AMERICAN HEALTH CONSULTANTS® A Medical Economics Company

Providing the Highest Quality Clinical Information for 19 Years

# INFECTIOUS DISEASE ALERT®

*A twice-monthly update of developments in infectious disease, hospital epidemiology, microbiology, infection control, emporiatrics, and HIV treatment*

American Health Consultants Home Page—http://www.ahcpub.com

CME for Physicians—http://www.cmeweb.com



## Welcome to Jurassic Park: Reptile-Associated Salmonellosis

ABSTRACT & COMMENTARY

***Synopsis:*** *It is not even necessary to travel all that far to contract diseases from lizards, snakes, and turtles, as many of us may have the opportunity to visit some of the numerous U.S. households that have included pet reptiles as part of their family—and its microbial flora.*

**Source:** Reptile-associated salmonellosis—Selected states, 1996-1998. *MMWR Morb Mortal Wkly Rep* 1999;48:1009-1013.

A series of four cases, reported in a recent issue of the CDC's *Morbidity and Mortality Weekly Report*, highlighted the clinical and epidemiological characteristics of salmonellosis transmitted from reptiles to humans. Many more cases had been reported from 16 state health departments (*see Figure*). Syndromes of fever, vomiting, bloody diarrhea, and even death in one young patient from salmonellosis, were linked to positive *Salmonella* cultures in pet iguanas and corn snakes. These occurred in a 3-week-old boy, a 6-year-old and his 3-year-old brother, an 8-month-old, and a 5-month-old boy who died.

### COMMENT BY MARIA D. MILENO, MD

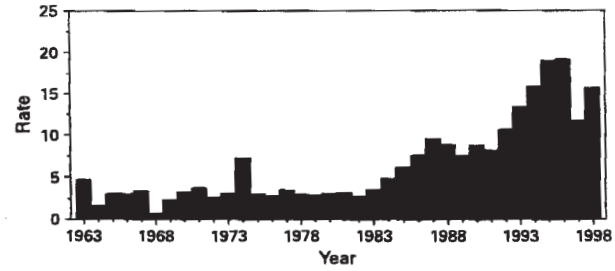
*Salmonella* infections can result in severe invasive illnesses, including sepsis and meningitis, particularly in infants. Despite considerable educational efforts, some reptile owners remain unaware that pet reptiles place them and their children at risk for salmonellosis. Commercial distribution of pet turtles, shorter than 4 inches long, was banned in 1975; until that time, pet turtles were an important source of salmonellosis for young pet owners. The popularity of other common and exotic reptiles is growing and continues to pose a substantial threat. More than 93,000 reported cases (7%) of *Salmonella* infections each year are attributable to pet reptiles for children. Most persons who



## INSIDE

**Figure**

## Rate of Reptile-Associated Salmonella Serotypes Isolated from Humans—United States, 1963-1998




* Per 10,000,000 population

† Reptile-associated serotypes are isolates from nonhumans reported to CDC and the U.S. Department of Agriculture that are isolated from reptiles ≥ 50% of the time.

**Source:** *MMWR Morb Mortal Wkly Rep* 1999;48:1011.

contract reptile-associated salmonellosis are infants and young children who are infected with *Salmonella* spp. after handling either a reptile or objects contaminated by a reptile, and then failing to wash their hands properly. To draw attention to this issue for the U.S. public, several important recommendations have been made (*see Table*).

To make matters worse, "man's best friend," the dog, may be also be subject to *Salmonella* infections acquired from dog treats that were manufactured from pig ears. To date, 30 cases of salmonellosis have been linked to such exposures, and 30% of *Salmonella infantis* infections occurred in children younger than 2 years of age; 48% in children younger than 4 years old. Health Canada has issued a public health warning that infants, the elderly, and immunocompromised persons should avoid handling dog treats manufactured from sources such as pig ears, which can be contaminated with *Salmonella* spp. (*Dr. Mileno is Director, Travel Medicine, The Miriam Hospital, Assistant Professor of Medicine, Brown University, Providence, RI.*) ❖

**Table**

## Recommendations for Preventing Transmission of Salmonella from Reptiles to Humans

- Pet store owners, veterinarians, and pediatricians should provide information to owners and potential purchasers of reptiles about the risk for acquiring salmonellosis from reptiles.
- Persons should always wash their hands thoroughly with soap and water after handling reptiles or reptile cages.
- Persons at increased risk for infection or serious complications of salmonellosis (e.g., children aged < 5 years and immunocompromised persons) should avoid contact with reptiles.
- Pet reptiles should be kept out of households where children aged < 1 year and immunocompromised persons live. Families expecting a new child should remove the pet reptile from the home before the infant arrives.
- Pet reptiles should not be kept in child care centers.
- Pet reptiles should not be allowed to roam freely throughout the home or living area.
- Pet reptiles should be kept out of kitchens and other food preparation areas to prevent contamination. Kitchen sinks should not be used to bathe reptiles or to wash their dishes, cages, or aquariums. If bathtubs are used for these purposes, they should be cleaned thoroughly and disinfected with bleach.

**Source:** *MMWR Morb Mortal Wkly Rep* 1999;48:1012.

***Infectious Disease Alert,*** ISSN 0739-7348, is published twice monthly by American Health Consultants, 3525 Piedmont Rd., NE, Bldg. 6, Suite 400, Atlanta, GA 30305.

**VICE PRESIDENT/GROUP PUBLISHER:** Donald R. Johnston.

**EXECUTIVE EDITOR:** Glen Harris.

**MARKETING PRODUCT MANAGER:** Schandale Kornegay.

**ASSOCIATE MANAGING EDITOR:** Robin Mason.

**COPY EDITORS:** Neill Larmore, Michelle Moran, Holland Johnson.

**GST Registration Number:** R128870672.

Periodical postage paid at Atlanta, GA.

**POSTMASTER:** Send address changes to ***Infectious Disease Alert***, P.O. Box 740059, Atlanta, GA 30374.



**Back issues: $18.**

Missing issues will be fulfilled by customer service free of charge when contacted within one month of the missing issue's date.



### Questions & Comments

Please call **Robin Mason,** Associate Managing Editor, at (404) 262-5517, or e-mail to robin.mason@medec.com, or **Neill Larmore,** Copy Editor, at (404) 262-5480, or e-mail to neill.larmore@medec.com between 8:30 a.m. and 4:30 p.m. ET, Monday-Friday.

### Subscriber Information

Customer Service: 1-800-688-2421

**Customer Service E-Mail Address:** customerservice@ahc.com

**E-Mail Address:** neill.larmore@medec.com

**World-Wide Web:** http://www.ahcpub.com

### Subscription Prices

**United States**
$219 per year (Student/Resident rate: $110).

**Multiple Copies**
1-9 additional copies: $197; 10 or more copies: $175.

**Canada**
Add GST and $30 shipping.

**Elsewhere**
Add $30 shipping.

**For 40 Category 1 CME credits, add $75**

### Accreditation

American Health Consultants (AHC) designates this continuing medical education (CME) activity for up to 40 hours in Category 1 credit toward the AMA Physician's Recognition Award. Each physician should claim only those hours of credit that he/she actually spent in the educational activity.

AHC is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide CME for physicians.

This CME activity was planned and produced in accordance with the ACCME Essentials.

### Statement of Financial Disclosure

American Health Consultants does not receive material commercial support for any of its continuing medical education publications. In order to reveal any potential bias in this publication, and in accordance with Accreditation Council for Continuing Medical Education guidelines, we disclose that Dr. Kemper serves on the speaker's bureau and is involved in research with SmithKline Beecham, DuPont, Merck, Gilead, and Virologics. Dr. Kuritzky is on the speaker's bureau for Glaxo Wellcome, 3-M, Pfizer, Wyeth-Ayerst, Novartis, Bristol-Myers Squibb, Zeneca, Jones, and Boehringer Ingelheim. Dr. Donnelly and Dr. Mileno report no speaker's bureau, research, stockholder, or consulting relationships having ties to this field of study.

# Fecal and Oral Shedding of *H. pylori*

ABSTRACT & COMMENTARY

***Synopsis:*** *This study was directed to learn, by using polymerase chain reaction (PCR) testing, the frequency of H. pylori in saliva, stool, and vomitus of infected volunteers. Immunomagnetic separation (IMS)-PCR was chosen as the detection method because of its superior ability to identify live organisms.*

**Source:** Parsonnet J, et al. Fecal and oral shedding of *Helicobacter pylori* from healthy infected adults. *JAMA* 1999;282: 2240-2245.

Several important unresolved questions about *Helicobacter pylori*, the causative agent of almost all non-NSAID related peptic ulcers and a likely cause of gastric cancer, remain unanswered. The path by which *H. pylori* leaves a host to enter the environment, the environmental location, method of human acquisition, and individual susceptibility to this organism are uncertain. This study was directed to learn, by using polymerase chain reaction (PCR) testing, the frequency of *H. pylori* in saliva, stool, and vomitus of infected volunteers. Immunomagnetic separation (IMS)-PCR was chosen as the detection method because of its superior ability to identify live organisms.

After sodium phosphate-induced catharsis, ipecac-induced emesis, and volitional saliva expectoration, *H. pylori* detection by IMS-PCR was performed (n = 16).

Stool culture obtained prior to catharsis was culture negative in all 16 patients, but positive in five of 16 using IMS-PCR. Post-cathartic stools were *H. pylori*-positive in 11 of 16 subjects by IMS-PCR, but only 50% of specimens were culture-positive. All vomitus samples from infected person were culture-positive as well as IMS-PCR positive. Saliva was culture-positive in only 18.8% of subjects but IMS-PCR positive in 43.8%.

### COMMENT BY LOUIS KURITZKY, MD

Despite the ready retrieval of *H. pylori* from saliva, there is little evidence of oral-oral transmission (e.g., the *H. pylori* strain present in married couples is rarely concordant and, thus far, studies of treated patients, whose infected partners are not treated, do not show significant risk of reinfection).

Saliva, stool, and vomitus all harbor *H. pylori*, which might serve as sources of transmission. Since up to half of middle-aged adults have been infected, the question might best be reframed to seek how the other half remain uninfected. *(Dr. Kuritzky is Courtesy Clinical Assistant Professor, University of Florida, Gainesville, FL.)* ❖

## *Special Feature*

# Fever and Neutropenia: More Challenges than Changes in the Last 20 Years

*By J. Peter Donnelly, PhD*

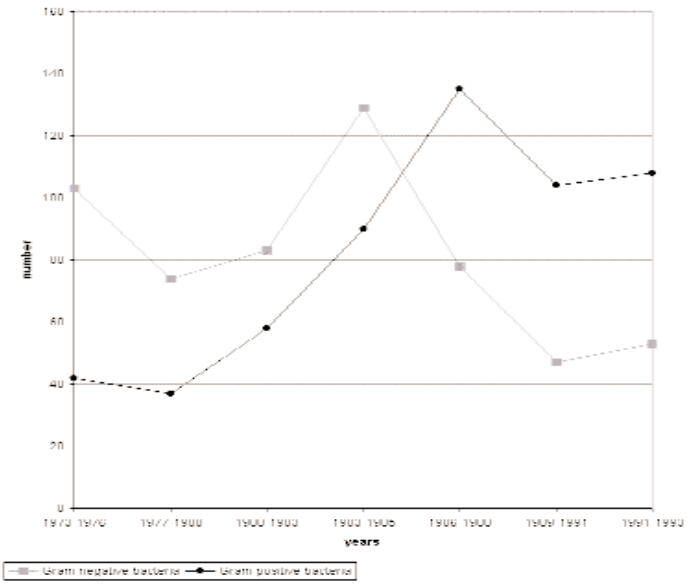
The number of neutropenic patients has increased considerably since Pizzo wrote his first editorial on fever in the immunocompromised host in 1983. Not only are there more patients being treated for malignancies but also more are receiving bone marrow transplants.[1] These patients are compromised at virtually every level of their immunity—phagocytic, cellular, and humoral—and also have breaches to the integument affecting the skin and mucosal defense barriers. This gives rise to complications that may not be infectious but that are nonetheless accompanied by fever. But, because pyrexia is often the only sign of infectious disease, empirical antimicrobial therapy is still started promptly once an attempt at diagnosis has been made.

### Risks Differ

All patients who are profoundly neutropenic (an absolute neutrophil count < 500 per cubic millimeter, < $0.5 \times 10^9$ L) and who develop a fever (temperature > 101°F or > 38°C sustained for several hours or a single temperature > 101°F or > 38.3°C) should be assumed to have a potentially life-threatening infection and treated accordingly until proven otherwise. This is still the most important principle governing management of potentially infectious complications that occur during neutropenia. At the same time, it is generally acknowledged that not all patients with neutropenia are at equal risk. For instance, those who develop neutropenia after cytotoxic chemotherapy or immediately after preparation for transplantation nearly always have concurrent breaches of the physical defense barriers, particularly the mucosa of the oral cavity and gastrointestinal tract. Such damage allows potentially pathogenic microorganisms that reside on these surfaces to establish local infection and

**Figure 1**

**Shift in Pathogens Through the Years**




**Source:** Zinner SH. *Clin Infect Dis* 1999;29:490-494.

gain entry into the tissues. Patients in this category should always be given empirical therapy promptly and in a hospital under the watchful eye of experienced doctors and nurses. By contrast, other less severely compromised individuals may require nothing more than careful observation and "watchful waiting" as outpatients. Several approaches to discriminating those at risk from those who are not at risk have been proposed as discussed by Rolston (*see Table 1*) but, as yet, none has been tested thoroughly enough nor for long enough to determine the true costs and principal benefits.[2] Nonetheless, there is a clear desire to allow as many patients as possible to be managed at home rather than in hospitals.

### Pathogens

At first sight, the range of potential opportunistic and professional pathogens capable of causing infection in neutropenic patients is daunting, since virtually any organism can become invasive if host defenses are severely impaired. But, in practice, a few species of bacteria and fungi predominate. Bacteria can represent an immediate threat but there has been a remarkable and consistent change in the species of bacteria responsible for infection. Twenty years ago, the gram-negative bacilli such as *Escherichia coli*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa* accounted for almost two- thirds of episodes of bacteremia and were rightly feared for the havoc they wreaked. Now the reverse is true, with the gram-positive bacteria predominating.[3] (*See Figure 1.*) In fact, the skin commensal coagulase-negative staphylococci (mainly *Staphylococcus epidermidis*) and the oral viridans (or alpha-

**Table 1**

**Paradigm for Risk-Based Therapy of Febrile Neutropenic Patients**

| Risk Group | Neutropenia | Malignancy | Procedure | Comorbidity | Clinical State | Anticipated Response to Empirical Therapy | Treatment Place | Treatment Approach | Treatment Administration |
|---|---|---|---|---|---|---|---|---|---|
| **High risk** | > 14 days | hematological | allogeneic HSCT, autologous HSCT, chemotherapy | substantial | unstable | slow | in-patient | empirical therapy until end of febrile episode | parenteral |
| **Moderate risk** | 7-14 days | solid tumor | autologous HSCT | minimal | stable | rapid | in-patient with early discharge | empirical therapy until end of febrile episode, then follow-up as outpatient | parenteral or parenteral then oral |
| **Low risk** | < 7 days | solid tumor | chemotherapy | none | stable | — | out-patient | appropriate out-patient treatment | oral, parenteral, then oral or parenteral |

**Source:** Rolston KV. *Clin Infect Dis* 1999;29:515-521.

**Table 2**

**Outcome of Monotherapy for the Initial Treatment of Fever During Neutropenia**

| | Percent of Episodes | | | |
|---|---|---|---|---|
| **Success with monotherapy** | **Cefepime** | **Ceftazidime** | **Meropenem** | **Ceftazidime plus amikacin** |
| **Overall** | 53 | 55 | 56 | 52 |
| **MDI** | 47 | 43 | 43 | 42 |
| **Glycopeptides added** | 22 | 27 | 33 | 42 |
| **Glycopeptides added for MDI** | 21 | 36 | - | - |
| **Further infections** | 10 | 15 | 12 | 12 |

**Source:** Ramphal R. *Clin Infect Dis* 1999;29:508-514.

haemolytic) streptococci (principally *S. mitis* and *S. oralis*) are now the two most frequent isolates from blood cultures. The steady rise to prominence of the skin staphylococci can be attributed to the increased use of indwelling intravenous-access devices that remain in place for weeks and even months, whereas the occurrence of oral mucositis induced by more intensive chemotherapy seems to have allowed the viridans streptococci to make their debut. It must also be acknowledged that the shift away from the gram-negative bacilli toward these bacteria also coincided with more extensive use of co-trimoxazole (trimethoprim-sulfamethoxazole) and especially the fluoroquinolones such as ciprofloxacin for antibacterial prophylaxis. These drugs are effective in selectively decontaminating the gastrointestinal tract of gram-negative bacilli but they also exert considerable selective pressure on the commensal flora favoring the less susceptible bacteria such as those that reside on the skin and mucous membranes. It must also be said that these changes have yet to become apparent beyond the borders of northern Europe and North America, since in developing countries the old foe, gram-negative bacilli, still reigns supreme.

### Initial Evaluation of Fever

The initial evaluation of a febrile, neutropenic patient should include a thorough inventory of the body to disclose sites of potential infection, particularly the oral cavity, lungs, gastrointestinal tract (including the perineal area), skin, and soft tissues. True, there is no clinical evidence whatsoever of such infection in up to two-thirds of cases, but the effort can be rewarding when a site is identified, such as an exit site infection of a central venous catheter or an anal fissure. These would be cases for considering including a focused-spectrum antibiotic in the empirical regimen.

### Which Empirical Regimen?

There has been a protracted dispute about whether combination therapy is obligatory or monotherapy will suffice. In many respects the debate is more a matter of taste than substance since there are several antibiotics, such as the cephalosporins, ceftazidime and cefepime, and the carbapenems, imipenem and meropenem, that clearly are effective as single agents for empirical therapy (*see Table 2*).[4] However, with the changing pattern of pathogens the issue deserves to be looked at afresh but there seems little willingness to do so. Instead, most physicians prefer to complement the initial regimen when they know what the cause of the fever is and some even when they do not. However, the fact remains that no matter which regimen is used, sooner or later other antimicrobial agents will be added to complement the core regimen. In many cases, the choice of drug will be driven by persistent fever that is as refractory to antibiotics as it is to diagnosis and is naturally assumed to be the result of a cryptic infection due to gram-positive cocci such as the coagulase-negative staphylococci. Thus, vancomycin will be chosen (or teicoplanin in Europe). Others will fear the worst and prescribe amphotericin B assuming that a fungus like *Aspergillus fumigatus* is lurking in the lung shadows. Many of these cases of persistent fever will remain unexplained and there will be no evidence to support the anxiety of the physician. But instinct and experience often provide better results at the bedside than guidelines arrived at by consensus. One issue does seem clear, however. Vancomycin (or teicoplanin) is seldom necessary upfront.[4] These drugs contribute little in managing persistent fever, they can always be added when infection is clinically or microbiologically attributable to gram-positive bacteria and, importantly, the specter of vancomycin-resistant enterococci looms large and has already proved troublesome in some centers. So, the lesson here is to stay your hand and use vancomycin and teicoplanin sparingly.

### Resistant or Not?

Disturbingly, at least in North America, resistance to several antibiotics now exceeds 10% (*see Figure 2*), making it difficult to choose a made-to-measure, one-size-fits-all empirical regimen.[6] The situation in Europe is more varied and resistance seems less pronounced. But the principal message to convey is that each institution should know its own resistance patterns and select

empirical regimens as well as the most reliable agents for complementing this. Also, there should be a protocol to guide antibiotic use in each unit and a policy throughout the hospital. Regular antimicrobial surveillance of pathogens should be in place and the alarm should be raised whenever resistance rates start drifting in an upward direction. This, of course, requires resources that providers may be unwilling to commit. Indeed, it may seem cheaper just to choose the broadest regimen possible and apply it to every situation in the forlorn hope that overall costs will be contained and no one will suffer unduly. History suggests otherwise—blind, profligate use of antibiotics is dangerous, and has undoubtedly provided the greatest impetus for crafty bacteria to pull out all the stops and reinvent themselves in resistant clones. Moreover, it is no accident that high resistance rates run parallel with high consumption of antibiotics that only the wealthiest of countries can afford.

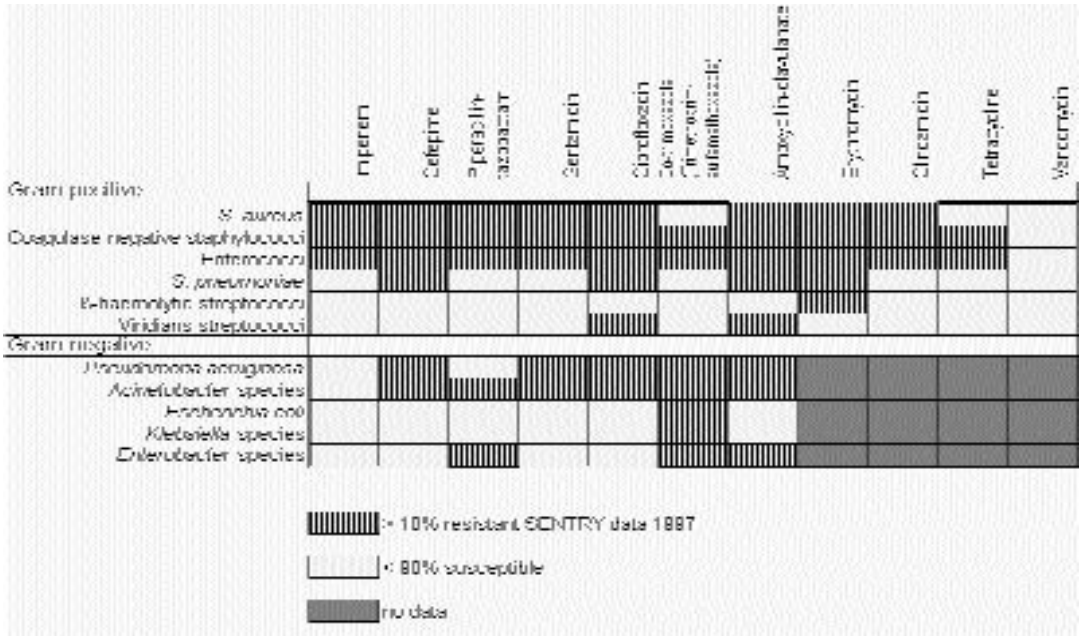
### Beyond Managing Fever

Patients with prolonged immunosuppression may have several febrile episodes or persistent fever despite empirical therapy. One approach is to change therapy if there is no immediate response or by the next ward round, usually by increasing the number of drugs in direct proportion to the level of anxiety. Sometimes the regimen is repeatedly changed for as long as fever persists. This has been variously termed planned progressive therapy, and even escalatory therapy, and is often justified by the fact that with each change in therapy more patients become afebrile, supporting the belief that each change adds an incremental value to the ultimate response rate. However, in many cases, the putative increment is no more than what would be expected were no changes to therapy made.

Many patients with prolonged neutropenia require continued antimicrobial treatment but this does not exonerate the physician from carefully examining the patient with neutropenia, at least daily, for any signs and symptoms of progressive initial infection or new further infections which may develop over time. For instance, blood cultures should be done every 3-4 days for as long as fever persists. But it is remarkable how little attention is paid to the practice of microbiology in these articles. For instance, while we are still heavily reliant on blood cultures, we don't take enough blood. Nor do we obtain proper specimens when we do see lesions on the skin or in the mouth and prefer to order a swab, having briefly entertained the idea of taking a biopsy only to dismiss it on the grounds that the results will prove of little value. True, we are now more inclined to ask for a bronchoscopy when a pulmonary infiltrate develops but remain in doubt as to its value, especially when negative, and so continue to treat empirically. In fact, although the empirical approach is based on the principle that fever is assumed infectious until there is proof

**Figure 2**

**Susceptibility Patterns of Bacterial Isolates from Neutropenic Patients During 1997**




**Source:** Jones RN. *Clin Infect Dis* 1999;29:495-502.

beyond all reasonable doubt to the contrary, antimicrobial treatment will continue regardless of the results. The advent of better imaging techniques, such as high-resolution computed tomography and indirect means of detecting pathogens, should make it easier to diagnose infectious complications. For instance, microbiologically defined infections can now be diagnosed by detecting antigens such as *Aspergillus* galactomannan and the presence of microorganisms can de determined using PCR techniques. But whether they will bring about a change in attitude, only time will tell. ❖

### References


1. Pizzo PA. Fever in immunocompromised patients. *N Engl J Med* 1999;341:893-900.
2. Rolston KV. New trends in patient management: Risk-based therapy for febrile patients with neutropenia. *Clin Infect Dis* 1999;29:515-521.
3. Zinner SH. Changing epidemiology of infections in patients with neutropenia and cancer: Emphasis on gram-positive and resistant bacteria. *Clin Infect Dis* 1999;29:490-494.
4. Ramphal R. Is monotherapy for febrile neutropenia still a viable alternative? *Clin Infect Dis* 1999;29: 508-514.
5. Feld R. Vancomycin as part of initial empirical antibiotic therapy for febrile neutropenia in patients with cancer: Pros and cons. *Clin Infect Dis* 1999;29:503-507.
6. Jones RN. Contemporary antimicrobial susceptibility patterns of bacterial pathogens commonly associated with febrile patients with neutropenia. *Clin Infect Dis* 1999;29:495-502.


## *CME Questions*

**18. Which of the following is correct?**

a. Pet amphibians have been identified as an important source of *Salmonella* infection in children in the United States.
b. Pet turtles are currently an important source of *Salmonella* infection in children in the United States.
c. Pet reptiles kept in child care centers can be considered not to be a potential source of salmonellosis if the reptiles appear to be healthy.
d. Immunocompromised persons and children aged younger than 5 years should avoid contact with reptiles.

**19. Which of the following is correct?**

a. In developed countries, aerobic gram-negative bacilli remain a more common cause of bacteremia in neutropenic cancer patients than do gram-positive cocci.
b. All patients with febrile neutropenia must be given empiric parenteral broad spectrum antibiotics.
c. Solid tumor patients with chemotherapy-related neutropenia expected to be of less than seven days duration may be managed as outpatients.
d. Patients with hematological malignancies and chemotherapy-related neutropenia expected to last for more than 14 days may be managed as outpatients.

**20. Which of the following is correct?**

a. There remains no evidence that avian influenza virus (H5N1) can be transmitted from human to human.
b. The peroneal anatomy of young women (e.g., the distance from the urethra to the anus) is reported to be an important risk factor for the development of urinary tract infection in young women.
c. Granulocyte-macrophage colony-stimulating factor (GM-CSF) accelerates the intracellular replication and growth of *Mycobacterium avium* in macrophages.
d. *Helicobacter pylori* is absent from the vomitus of patients with gastric infection due to this organism.



## In Future Issues:

Reducing Surgical Wound Infections with Supplemental Oxygen

# UPDATES

By Carol A. Kemper, MD, FACP

## GM-CSF Potentiates Anti-Mycobacterial Activity

**Source:** Kedzierska K, et al. *J Infect Dis* 2000;181:390-394.

Granulocyte-macrophage colony-stimulating factor (GM-CSF) is known to play a significant role in the maturation and activation of granulocytes and macrophages. Kedzierska and colleagues describe an HIV-infected patient with multidrug resistance disseminated *Mycobacterium avium* complex (MAC) infection who received GM-CSF (200-400 mcg/day) for 40 days without specific antimycobacterial therapy. Peripheral circulating monocytes obtained before treatment with GM-CSF demonstrated impaired phagocytosis in vitro of MAC (probably due to his underlying HIV infection), which was subsequently partially reversed with GM-CSF therapy. Clinical improvement was difficult to demonstrate although Kedzierska et al believe that his level of MAC bacteremia decreased during GM-CSF therapy based on a prolongation in time for blood specimens to yield a positive MAC culture.

Similar results have been reported by Drs. Deresinski and Bermudez with HIV+ patients with disseminated MAC, as well as a non-HIV-infected patient with disseminated *M. kansasii* (Kemper CA, et al. *J Infect Dis* 1998;177:914-920; Bermudez LE, et al. *Biotherapy* 1995;4:3-10). Blood monocytes obtained from four HIV-infected patients with MAC bacteremia treated with azithromycin and GM-CSF for up to six weeks had significantly enhanced activation and intracellular killing of MAC ex vivo compared with patients receiving azithromycin alone. The effect was apparent within seven days of administration of dosages as low as 50-125 mcg/$m^2$. Similar results have also been reported with candidal infection, although it has been difficult to demonstrate a direct clinical benefit in many of these unusual infections. Nevertheless, there are increasing data to suggest that GM-CSF may be a useful adjuvant in patients with fungal and mycobacterial infections poorly responsive or resistant to conventional therapies. ■

## Peroneal Anatomy and UTIs in Women

**Source:** Hooton TM, et al. *Clin Infect Dis* 1999;29:1600-1601.

In order to test the hypothesis that physiogomy and urine-voiding characteristics may affect the risk of urinary tract infection (UTI), Hooton and colleagues examined healthy nonpregnant women aged 18-30 years. Case subjects (n = 98) had a history of frequent UTI (> 3 in the past 12 months or > 2 in the past 6 months), while control subjects (n = 107) had no history of UTI during the previous year and no more than one UTI in any preceding year.

No difference in urinary flow characteristics (peak and average flow rate, volume, and voiding time) or post-void residuals were identified. Remarkably, however, the distance from the urethra to the anus as well as from the posterior fourchette to the anus in women with more frequent UTI was significantly shorter than that of control subjects (although the mean difference averaged only 0.2 cm). In women who did not use spermicides, a distance from the urethra to the anus of less than 4.5 cm was significantly more frequent in case subjects than controls (38% vs 10%, P = 0.0013), although this association was not observed in spermicide users. No difference in urethral length (average length ~3.5 cm) was detected.

In the absence of other risk factors, such as frequent sex or use of spermicides, Hooton et al argue that anatomic differences in peroneal anatomy may contribute to the frequency of UTI. While an interesting theory, I'm baffled as to how the seemingly minor differences detected in this study could be an important factor. Fecal pathogens can readily colonize Foley catheters in men within days of insertion, which entails migration from the perirectal area to the penile meatus (presumably a much longer distance). Furthermore, peroneal anatomy in this study was significantly associated with weight, height, and body mass index, but I know of no data suggesting that thin women are at greater risk for UTI than overweight ones. This seems like one of those statistical observations that deserves further exploration. ❖

## Human-to-Human Transmission of Avian Flu

**Source:** Bridges CB, et al. *J Infect Dis* 2000;181:344-348.

A central concern during the outbreak of avian influenza (H5N1) among humans in Hong Kong in 1997 was the possibility of human-to-human transmission which could lead to a larger pandemic. This retrospective surveillance study investigated whether 217 health care workers (HCWs) exposed to at least one patient hospitalized were at risk of H5N1 viral infection compared with 309 non-exposed HCWs. No difference in the frequency of poultry exposure was found between the two groups. Antibody to H5N1 virus was found in 10 HCWs, including eight (3.7%) with exposure to a hospitalized patient vs. two (0.7%) non-exposed HCWs. Two HCWs with exposure had evidence of seroconversion in paired serum samples—neither reported exposure to poultry. One of these reported a respiratory illness within two days of exposure to a case, although viral cultures remained negative.

Although paired specimens were not available from all exposed HCWs, these data strongly support the limited occurrence of human-to-human transmission of avian influenza during the outbreak in Hong Kong. ■