pyelonephritis is one of the disease entities that is now being frequently treated out of the hospital.

References

Mombelli: Oral vs intravenous ciprofloxacin in the initial empirical management of severe pyelonephritis or complicated urinary tract infections: a prospective randomized clinical trial. *Arch Intern Med*, 159(1), Jan. 11, 1999, pp. 53-58.

Nelson D et al. Management of febrile children with urinary tract infections. *Am J Emerg Med* 1998;16:643-647..

2. Treatment of upper respiratory tract infections in children

In an attempt to promote more judicious use of antimicrobial agents, and thereby decrease the development of drug resistance, the following recommendations have been put forth:

a. Otitis media

Uncomplicated acute otitis media in patients 2 years and older may be treated with a shortened (5-7 day) course of antimicrobials.

Otitis media with effusion

Fluid in the middle ear but the absence of signs or symptoms of acute infection may have antimicrobial treatment deferred.

b. Pharyngitis

Antimicrobial therapy should not be given unless group A streptococcal or other bacterial infection is diagnosed on the basis of laboratory tests in conjunction with clinical findings. Penicillin remains the drug of choice for group A streptococcal pharyngitis.

c. Acute sinusitis

Diagnosis requires prolonged (>10 days) non-specific symptoms (rhinosinusitis and cough without improvement) or more severe signs and symptoms (fever>39^{o} C, facial swelling or facial pain). The most narrow-spectrum agent that is active against the likely pathogen should be employed

d. Cough illness/bronchitis

Regardless of duration, non-specific cough illnesses rarely warrant antimicrobial treatment. *Mycoplasma pneumoniae* can cause prolonged cough (usually in children over 5 years of age). Treatment is a macrolide (or tetracycline for children 8 or more years of age).

e. Common cold

Antimicrobial agents are not indicated even when mucopurulent rhinitis is present (unless this symptom persists for more than 10-14 days).

Reference

Dowell, Scott F., Principles of judicious use of antimicrobial agents for pediatric upper respiratory tract infections, *Pediatrics,* 1998; 101(suppl): 163-184.

G. The role of the patient

For reasons ranging from increasing patient satisfaction, decreasing the cost of medical care and promoting public health, patients are being increasing involved in decisions regarding their care. They may be asked to deliver medication to their sexual partner to treat or prevent recurrent STD's. Patients are increasingly exposed to advertisements in the media for both non-prescription and prescription medications. Furthermore, it appears that social stress and social status influence susceptibility to infections in both non-human and human primates.

References

Kissinger P, et al: Effectiveness of patient-delivered partner medication for preventing recurrent *Chlamydia trachomatis. Sex Trans Inf* . 1998;74:331.

CohenS, Line S, et al: Chronic social stress, social status, and susceptibility to upper respiratory infections in nonhuman primates. *Psychosomatic Medicine*. 59(3):213-21, 1997, May-June.

Cohen S, Doyle WJ, et al: Social ties and susceptibility to the common cold. *JAMA*, 227(24):1940-4, 1997 Jun 25.

III. Summary

A. The Ten Commandments

I. Be aware of emerging infections
II. Don't prescribe unnecessary antibiotics
III. Beware drug resistant S.pneumoniae, S. aureus and Enterococci
IV. Respect travel and macaque monkey exposure
V. Beware of bats

VI. Consider out patient treatment of pyelonephritis
VII. Get a hepatitis A vaccination
VIII. Wash your hands
IX. Involve your patients in their care
X. Eat, drink and be merry

B. Where to look

1. Your desk:

Bosker, G: Antibiotic update 1998: outcome effective treatment guidelines for bacterial infections managed in the primary care and emergency department settings**.** ***Emergency Medicine Reports,*** 1997; 18(26), 257-280.

2. Your computer

CDC website http://www.cdc.gov/
Includes online *Emerging Infectious Disease* journal *MMWR*, down loadable slide presentations, etc.

3. Your pocket

The **Sanford** Guide to Antimicrobial Therapy, 1999 (29 ed.) Gilbert DN, Moellering RC, Sande MA, Vienna, VA

The 1999 Tarascon Pocket **Pharmacopoeia**, Loma Linda, CA