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Meanwhile, Back at the Farm . . .

ABSTRACTS & COMMENTARY

Synopsis: *Antibiotic-resistant Enterococcus faecium and Salmonella spp are widespread in meat obtained from US supermarkets. The high prevalence of resistance is the likely consequence of the practice of adding antimicrobials to animal feed.*

Sources: McDonald LC, et al. *N Engl J Med*. 2001;345:1155-1160; Sorensen TL, et al. *N Engl J Med*. 2001;345:1161-1166; White DG, et al. *N Engl J Med*. 2001;345:1147-1154.

Virginiamycin is a streptogramin antibiotic commonly used in animal feeds in the United States as a growth promoter. Because resistance to virginiamycin is associated with resistance to other streptogramins, widespread use of virginiamycin could lead to the development of quinupristin-dalfopristin resistance among the bacterial flora of farm animals. Resistance to the latter agent has been identified among turkeys fed virginiamycin.[1]

In order to assess potential human exposure to quinupristin-dalfopristin-resistant *Enterococcus faecium*, McDonald and colleagues undertook a multistate survey of chickens purchased in Georgia, Maryland, Minnesota, and Oregon. Using selective media, they sampled 407 chickens from 26 stores. In addition, they examined 334 human stool samples from specimens submitted to clinical laboratories for routine culture. A total of 58% of chicken carcasses yielded quinupristin-dalfopristin *E faecium*. Resistant isolates were identified in all 4 regions, ranging from a low of 17% in Minnesota to 87% in Oregon. Only 3 (1%) of the human stool specimens were positive for resistant *E faecium*.

In order to assess the ability of resistant *E faecium* to colonize the human intestinal tract, Sorensen and colleagues fed 10^7 CFU of 3 different strains of *E faecium* of animal origin to healthy volunteers in a randomized, double-blind study. One group received 2 strains resistant to glycopeptides, one group received a strain resistant to streptogramins, and a third group received a strain susceptible to both classes of agents. Stools were cultured on selective media on days 0 through 6, 14, and 35. All subjects receiving the test strains

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excreted resistant *E faecium* through day 6; stools were cleared of the test strains in all but 1 patient at day 14 and in all patients at day 35.

In the same issue of the *New England Journal of Medicine*, White and colleagues reported sampling of ground chicken, turkey, beef, and pork obtained from 3 supermarkets for *Salmonella*. Of 200 samples tested, 20% yielded *Salmonella*, representing 13 different serotypes. Eighty-four percent of isolates were resistant to at least 1 antimicrobial; 53% were resistant to 3 or more. Five isolates of *Salmonella enterica* serotype *agona* were resistant to 9 antimicrobials; 2 isolates of serotype *typhimurium* were resistant to 12 agents. Prevalence of resistance to selected agents is displayed in the table.

Table

Resistance to Selected Antimicrobials of Salmonella Isolates from Ground Meat

Agent	Resistant (n = 45)
Ampicillin	27%
Ceftriaxone	16%
Gentamicin	4%
TMP/SX	18%
Ciprofloxacin	0%

COMMENT BY ROBERT MUDER, MD

Antimicrobial resistance is widespread among bacterial isolates of agricultural animals, and the likely cause is the practice of adding antibiotics to animal feed in order to enhance growth. This is not a new phenomenon. For example, avoparcin, a glycopeptide similar in structure to vancomycin, was widely used as a growth promoter in Europe until 1997, when it was banned due to the widespread presence of vancomycin-resistant enterococci in farm animals.

The 3 articles presented here provide troubling evidence that resistant bacteria are developing as a result of agricultural practices and these bacteria are a potential threat to human health. In the United States, virginiamycin, a streptogramin antibiotic, is widely used in animal feeds. As a consequence, streptogramin resistance, and—in particular—quinupristin-dalfopristin resistance, appears to be widespread among *E faecium* strains isolated from poultry. Although streptogramin resistance among human stool isolates of *E faecium* is currently rare, the study of Sorensen et al demonstrates that ingestion of resistant *E faecium* in the amount likely to be encountered in food results in at least transient multiplication and carriage of the strain in the human intestine. Although carriage in healthy subjects lasted about a week, it should be noted that none of the volunteers had underlying conditions associated with prolonged carriage of resistant *E faecium*, such as coadministered antibiotics or abdominal surgery. Given the enormous reservoir of resistant enterococci that exists in the food supply, establishment of persistent colonization in susceptible humans seems likely.

The potential for widespread dissemination of quinupristin-dalfopristin resistance among human isolates of *E faecium* is of tremendous concern. Since many strains of nosocomially acquired *E faecium* are resistant to vancomycin, therapeutic options are limited. Spread of streptogramin resistance from animals into the human population would further diminish the number of potentially effective therapies.

White et al demonstrate that multiple antibiotic-resistant *Salmonella* are widely distributed in the food supply. Given that there are more than 1 million cases of salmonellosis occuring annually, and that at least 80% of these are food borne, this is a significant threat to public

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health. A number of strains are resistant to 3rd-generation cephalosporins; this is most likely due to the agricultural use of ceftiofur, a cephalosporin licensed for use in livestock. A plasmid-mediated beta-lactamase mediating resistance to both ceftiofur and ceftriaxone was identified among the *Salmonella* isolates studied. Ceftriaxone is considered by many to be the drug of choice in the treatment of salmonellosis in children; this agent may be "lost" if cephalosporin resistance increases among *Salmonella* isolates.

Each year in the United States, 25 million pounds of antimicrobials are given to animals for nontherapeutic purposes, primarily for growth promotion. In contrast, "only" 3 million pounds are given to humans.[2] Current agricultural practices clearly promote antibiotic resistance among the bacterial flora of farm animals. Spread of antimicrobial resistance from animals to humans can occur either through direct spread of resistant strains, or by transfer of resistance determinants from animal strains to human strains. One wonders about the ultimate effectiveness of our attempts to control the spread of resistant bacteria within hospitals when there appears to be an enormous reservoir of resistance in the food supply. Clearly, the nontherapeutic use of antimicrobials in agriculture must be curtailed. ❖

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Erythromycin and Infantile Hypertrophic Pyloric Stenosis

ABSTRACT & COMMENTARY

Synopsis: *A retrospective study of 14,876 newborns found that infants prescribed systemic erythromycin during the first 2 weeks of life had a significantly increased risk of developing infantile hypertrophic pyloric stenosis.*

Source: Mahon BE, Rosenman MB, Kleiman MB. *J Pediatr.* 2001;139:380-384.

A retrospective cohort study of 14,876 infants born from June 1993 through December 1999 found 43 (0.29%) developed infantile hypertrophic pyloric stenosis (IHPS). The highest risk was with systemic erythromycin use during the first 2 weeks of life, with a relative risk (RR) of 10.51 (95% CI, 4.48, 24.66). Prescriptions for longer treatment periods were associated with higher risk; 6 (3%) of the 201 infants with prescriptions for ≥ 14 days developed IHPS. Erythromycin ophthalmic ointment was not associated with an increased risk for IHPS. Only 6 infants received azithromycin, none of which developed IHPS. No infants were prescribed clarithromycin. Maternal macrolide antibiotics (erythromycin, azithromycin, or clarithromycin) administered within 10 weeks of delivery may have been associated with higher risk of IHPS (RR 1.47; 95% CI 0.7, 3.3).

COMMENT BY HAL B. JENSON, MD, FAAP

An association of erythromycin and IHPS was first reported in 1976 by SanFilippo.[1] In 1999, another report of a cluster of cases of IHPS among infants treated with erythromycin after exposure to pertussis found an absolute risk of IHPS of 4.5% among the 157 infants treated with erythromycin compared to no cases among 125 untreated control infants.[2] This new study confirms the association of erythromycin use during early infancy with IHPS. There is a plausible biologic basis for this association. Erythromycin is a motilin agonist and at doses used as an antibiotic can result in strong, nonprogagated contractions that may lead to hypertrophy of the pylorus.

Erythromycin (40-50 mg/kg/d in 4 divided doses for 14 days; maximum, 2 g/d) is the recommended drug in children for treatment of pertussis and prophylaxis following exposure to pertussis. Studies suggest that the newer drugs azithromycin (10-12 mg/kg/d orally in 1 dose) or clarithromycin (15-20 mg/kg/d orally in 2 divided doses; maximum, 1 g/d), may be effective in shorter courses of 5-7 days; however, their efficacy is unproven. The risk of IHPS after treatment with these drugs is unknown. Trimethoprim-sulfamethoxazole is another possible alternative, but its efficacy is also unproven. Since alternative therapies are not as well studied, the American Academy of Pediatrics continues to recommend erythromycin for treatment and prophylaxis of disease caused by *B pertussis*.

Erythromycin (50 mg/kg/d in 4 divided doses for 14 days) is also recommended in infants for treatment of *Chlamydia trachomatis* infection, which is the most common cause of afebrile pneumonia in early infancy and causes 20-30% of all pneumonia among hospitalized infants < 6 months of age. However, this usually has onset from 4-18 weeks of age (median, 9 weeks), apparently beyond the period of greatest risk for erythromycin-associated IHPS. The American Academy of Pediatrics continues to recommend erythromycin for treatment of *C trachomatis* infection in infants.

Despite the historically safe record of erythromycin, it should be used with prudence in early infancy. Physicians who prescribe erythromycin—and possibly other macrolides—to newborns and young infants should be aware of this association with IHPS and inform parents about the potential risks of developing IHPS and the signs of IHPS. Reports of IHPS associated with erythromycin can be reported to MedWatch, the Food and Drug Administration (FDA) Medical Products Reporting Program (by fax at 800-FDA-0178), or by using the interactive form on the MedWatch website (www.fda.gov/medwatch). ❖

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Yellow Fever Vaccine—Adverse Events

ABSTRACTS & COMMENTARY

Synopsis: *Yellow fever vaccine has been one of the most extensively used vaccines in the world during much of the 20th century. Recent evidence, however, indicates an increased risk of adverse events in the elderly.*

Sources: Martin M, et al. *Lancet*. 2001;358:98-104; Vasconcelos PFC, et al. *Lancet*. 2001;358:91-97; Chan RC, et al. *Lancet*. 2001;358:121-122.

While serious adverse events associated with yellow fever (YF) vaccination remain rare, several recent reports have raised concern. YF remains a serious risk in South America and Africa, and vaccination for persons at risk should be continued. However, physicians should be vigilant in detecting and reporting adverse events associated with YF vaccination, and the safety of the vaccine is being further evaluated.

Seven cases of serious adverse events in YF vaccinees were reported in the July 14, 2001, issue of the Lancet. Four cases occurred in the United States, and 1 in Australia following use of the 17D-204 vaccine. Two cases were reported from Brazil, following use of the 17DD vaccine.

In US and Australian patients, illness occurred 2-5 days after administration of the 17D-204 YF vaccine. All US patients were older than 62 years of age, and the Australian patient was 56 years old. All cases presented with fever and subsequently developed thrombocytopenia, lymphopenia, bandemia, significant hyperbilirubinemia, and hypotension. All patients developed renal failure, respiratory failure, or both. The vaccine strain of YF virus was isolated from the serum of 2 US patients and the cerebrospinal fluid of 1 US patient. One patient's liver biopsy, performed 28 days after vaccination, showed YF fever virus antigen by immunohistochemical assay. The Australian patient's serum samples as well as multiple organs showed the vaccine strain of YF virus.

The 2 Brazilian cases presented similarly with fevers, myalgia, and vomiting. Following immunization with the 17DD YF vaccine, the patients developed icterus, hemorrhage, and multi-organ involvement. In contrast to the other patients, the Brazilian patients were only 5 and 22 years old. None of the patients were known to be immunosuppressed at the time of vaccination. YF virus was isolated from blood and multiple organs in both patients.

COMMENT BY LIN H. CHEN, MD

Yellow fever virus is an enveloped, single-stranded RNA virus in the *Flaviviridae* family. The vectors are tree hole-breeding mosquitoes, which feed primarily on monkeys in the jungle, and *Aedes aegypti*, a domestic mosquito that thrives in urban settings. YF occurs only in sub-Saharan Africa and parts of South America. It has never occurred in Asia, the Indian subcontinent, the Middle East, and Australia, although the mosquito vector is present.

The incidence of YF is thought to be greater than 200,000 cases annually in Africa, with a case-fatality rate of 23%.[1] In comparison, the incidence in South America is estimated to be 1000-20,000 cases annually, with a case-fatality rate of 65%.[1] Epidemics in the 1990s, which occurred in Nigeria, Cameroon, Ghana, Liberia, Gabon, Senegal, Benin, and Kenya, have contributed to a resurgence of YF.[1,2]

Clinical presentation for YF is variable, ranging from an influenza-like illness to hemorrhagic fevers. Following the bite of an infected mosquito, the infection incubates for 3-6 days before fever develops. Patients then enter a "period of infection" in which they are viremic up to several days.[1] Symptoms during this period include fever, chills, malaise, headache, myalgia, nausea, and anorexia. Findings include toxic appearance, conjunctival congestion, pointed red tongue with a central white coating, relative bradycardia, leukopenia, and neutropenia. A "period of remission" follows and lasts 2-24 hours.[1] Some patients may recover at this point, but many go on to a "period of intoxication" where fever increases along with nausea, vomiting, abdominal pain, jaundice, renal failure, and hemorrhages.[1] A "terminal period" follows with death occurring on the 7th to 10th day of illness.[1]

A diagnosis of YF may be made by culturing the virus

from blood or serum during the first 4 days of symptoms.[1] Serologic studies with the enzyme-linked immunosorbent assay (ELISA), especially the IgM-capture immunoassay, can also establish a diagnosis. Postmortem diagnosis can be made by histopathology as well as immunocytochemical staining of liver tissue sections to detect YF antigen. Biopsy of the liver is, however, often precluded by the presence of a coagulopathy.

The YF vaccine has long been considered a safe vaccine, and it has been successful in controlling YF. Live attenuated vaccines were developed shortly after isolation of the YF virus in 1927, and the 17D vaccine has been in use since 1937. The 17D-204 and 17DD vaccines are substrains derived from the 17D strain. Approximately 300 million doses of the 17D YF vaccines have been administered in endemic areas, and approximately 8 million US travelers have been vaccinated since 1965.[3] The World Health Organization estimated that 54 million doses of the vaccine were administered in Brazil in the past 4 years, during which the 2 cases of serious adverse events were reported.[4]

Adverse events following administration of the 17D vaccines have been reported in the past, although most have been mild. These include fever, headache, backache, local reactions, and mild flu-like symptoms.[5] Encephalitis following vaccination has occurred rarely and primarily in very young infants, with an estimated incidence of 0.5-4/1000,[5] which is the reason the vaccine is generally not recommended for children younger than 9 months of age. Allergic reactions associated with the 17D vaccine have been reported, and the incidence is estimated at 5-20 per million doses.[5]

The reported rate for YF vaccine-associated serious illness appears to be higher in the elderly. The rate is estimated to be 3.5 per 100,000 among people 65-75 years old and 9.1 per 100,000 for people 75 or older.[6] However, the overall systemic adverse events are still rare at 2.4 per 100,000 doses in the United States.[6] The itinerary of each traveler should be carefully assessed for necessity of the vaccine. YF remains a serious threat to travelers going to endemic areas in Africa and South America, and vaccination should be continued for the travelers at risk.

VAERS report forms can be obtained by telephone (800-822-7967) or at http://www.vaers.org. Reports can be submitted by fax (877-721-0366), mail (P.O. Box 1100, Rockville, MD 20849-1100), or e-mail (info@vaers.org). The CDC will perform virologic and immunohistochemical studies on specimens available. ❖

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Pharmacology Update

Ribavirin Unbundled—New Flexibility in Treatment of HCV Infection

By William T. Elliott, MD, FACP, and James Chan, PharmD, PhD

The fda recently approved a "stand-alone package" of ribavirin capsules for the treatment of hepatitis C. Ribavirin is used in combination with interferon—either interferon alfa-2b or peginterferon alfa-2b. In 1998 the FDA approved a combination package of ribavirin and interferon alfa-2b that has been marketed under the trade name Rebetron. With the recent approval of a pegylated interferon alpha (PEG-Intron, Schering) and another on the way (Pegasys-Roche), ribavirin as a stand-alone product allows the flexibility to use these drugs in combination.

Indication

Ribavirin is indicated for use in combination with interferon alfa-2b (Intron A) for the treatment of chronic hepatitis C in adult patients with compensated liver disease previously untreated with alpha interferon or who have relapse after interferon therapy.[1] It is also indicated in combination with peginterferon alfa-2b (PEG-Intron) for the treatment of chronic hepatitis C in patients with compensated liver disease who are naïve to interferon alpha therapy.[2]

Dosage

The recommended dose of ribavirin with interferon alfa-2b is based on body weight. For patients < 75 kg the dose is 400 mg (2 × 200 mg) in the am and 600 mg (3 × 200 mg) in the pm. For patients > 75 kg, the dose is 600 mg (3 × 200 mg) in the am and pm. This is administered with 3 million IU of interferon alfa-2b (Intron A) 3 times weekly. In patients with a history of stable cardiovascular disease, a permanent dose reduction is needed if the hemoglobin decreases by 2 g/dL or greater during any 4-week period. Ribavirin should be discontinued if the hemoglobin remains below 12 g/dL after 4 weeks of a reduced dose. In patients with no cardiac history, the dose should be reduced to 600 mg daily (200 mg am and 400 mg pm) if hemoglobin falls below 10 g/dL and discontinued if it falls below 8.5 mg/dL.[1]

In combination with peginterferon (1.5 mg/kg/wk), the recommended dose is 800 mg in 2 divided doses (with breakfast and dinner). If hemoglobin drops below 10 mg/dL, but not below 8.5 mg/dL, the dose should be reduced by 200 mg/d.[2] In those with a history of stable cardiovascular disease, the dose of peginterferon should be reduced by half and the dose of ribavirin by 200 mg/d if the there is a > 2 g/dL decrease in hemoglobin in any 4-week period, and discontinued if Hgb is < 12 g/dL. Ribavirin should be discontinued if there is significant decrease in WBC, neutrophils, or platelets.[2]

Treatment is generally 24-48 weeks for treatment-naïve patients and 24 weeks for treatment-relapse patients.

Ribavirin is supplied as 200-mg capsules in packages of 84. The bottles should be stored at 25°C or 77°F.

Potential Advantages

The approval of the "stand alone" ribavirin provides more dosing flexibility in tailoring individualized therapy for those patients requiring dosage reduction as well as allowing use with peginterferon. In the clinical trials, about 26% of patients required modification in the dose of ribavirin. These included dose reduction or discontinuation. The combination package (Rebetron) contains a week's supply of ribavirin (35 or 42 capsules) and does not allow for the flexibility of dose reduction in patients with anemia associated with ribavirin therapy.

Potential Disadvantages

Ribavirin is not effective as monotherapy for hepatitis C. Hemolytic anemia, which occurs in about 10% of patients, is the primary adverse effect of ribavirin.[1] The drug can also potentiate the neutropenia induced by interferon alpha.[2] Ribavirin should not be used in pregnant patients or those with a creatinine clearance < 50 mg/min.

Comments

The combination of ribavirin and interferon alfa-2b has been approved for the treatment of patients who have relapsed following interferon alfa-2b therapy as well as those naïve to treatment. The combination has been reported to be more effective than interferon alone in both relapsing as well as naïve patients.[1,3,4,7] Ribavirin was recently approved for use in combination with peginterferon alfa-2b (PEG-intron) which is a conjugate of monomethoxy polyethylene glycol (PEG) with recombinant interferon alfa-2b. The pegylated interferon permits a more convenient once-weekly dosing. In interferon treatment-naïve patients, the combination of ribavirin (800 mg daily) plus peginterferon (1.5 µg/kg week) produced a better overall response (undetectable virus in the serum in 24 weeks) than ribavirin (1000 or 1200 mg) plus interferon 3 MIU 3 times a week (52% vs 46%, respectively). The difference was seen in genotype 1 hepatitis C compared to genotypes 2-6.[2,6] A recent report of a 24-week interim analysis suggests that ribavirin/peginterferon may be effective in patients who have previously failed on other interferon therapy.[5]

Clinical Implications

It is estimated that about 4 million Americans are chronically infected with hepatitis C and it is the leading reason for liver transplantation in this country. The combination of ribavirin and interferon is currently considered the standard of care. The approval of "stand alone" ribavirin permits its use with peginterferon and also allows for more flexibility in dosage modification due to adverse effects. As more data are published, peginterferon may become the standard interferon. Schering has agreed to conduct several postmarketing studies including the comparison of weight-adjusted doses of ribavirin with the currently approved fixed dose which is underway. Data suggest that body weight is an important predictor of response to interferon.[6] Rebetol is expected to be available in November and a combination PEG-Intron/Rebetol product is also pending. ❖

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Pharmacology Update

Cefditoren Pivoxil Tablets—A New Cephalosporin

By William T. Elliott, MD, FACP, and James Chan, PharmD, PhD

Cefditoren is a new semisynthetic "third/fourth generation" cephalosporin recently approved by the FDA. It has good antimicrobial activity against common pathogens of the respiratory tract such as *Streptococcus pneumoniae, Haemophilus influenzae,* and *Moraxella catarrhalis*. TAP Pharmaceuticals licensed cefditoren pivoxil from a Japanese pharmaceutical company. The drug has been in wide use in Japan for 7 years, where 41 million prescriptions have been dispensed. Cefditoren is marketed by TAP as Spectracef.

Indications

Cefditoren is indicated for use in adults or adolescents for the treatment of the following infections: acute bacterial exacerbation of chronic bronchitis caused by *H influenzae*, *Streptococcus parainfluenzae*, *S pneumoniae*, or *M catarrhalis*; pharyngitis/tonsillitis caused by *Streptococcus pyogenes*; uncomplicated skin and skin-structure infections caused by *Staphylococus aureus*, or *S pyogenes*.[1]

Dosage

The recommended dose for acute bacterial exacerbation of chronic bronchitis is 400 mg twice daily for 10 days. For pharyngitis/tonsillitis or uncomplicated skin and skin structure infections, the dose is 200 mg twice daily for 10 days. The drug should be taken with meals to improve absorption. It should not be taken with antacids, histamine-2 receptor antagonists, and, possibly proton pump inhibitors. No dose adjustment is required in patients with mild renal impairment or mild-to-moderate hepatic impairment.[1]

Potential Advantages

Cefditoren has demonstrated in vitro activity against intermediate and penicillin-resistant strains of *S pneumoniae* as well as beta lactam and macrolide resistant *S pyogenes*.[1-3]

Potential Disadvantages

Cefditoren, as with other cephalosporins, is not active against atypical respiratory pathogens such as *Chlamydia pneumonia*, *Mycoplasma pneumoniae*, and *Legionella pneumophilia*. It is not recommended for long-term use because pivalate-containing compounds have been associated with carnitine deficiency when used over a period of months. Patients with milk protein hypersensitivity should not take cefditoren because the tablets contain sodium caseinate.[1] The most frequent side effect is diarrhea (12-14%) and the primary reason for discontinuation of therapy is diarrhea or nausea. Approximately 2-3% of patients discontinue therapy because of intolerance.[1]

Comments

Cefditoren pivoxil is considered a "third/fourth" generation cephalosporin. It is administered as the prodrug (pivoxil ester) which is hydrolyzed by esterases after oral absorption. It has excellent in vitro activity against many respiratory tract pathogens such as *S pneumonia*, *H influenzae*, and *M catarrhalis*. It is not active against atypical respiratory pathogens, *Pseudomonas aeruginosa* or *B fragilis*. Data from clinical trials indicate that the efficacy and safety of cefditoren are comparable to other similar antibiotics in the treatment of acute exacerbation of chronic bronchitis, pharyngitis, sinusitis, and uncomplicated skin and skin structure infections.[4,5] Comparative antibiotics included penicillin VK for pharyngitis, cefuroxime or clarithromycin for acute exacerbation of chronic bronchitis, cefadroxil or cefuroxime for uncomplicated skin and skin structure infections, and amoxicillin/clavulanate for acute maxillary sinusitis.

Cefditoren is expected to be launched in December. Costs are not available at this time.

Clinical Implications

Cefditoren appears to be safe and efficacious for approved indications but does not appear to offer any clear clinical advantages over available agents. It is currently not approved for community-acquired pneumonia or sinusitis. Antibiotic resistance is regarded by several expert committees as a major public health threat. Misuse and overuse of antibiotics is considered a major driver.[7] Therefore, judicious use of cefditoren or any antibiotic is essential. ❖

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PS Form **3526**, September 1999 *(Reverse)*

CME Questions

35. Which one of the following statements regarding the 17D yellow fever vaccine is *false*?

a. The 17D yellow fever vaccine is a live-attenuated virus vaccine.
b. The 17D vaccine has been in use for more than 60 years.
c. The 17D yellow fever vaccine has commonly been associated with adult encephalitis.
d. The 17D vaccine is generally not recommended for children younger than 9 months of age.
e. Serious adverse events associated with the yellow fever vaccine should be reported.

36. Which one of the following is *not* true about ribavirin?

a. It is indicated for the treatment of hepatitis C only in combination with interferon.
b. Hemolytic anemia is the primary adverse reaction to the drug.
c. Data suggest that ribavirin/peg-interferon may have some benefits over ribavirin-interferon.
d. Treatment regimens are generally 12 weeks.

37. Which one of the following statements is correct?

a. The most uncommon side effect of cefditoren is diarrhea.
b. Patients with milk protein hypersensitivity should not take cefditoren as the tablets contain sodium caseinate.
c. Cefditoren should not be taken with meals.
d. Cefditoren is recommended for long-term use.
e. None of the above

38. Which one is recognized to be associated with infantile hypertrophic pyloric stenosis?

a. Maternal azithromycin during pregnancy
b. Any maternal macrolide during pregnancy
c. Erythromycin during the first 2 weeks of life
d. Any macrolide during the first 2 weeks of life

In Future Issues:

C difficile Continues to Confound Clinicians