INFECTIOUS DISEASE

The four articles reviewed in this year's Update cover a range of subjects:

1. important new information regarding the effectiveness of hepatitis A vaccine for postexposure prophylaxis

2. the need to confirm antimicrobial susceptibility of group B streptococcus (GBS) isolates in pregnant women who are allergic to penicillin

3. a new guideline on administering antibiotic prophylaxis for cesarean delivery

4. a valuable overview of diverticulitis, a disease that we will all see with increasing regularity as the US population ages

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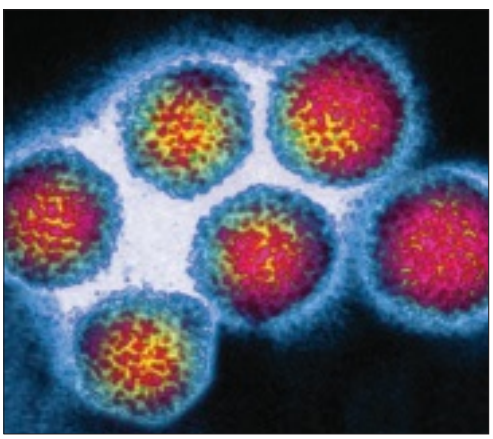
For most, the best hepatitis A post-exposure prophylaxis is vaccination

Victor JC, Monto AS, Surdina TY, et al. Hepatitis A vaccine versus immune globulin for postexposure prophylaxis. N Engl J Med. 2007;357:1685–1694.

The objective of this investigation, conducted in Almaty, Kazakhstan, was to compare the relative effectiveness of hepatitis A vaccine with that of immune globulin for prophylaxis after exposure to the hepatitis A virus. Participants were 2 to 40 years old and were household or day-care contacts of people who had hepatitis A. Five hundred sixty-eight susceptible patients received hepatitis A vaccine within 14 days of exposure; 522 susceptible patients received an age-appropriate dose of immune globulin. The primary endpoint was laboratory-confirmed, symptomatic hepatitis A within 15 to 56 days of exposure.

Symptomatic infection occurred in 25 of 568 (4.4%) vaccine recipients and 17 of 522 (3.3%) recipients of immune globulin. The relative risk of infection after the vaccine was 1.35 (95% confidence interval [CI], 0.70–2.67). No serious adverse effects occurred as the result of administration of either the vaccine or

FIGURE 1 Hepatitis A virus



Hepatitis A virus has single-stranded RNA, no envelope, and is approximately 27–30 nm in diameter.
JAMES CAVALLINI / PHOTO RESEARCHERS, INC.

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Hepatitis A is usually symptomatic, and the risk of perinatal transmission is low

Hepatitis A is caused by an RNA virus that is transmitted by fecal–oral contact. It is highly contagious and endemic in areas of the world where poverty, poor sanitation, and overcrowded living conditions prevail. Hepatitis A usually causes a symptomatic illness characterized by fever, malaise, anorexia, jaundice, acholic stools, darkened urine, and hepatic pain and tenderness. In poorly nourished or immunocompromised patients, severe morbidity and, rarely, mortality, may occur. Unlike other forms of hepatitis, hepatitis A does not cause a chronic carrier state, and perinatal transmission is extremely unlikely.

Best strategy? Prevention

At present, there is no specific antiviral therapy that is routinely used for treatment of hepatitis A. However, highly effective preventive measures are available. For preexposure prophylaxis, time permitting, the ideal agent is inactivated hepatitis A vaccine.[1]

The vaccine is usually given in two doses separated by 6 to 12 months and is highly immunogenic. In the United States, key candidates for vaccination are

- gay men
- residents and staff of chronic care facilities
- intravenous drug users
- individuals who live in areas where hepatitis A is endemic
- primate laboratory workers
- people 30 years of age and older who have chronic liver disease
- international travelers
- people who have received a liver transplant or are awaiting one.

The vaccine is safe for administration in pregnancy and is now recommended for children.

FAST TRACK

Immune globulin is preferred for postexposure prophylaxis in older or immunocompromised patients

immune globulin. The authors concluded that both agents provide effective postexposure prophylaxis against hepatitis A infection.

After exposure, vaccine trumps immune globulin in healthy patients

The standard agent for prophylaxis after exposure to the hepatitis A virus has been immune globulin 0.02 mL/kg, administered intramuscularly. Immune globulin is highly effective in this application and, in the present investigation, it was slightly more effective than the vaccine.

Despite the modest difference in effectiveness, however, hepatitis A vaccine offers several unique advantages for postexposure prophylaxis:

- It confers long-term immunity rather than just temporary protection.
- Because the volume of fluid injected is lower, the vaccine causes less pain upon administration.
- Immune globulin is now produced by a single manufacturer, and its supply has been limited. Its price also approaches that of the vaccine.
- Administration of immune globulin to a child may disrupt the normal childhood immunization schedule.

In older and immunocompromised patients, use immune globulin

For most patients, hepatitis A vaccine is the indicated method of postexposure immunoprophylaxis.

Because it is slightly more effective, however, immune globulin probably should remain the preferred agent for hepatitis A postexposure prophylaxis in older or immunocompromised patients who are more likely to develop severe illness if they become infected.

Reference

1. Duff B, Duff P. Hepatitis A vaccine: ready for prime time. Obstet Gynecol. 1998;91:468–471.

We're not following guidelines on GBS prophylaxis in penicillin allergy

Matheson KA, Lievense SP, Catanzaro B, Phipps MG. Intrapartum group B streptococci prophylaxis in patients reporting a penicillin allergy. Obstet Gynecol. 2008;111:356–364.

In this study, conducted at a single institution (Brown University), Matheson and colleagues sought to assess the adequacy of prophylaxis for GBS infection in women who had an allergy to penicillin. Specifically, the authors sought to determine how well practitioners at their institution adhered to the 2002 Centers for Disease Control and Prevention (CDC) guidelines, which specify that cefazolin should be used for prophylaxis in patients who are penicillin-allergic but not at high risk for anaphylaxis.[1] For patients at high risk for anaphylaxis, clindamycin may be used for prophylaxis if the organism is known to be susceptible. If susceptibility has not been documented, vancomycin should be administered.[1]

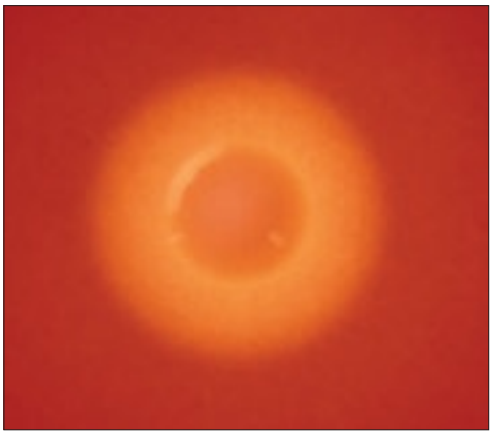
Overall, 95% of GBS-positive, penicillin-allergic patients received prophylaxis (95% CI, 91–97). However, only 15% of these women received appropriate prophylaxis as defined by the CDC (95% CI, 11–12). Clindamycin was administered to 83% of patients, but susceptibility testing was performed in only 11%. At the time of this study, 26% of all GBS isolates at Brown were resistant to clindamycin; 37% were resistant to erythromycin.

The authors concluded that adherence to CDC guidelines was clearly less than optimal. Even at 1 year after adoption of the guidelines, only 20% of patients received appropriate prophylaxis.

Type of allergic reaction is key to selection of prophylactic agent

GBS is uniformly sensitive to penicillin and ampicillin. It also is 100% sensitive to cefazolin, the preferred drug for intrapartum prophylaxis in penicillin-allergic women who have a low risk of anaphylactic reaction to penicillin.

FIGURE 2 Group B streptococcus



A clear zone of hemolysis on blood agar is a key characteristic of group B streptococcus.

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However, it probably is better to avoid cephalosporins in patients who report a previous anaphylactic reaction to penicillin or ampicillin, even though the risk of cross-reactivity between penicillin and cephalosporin is low. In such patients, possible alternatives include erythromycin, clindamycin, and vancomycin.

Erythromycin is no longer recommended

At the University of Florida, we reported that 21% of GBS strains were resistant to erythromycin.[2] At Brown University, Matheson and colleagues reported that 37% of GBS isolates were resistant to erythromycin. On the basis of similar reports, the CDC has concluded that erythromycin no longer should be used for GBS prophylaxis.

At our institution, we also have noted a disturbing trend of increased GBS resistance to clindamycin. In our recent report, 9% of GBS strains were resistant to this antibiotic. Similarly, Matheson and coworkers observed that 26% of GBS isolates in their center were resistant to clindamycin.

FAST TRACK

Increasing GBS resistance to clindamycin has been reported

CONTINUED

Proper GBS testing and prophylaxis are medicolegally prudent

Neonatal GBS infection is now one of the leading causes for malpractice suits in obstetrics. Key issues presented in these suits include:

- failure to screen
- failure to use the correct culture medium for screening
- failure to obtain test results in a timely manner
- failure to use the correct drug for prophylaxis.

In GBS-positive patients, practitioners should inquire about penicillin allergy and document the exact type of reaction experienced by the patient, if it is accurately known. If the reported reaction to penicillin was not life-threatening, patients should receive cefazolin, 2 g IV initially, then 1 g every 8 hours until delivery. If the reaction to penicillin was immediate and life-threatening, the patient should receive clindamycin, 900 mg IV every 8 hours, if the organism is confirmed to be susceptible. Susceptibility testing should be documented in the medical record.

If such testing is unavailable, vancomycin is the drug of choice.

FAST TRACK

CDC recommends that clindamycin be used for GBS prophylaxis only if antimicrobial susceptibility testing confirms that the organism is sensitive

Susceptibility testing is vital in penicillin-allergic women

Because of observations such as these, the CDC now recommends that clindamycin be used for GBS prophylaxis only if antimicrobial susceptibility tests have confirmed that the organism is sensitive. If susceptibility testing cannot easily be performed, practitioners should use intravenous (IV) vancomycin, 1 g every 12 hours, for prophylaxis. Potential side effects of vancomycin include allergic reactions, gastrointestinal irritation, ototoxicity, and nephrotoxicity. The latter two effects are extremely unlikely in patients who receive only one or two IV doses of the drug.

20% to 30% of gravidas are colonized with GBS

GBS is one of the two major causes of pneumonia, meningitis, and sepsis in both preterm and term newborns. Approximately 20% to 30% of women are colonized with the organism at some point during pregnancy. Universal screening for GBS at 35 to 37 weeks' gestation, combined with intrapartum antibiotic prophylaxis, has been highly effective in reducing the frequency of invasive GBS infection.

References

1. Schrag S, Gorwitz R, Fultz-Butts K, Schuchat A. Prevention of perinatal group B streptococcal disease. Revised guidelines from CDC. MMWR Recomm Rep. 2002;51:1–24.
2. Edwards RK, Clark P, Sistrom CL, Duff P. Intrapartum antibiotic prophylaxis 1: relative effects of recommended antibiotics on gram-negative pathogens. Obstet Gynecol. 2002;100:534–539.

New data suggest that preincision prophylaxis is best for C-section

Sullivan SA, Smith T, Chang E, Hulsey T, Vandorsten JP, Soper D. Administration of cefazolin prior to skin incision is superior to cefazolin at cord clamping in preventing postcesarean infectious morbidity: a randomized, controlled trial. Am J Obstet Gynecol. 2007;196:455.e1–455.e5.

Is preoperative antibiotic prophylaxis superior to intraoperative prophylaxis in preventing postcesarean infection? Sullivan and colleagues set out to answer this question in a prospective, randomized, double-blinded, placebo-controlled study at the Medical University of South Carolina.

In the study group, 175 women undergoing cesarean delivery were randomized to receive 1 g of IV cefazolin 15 to 60 minutes before surgery, followed by a placebo infusion immediately after the umbilical cord was clamped. In the control group, 182 women received preoperative placebo, followed by 1 g of cefazolin immediately after cord clamping.

Two patients in the study group developed endomyometritis, compared with 10 in the control group (relative risk [RR], 0.2; 95% CI, 0.15–0.94). Five patients in the study group developed a wound infection, compared with 10 in the control group (RR, 0.52; 95% CI, 0.18–1.5, not significant). Overall, eight women in the study group and 21 women in the control group met the criteria for infectious morbidity (RR, 0.4; 95% CI, 0.18–0.87).

There were no differences between the groups in the frequency of neonatal sepsis, neonatal intensive care unit (NICU) admission, total length of hospital stay, metabolic acidosis, or sepsis evaluation. Infants in the study group had significantly fewer days in the NICU ($P<.01$).

How this study differs from earlier investigations

The classic studies of antibiotic prophylaxis were performed in an animal model by Burke.[1] He demonstrated that prophylaxis had its greatest effect when the antibiotic was administered before the surgical incision. Essentially, no effect of prophylaxis was evident when antibiotic administration was delayed more than 4 hours beyond the start of surgery.

Early studies of antibiotic prophylaxis for cesarean delivery, conducted in the 1970s, administered antibiotics preoperatively and continued administration for several days after surgery. In 1979, Gordon and colleagues published an important investigation demonstrating that delay in administration of antibiotics until after the umbilical cord was clamped did not compromise the effectiveness of prophylaxis and significantly decreased the number of infants who required sepsis evaluations.[2] This latter effect presumably occurred because infants were not exposed to antibiotics before delivery. Gordon's investigation and subsequent reports also demonstrated that effective prophylaxis could be achieved with one to three doses of antibiotics.[3]

Why this new study may alter practice

Before Sullivan and colleagues published their findings, I believe that the best available evidence supported the use of a single dose of antibiotic, such as cefazolin, immediately after cord clamping. There are no convincing data that demonstrate an advantage for extended-spectrum agents (second- and third-generation cephalosporins, broad-spectrum penicillins, or carbapenems) over cefazolin.[3]

However, if the findings of Sullivan and coworkers are confirmed by other investigations in different patient populations, they definitely should lead to a change in the standard of care for prophylaxis. This investigation was exceptionally well designed and executed. The reduction in the frequency of endomyometritis and overall rate of infectious morbidity was impressive. This advantage was achieved without increasing the rate of neonatal sepsis evaluation.

References

1. Burke JF. The effective period of preventive antibiotic action in experimental incisions and dermal lesions. Surgery. 1961;50:161–168.
2. Gordon HR, Phelps D, Blanchard K. Prophylactic cesarean section antibiotics: maternal and neonatal morbidity before or after cord clamping. Obstet Gynecol. 1979;53:151–156.
3. Duff P. Prophylactic antibiotics for cesarean delivery: a simple cost-effective strategy for prevention of postoperative morbidity. Am J Obstet Gynecol. 1987;157:794–798.

DID YOU SEE IT?

Does a short course of nitrofurantoin cure acute uncomplicated cystitis?

› Sebastian Faro, MD, PhD

See Examining the Evidence (May 2008) in our archive at **www.obgmanagement.com**

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This early study suggests there is good reason to administer C-section antibiotic prophylaxis before the incision, instead of intraoperatively

CONTINUED

Expect to see more women with diverticulitis as the population ages

Jacobs DO. Diverticulitis. N Engl J Med. 2007;357:2057–2066.

FAST TRACK

Diverticulitis is present in 40% to 70% of people 80 years of age or older

ObGyns continue to play a major role in providing primary care to women. With the steady aging of the American population, practitioners certainly can expect to care for more and more women who are 50 years of age or older, and diverticulitis is likely to turn up in an increasing number of these patients.

Diverticulitis is a relatively common condition in older patients and must consistently be considered in the differential diagnosis of women with acute abdominal pain—particularly left-sided pain.

It is present in approximately 10% of adults younger than 40 years of age and in 40 to 70% of people 80 years of age or older. It primarily affects the sigmoid and descending colon and is associated with diets that are low in fiber and high in refined carbohydrates.

The condition probably results from stasis or obstruction in the narrow neck of a diverticulum, which, in turn, leads to an overgrowth of bacteria. The principal microorganisms isolated from affected patients are anaerobes, gram-negative aerobes, and some facultative gram-positive bacteria.

Range of severity can be wide

Presentation of diverticulitis may range in severity from mild to moderate lower abdominal pain associated with anorexia, nausea, and vomiting to abscess and fistula formation, colonic stricture, bowel obstruction, and peritonitis ("complicated diverticulitis"). Peritonitis may arise from rupture of a peridiverticular abscess or free rupture of an uninflamed diverticulum. Diverticulitis may be particularly severe in immunocompromised patients.

Classification of disease

The most accepted classification system for diverticulitis is the Hinchey system:

- in stage 1 disease, patients have small and confined pericolic or mesenteric abscesses
- in stage 2, the abscesses are larger but usually remain confined to the pelvis
- in stage 3, an abscess ruptures and causes purulent peritonitis
- stage 4 disease is distinguished by rupture of an uninflamed and unobstructed diverticulum (known as "free rupture"); this stage has the highest risk of adverse outcomes.

CT is best for diagnosis

The most useful diagnostic test for diverticulitis is a computed tomography (CT) scan. As a general rule, endoscopy should be avoided because of the risk of intestinal perforation.

Most patients can be treated as outpatients

Patients who have mild disease usually can be treated as outpatients. They should receive a 7- to 10-day course of oral antibiotics such as ciprofloxacin, 500 to 750 mg every 12 hours, plus metronidazole, 500 mg every 6 to 8 hours.

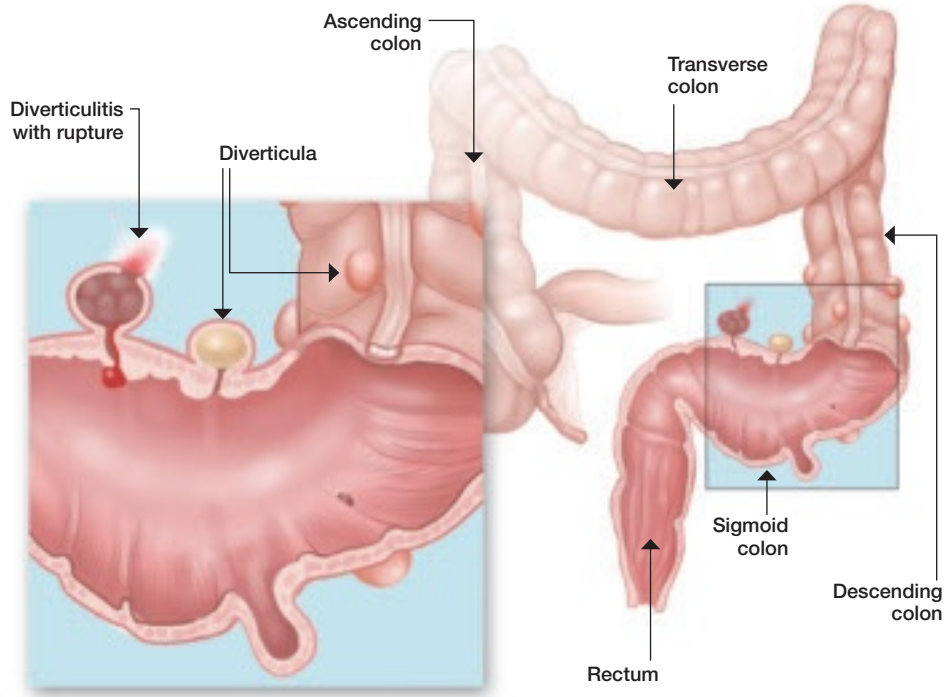
Alternate oral regimens include metronidazole, 500 mg every 6 to 8 hours, plus trimethoprim-sulfamethoxazole, double-strength, every 12 hours, or amoxicillin-clavulanate, 875 mg every 12 hours.

For seriously ill patients, hospitalization is warranted

Seriously ill patients—particularly those who are immunocompromised—should be hospitalized. If bowel obstruction is present, a nasogastric tube should be inserted. Appropriate IV antibiotic regimens for hospitalized patients include:

- metronidazole, 500 mg every 6 to 8 hours, plus ciprofloxacin, 400 mg every 12 hours
- metronidazole, 500 mg every 6 to 8 hours, plus ceftriaxone, 1 to 2 g every 24 hours

FIGURE 3 Consider diverticulitis in older women who complain of acute abdominal pain



Diverticulitis generally affects the sigmoid colon and descending colon and probably arises from stasis or obstruction in the narrow neck of a diverticulum, which leads to an overgrowth of bacteria and possible rupture.

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- ampicillin–sulbactam, 3 g every 6 hours
- piperacillin–tazobactam, 3.375 g every 6 hours
- ticarcillin–clavulanate, 3.1 g every 6 hours.

If an abscess is present and fails to respond promptly to medical therapy, drainage may be necessary. Some abscesses can be drained percutaneously under CT guidance. Large abscesses, in association with signs of generalized peritonitis, uncontrolled sepsis, or intestinal perforation, require surgical intervention, either via laparoscopy or open laparotomy. Preliminary data suggest that the laparoscopic approach may result in a shorter hospital stay, decreased postoperative pain, and an overall reduced rate of perioperative complication.

Diverticulitis may mimic appendicitis

The clinical presentation of diverticulitis is similar to that of appendicitis, except that the pain is usually on the left. Perforation, with resulting peritonitis, is an ever-present and potentially life-threatening complication. The dominant organisms are anaerobes and coliforms. The best diagnostic test is CT.

Patients in the early stages of disease can usually be treated as outpatients with antibiotics that are quite familiar to all ObGyns—i.e., metronidazole and a quinolone. More seriously ill patients should be hospitalized and treated with IV antibiotics and nasogastric suctioning.

Consultation with an interventional radiologist and general surgeon is recommended if operative intervention is necessary.

FAST TRACK

The clinical presentation of diverticulitis is similar to that of appendicitis