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Helicobacter Pylori and Houseflies: Are They Really to Blame?

ABSTRACTS & COMMENTARY

Sources: Grübel P, et al. Detection of *Helicobacter pylori* DNA in houseflies (Musca domestica) on three continents. *Lancet* 1998;352:788-789. Osato M, et al. Houseflies are an unlikely reservoir or vector for *Helicobacter pylori*. *J Clin Microbiol* 1998;36:2786-2788.

Grübel and colleagues have already shown that the humble housefly has the potential for harboring *Helicobacter pylori* for at least 30 hours after being fed pure cultures of the bacterium and have now shown the presence of the gene for isocitrate dehydrogenase (*icd*) elaborated by *H. pylori* among 97 groups of five flies collected from around North America, Poland, and Egypt. They used a PCR technique and found a positive reaction in one of 14 groups of flies collected from a dairy farm in South Carolina, four of 17 groups collected on a dairy farm in Florida, and five of 13 groups collected in a residential area in California. Similarly, five of the 14 groups of flies collected in Krakow, Poland, were positive as were three of the nine groups collected in Cairo, Egypt. However, none of the flies collected in three different Japanese cities were positive, nor were any of those collected at a turkey farm in North Carolina, from a pig farm and a chicken farm in South Carolina, or a dairy farm in Iowa. The specificity of the PCR was determined using other *Helicobacter* species, other bacteria, flies raised in the laboratory, and fecal material from patients known not to harbor *H. pylori*. Thus, Grübel et al conclude that the DNA found must represent colonization of the flies with *H. pylori* lending further weight to their argument that the housefly is both a vector and reservoir of the bacterium it acquires by eating infected feces.

Osato and colleagues doubt this conclusion and set about to disprove it by feeding the same species of laboratory-raised domestic houseflies fresh fecal material from a volunteer known to harbor *H. pylori* and another known to be free of infection. One group of flies was fed feces from the *H. pylori* positive volunteer, another group was fed feces from the negative volunteer, and the third group was fed the same feces seeded with almost 100 million

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viable *H. pylori*. Groups of five flies were killed at six hourly intervals between 24 and 72 hours after exposure, but *H. pylori* was not found in any of their midgut samples. Osato et al had already taken the precaution of removing all other sources of water to be sure that the flies were forced to eat the fecal material. Apparently, contrary to common belief, the domestic housefly, *Musca domestica*, does not have a predilection for feces although his subtropical cousin *Musca domestica* vicina does. This makes it unlikely that the domestic housefly acquires *H. pylori* in the first place. The experiments done by Osato et al indicate that even higher levels of *H. pylori* need to be present in fecal material if the fly is to become infected, much less become a carrier. Such levels are unlikely outside the stomach of an infected individual.

COMMENT BY J. PETER DONNELLY, PhD

So, we are left with a conundrum. If one has to force-feed houseflies with feces loaded with unattainably high numbers of viable *H. pylori*, how did the DNA get there? It is tempting to dismiss the positive results as contamination but, in fact, neither group has proved their case beyond all reasonable doubt. It is a pity that Grübel et al didn't culture the flies and that Osato et al didn't attempt to detect the *icd* gene. It is also tempting to inquire why anyone should be trying so hard to implicate the housefly as a vector of this gastric pathogen. If it is proven, will this lead to an attempt to protect potential victims from contact with the ubiquitous insect or, even more futile, a drive to eradicate the poor thing altogether? It seems much more likely that people acquire *H. pylori* like they do many other micro-organisms, namely, feces to fingers to mouth. There seems no need to invoke any role for the housefly. ❖

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Controlling Antibiotic Resistance: One Small Victory?

ABSTRACTS & COMMENTARY

Synopsis: *Control of virtually all cephalosporin use at one hospital was associated with a significant reduction in the prevalence of resistant Klebsiella containing extended spectrum beta lactamase. This was accomplished, however, with an increased use of imipenem as well as an increased prevalence of imipenem resistence in Pseudomonas aeruginosa.*

Sources: Rahal JJ, et al. Class restriction of cephalosporin use to control total cephalosporin resistance in nosocomial Klebsiella. *JAMA* 1998;280:1233-1237; Burke JP. Antibiotic resistance—squeezing the balloon? *JAMA* 1998;280: 1270-1271.

An outbreak of *Klebsiella* producing an extended spectrum B-lactamase (ESBL) occurred in Rahal and colleagues' hospital in 1990. Over the next five years, the prevalence gradually increased despite restrictions upon the use of third generation cephalosporins. In 1995, there were a total of 150 isolations of ESBL-producing *Klebsiella*, representing 19.6% of all *Klebsiella* isolates. Approximately 40% of the resistant isolates were resistant to cephamycins (cefotetan, cefoxitin) as well. Prior to 1996, use of third generation cephalosporins or imipenem required approval by the infectious disease service. Beginning in 1996, the hospital adopted new antibiotic use guidelines, requiring approval for use of all cephalosporins and cephamycins with few exceptions, such as the use of ceftriaxone for the treatment of meningitis or gonococcal infections. Restrictions of the use of imipenem continued.

Rahal et al measured the effect of the new restriction by comparing the isolation of ceftazidime-resistant

Klebsiella in 1996 with that noted in 1995. They also compared the isolation of imipenem-resistant *Pseudomonas* during the two-year period. Surveillance methods and infection control practices were identical during the two years.

In 1996, there was an 80% decrease in cephalosporin use hospital-wide, from 5558 g/month to 1106 g/month ($P < 0.001$) compared with 1995. However, imipenem use increased by 141% (197 g/month in 1995 to 474 g/month in 1996). During 1996, there was a 44% reduction in nosocomially acquired ceftazidime-resistant *Klebsiella* compared with 1995 (150 vs 84 isolates, respectively). The reduction was most apparent in the ICUs. There was a concomitant 69% increase in isolation of imipenem-resistant *Pseudomonas*.

COMMENT BY ROBERT MUDER, MD

ESBLs of *Klebsiella* are typically plasmid mediated, and confer high-level resistance to ceftazidime and aztreonam, and variable, often less marked, resistance to cefotaxime. Many, but not all, of these ESBL-producing strains remain susceptible to cephamycins. The plasmids often contain resistance determinants to other, unrelated antibiotics such as aminoglycosides. ESBL-producing *Klebsiella* (as well as other members of the Enterobacteriaceae) are widespread in hospitals and long-term care facilities throughout the world.

Efforts to control resistant microorganisms have generally consisted of a two-pronged approach—prevention of transmission by isolation practices and control of antibiotic use. The reported results of control measures have been (to put the best possible face on the situation) decidedly mixed. Rahal et al took a novel approach and hypothesized that restriction of the entire cephalosporin class, including the related cephamycins, would lead to withdrawal of the selective pressure favoring ESBL-producing *Klebsiella*. They were remarkably successful in reducing cephalosporin use, and, indeed, there was a marked and statistically significant reduction in resistant *Klebsiella* that was most apparent in the ICUs. Unfortunately, there was an increase in the frequency of isolation of imipenem-resistant *Pseudomonas*, in response, no doubt, to the increased use of imipenem during the period of intervention. In an accompanying editorial, Burke compares the result to "squeezing a balloon—constraining one end causes the other end to bulge."

It is difficult to judge the overall effect of the intervention by Rahal et al. Rahal et al don't provide outcome information in terms of infection rates or deaths due to infection. It would also be important to know what effect the change in antibiotic prescribing had on other resistant flora in the hospital, particularly other potentially cephalosporin-resistant agents such as *Enterobacter* and *Serratia*. One might surmise that a decrease in cephalosporin use might have led to a decrease in isolation of methicillin-resistant *Staphylococcus aureus* and resistant *Enterococcus*, for example. It would also be important to know the changes in the use of alternative agents such as ciprofloxacin and the effect of these changes upon the frequency of resistance to the these agents. It would also be important to know what happened to the total use of antibiotics and any changes in drug expenditures.

Hospitals can be likened to complex ecosystems, in which one change or perturbation is likely to have not only its intended effect but also multiple secondary effects that may not be predictable. It's not surprising that the "ecologic niche" occupied by resistant *Klebsiella* would be taken over something else that might be just as objectionable. It is, undoubtedly, overly optimistic to expect that changing the usage pattern of a single class of antibiotics will solve the problem of drug resistance. But, the experience of Rahal et al demonstrates that antibiotic usage patterns can be changed in a rational way over a prolonged period of time, and that at least some of the effects of the intervention can be quantified. Such studies are an important stepping stone if we hope to devise comprehensive control strategies to reduce the threat of antibiotic resistance. ❖

Which of the following is correct?

a. Extended spectrum beta-lactamases (ESBL) are usually chromosomally mediated.
b. ESBLs code for resistance to cephamycins but not cephalosporins.
c. ESBL-coded resistance is often associated with genes encoding resistance to antibiotics other than beta-lactams, such as aminoglycosides.
d. ESBL producing *Klebsiella* remain extraordinarily rare in U.S. hospitals.

Subcutaneous IVIG?

ABSTRACT & COMMENTARY

Synopsis: *The term intravenous immune globulin (IVIG) has become a misnomer. IVIG was safely and effectively administered to eight patients; this route is believed to be associated with reduced adverse effects, but the total volume that can be given is limited.*

Source: Stiehm ER, et al. Slow subcutaneous human intravenous immunoglobulin in the treatment of antibody immunodeficiency: Use of an old method with a new product. *J Allergy Clin Immunol* 1998;101:848-849.

Stiehm and colleagues describe eight patients that received 10% intravenous immune globulin (IVIG) via the subcutaneous route. Subcutaneous infusions of immune globulin were given weekly or biweekly using a battery-operated pump and a 20 mL syringe connected via tubing to a 1 cm × 24 gauge needle. The usual site of infusion was the abdominal wall 2 inches from the umbilicus. The site was rotated 90° at each visit and the typical infusion time was three hours. Usual doses given were 100 mg/kg/wk, although doses as high as 250 mg/kg were given every three weeks via this method.

In all patients, the subcutaneous route was chosen because of problems when IVIG was administered by the intravenous route. Four of the patients had poor venous access, two had prior anaphylactic reactions, one experienced severe aseptic meningitis, and another had rapid immunoglobulin catabolism. Three different brands of IVIG were used with comparable efficacy, lower side effects, and more consistent and sustained blood levels. While the concentration area under the curve after subcutaneous IVIG is equivalent to that when given intravenously, the peak level does not occur until four days later. This slow release of immunoglobulin into the blood stream is felt to be responsible for decreased side effects and more consistent blood levels, especially in patients with rapid immunoglobulin catabolism. To alleviate symptoms in some patients, they were premedicated with aspirin, acetaminophen, oral diphenhydramine, or intravenous hydrocortisone prior to infusions.

COMMENT BY THOMAS G. SCHLEIS, MS, RPh

Infectious disease specialists are often referred patients with chronic sinusitis or pulmonary infections who are found to have compromised immune systems. Often, the response of these patients to immune globulin therapy is dramatic, with a significant decrease in infection rate. Although the subcutaneous infusion of IVIG is not new,[1-4] I became aware of this method of administration at an immunology meeting. Most immunologists I spoke with feel this will be the preferred method of administration of IVIG in the future.

There are limitations to this method of adminstration, however. Infusions must be given more frequently—often weekly. This may present a problem for some patients, especially those who are used to receiving infusions on a monthly basis. It is also only suitable for relatively small volumes, such as 100-150 mL, making it unsuitable for treatment of certain autoimmune disorders, ITP, or other diseases where high doses are used. Nonetheless, for those patients experiencing significant side effects to immune globulin via the intravenous route, it does provide a potentially effective alternative. In the past, we have had several patients who experienced severe aseptic meningitis after IVIG infusions, despite decreasing the infusion rate in half and pretreatment with steroids and analgesics. These patients would certainly be candidates for subcutaneous therapy.

Another option may be a slow (24-48 hour) intravenous infusion of IVIG using an ambulatory infusion pump. To my knowledge, this has not been studied in patients experiencing side effects at more conventional infusion rates. A slow intravenous infusion may mimic the slow release of immunoglobulins into the bloodstream, which is felt to be responsible for the decreased side effects with subcutaneous infusions. This method would have the advantage of not being limited by dosage or volume. ❖

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3. Gardulf A, et al. The life situations of patients with primary antibody deficiency untreated or treated with subcutaneous gammaglobulin infusions. *Clin Exp Immunol* 1993;92:200-204.
4. Abrahamsen TG, et al. Home therapy with subcutaneous immunoglobulin infusions in children with congenital immunodeficiencies. *Pediatrics* 1996;98: 1127-1131.

Which of the following is correct?

a. All patients may be given immune globulin via the subcutaneous route.
b. Patients experiencing anaphylactic reactions to IVIG may tolerate immune globulin when given via the subcutaneous route.
c. Administration of immune globulin via the subcutaneous route is relatively new.
d. A specialized preparation of immune globulin is necessary in order to administer subcutaneously.

Candida dublinensis: New Species and Old Strains

ABSTRACTS & COMMENTARY

Synopsis: *Far from being a new species, Candida dublinensis was first isolated from oral samples*

obtained as far back as 1973 but was originally identified as Candida albicans. The species can be recognized by its unusual green color on CHROMagar and failure to grow at 45°C.

Sources: Odds FC, et al. Prevalence of *Candida dublinensis* isolates in a yeast stock collection. *J Clin Microbiol* 1998; 36:2869-2873; Kirkpatrick WR, et al. Detection of *Candida dublinensis* in oropharyngeal samples from human immunodeficiency virus-protected patients in North America by primary CHROMagar Candida screening and susceptibility testing of isolates. *J Clin Microbiol* 1998;36:3007-3012.

A sample of 2589 yeasts originally identified as *Candida albicans* were reexamined by Odds and colleagues by culturing them on the differential medium CHROMagar testing for the presence of the enzyme beta-glucosidase and hybridization with the *C. albicans* specific oligonucelotide sequence Ca3. An abnormal color of green was produced on the CHROMagar by 502 (19.4%) of which 93 (18.5%) failed to elaborate beta-glucosidase. Fifty-three of these strains failed to hybridize with Ca3 and, hence, were reidentified as *Candida dublinensis*. Forty-four (83%) of these yeasts originated from oral samples, eight from faces, and one each from sputum, the vagina, and an undisclosed site. Far from being recent isolates, *C. dublinensis* was being deposited from 1973 onward unbeknown to everyone. In 1986, there had already been six isolates from IV drug users deposited as well as 15 strains from oral surveillance cultures taken from patients treated for hematological malignancies in the same hospital. From 1988 on, 19 *C. dublinensis* isolated from the oropharynxes of patients with AIDS had been deposited. In the study by Kirkpatrick and associates, the oral rinses of 63 patients with HIV infection were screened prospectively using CHROMagar and *C. dublinensis* was detected in 23 cases. These isolates were then contrasted with 28 *C. albicans* isolated from the samples with the results shown in the Table.

Table

***C. dublinensis* vs. *C. albicans* in oral cultures**

Test	*C. dublinensis* (n = 23)	*C. albicans* (n = 28)
Germ tube production	100%	100%
Abundant chlamydospores	70%	4%
Correctly identified by API 20C	0%	89%
Ability to use xylose	0%	100%
Growth at 42°C	4%	100%
Growth at 45°C	0%	64%
Good hybridization with Ca3 probe	0%	100%

COMMENT BY J. PETER DONNELLY, PhD

No real difference in susceptibility to amphotericin B or the azole antifungal agents was noted. It is too early to claim any particular virulence for *C. dublinensis* but these studies serve to remind us that oral samples frequently yield more than one species of *Candida*. Armed only with CHROMagar and a hotter than normal incubator, it is possible to distinguish *C. dublinensis* from its cousin *C. albicans* and other *Candida* species so there is no longer any excuse for reporting yeasts as *C. albicans*, and *Candida* species not albicans when dealing with HIV-infected and other immunocompromised patients. ❖

Which of the following is correct?

a. *Candida dublinensis* is a newly emerged pathogen that first appeared in 1991.
b. In contrast to *Candida albicans*, *C. dublinensis* fails to grow at 45° C.
c. *C. dublinensis* produces a pink pigment on CHROMagar.
d. *C. dublinensis* has been exclusively isolated from patients with advanced HIV disease.

Prosthetic Joints—Loose or Infected?

ABSTRACT & COMMENTARY

Synopsis: *Prosthetic joint infections were identified using cultures taken by surgeons during surgery. The study found that surgeons should take at least three careful cultures and have them separately processed to determine if infection is present. Evaluating blood studies and culture fluid before surgery may also be beneficial.*

Source: Atkins BL, et al. Prospective evaluation of criteria for microbiological diagnosis of prosthetic-joint infection at revision arthroplasty. *J Clin Microbiol* 1998;36:2932-2939.

Atkins and colleagues in oxford, england, studied 297 cases of prosthetic knee and hip revisions over 17 months. Because of their concern that Gram stain results were not reliable and that specimen collection and culture methods were not well standardized, they asked their surgeons to take cultures at surgery, which included a swab of joint fluid, capsular tissue, femoral and tibial membrane, and other abnormal

tissue. Cultures were taken using separate sterile instruments for each specimen and processed for aerobic and anaerobic organisms. An average of 4.06 specimens was taken per patient.

Their definition of infection was the presence of five or more polymorphonuclear leukocytes per high power field on histology exam provided the patient did not have an inflammatory process such as rheumatoid arthritis. One pathologist read all histology specimens. Based on this criterion, 41 patients (13.8%) were diagnosed with infection—even though 35% of those had no growth on culture. Gram staining had a sensitivity of 6% and specificity of 99.7% for a positive culture and 12% and 98.8%, respectively for positive histopathology.

The culture results showed a variety of organisms, the most frequent being coagulase-negative staphylococci followed by corynebacterium, then propionibacterium, *Staphylococcus aureus*, and streptococci. The number of positive cultures from each patient was also examined. The histology results correlated well with microbiology results when at least three specimens were found to contain the same bacteria. A mathematical model was constructed from the data, which showed a relative likelihood of infection of 0.7 if one culture is positive. For two positive cultures showing the same organism, the likelihood was 4.3, and for three or more positive cultures, 25.9.

There is little information on the clinical evaluation, treatment, or outcome data for patients in the study, although Atkins et al do point out that their policy is to remove the prosthesis for six weeks before replacing it if a definite infection is established with positive histology.

COMMENT BY ALAN TICE, MD, FACP

The problem of appropriate treatment of prosthetic joint infections is a frequent and important one. This study provides some useful results and underscores the value of cultures in confirming an infection. It seems that all too often, infectious disease consultations are requested after the joint is replaced and a single culture of the wound grows a skin organism after three days.

A diagnosis of infection with a prosthetic joint may be easy in some cases but clinical indicators may not be able to distinguish between loosening of the joint and infection. It is not unusual for a surgeon to be unpleasantly surprised at surgery. The situation is further complicated by coagulase-negative staphylococci, which are not only the most frequent contaminants but the most likely pathogens as well. In addition, coagulase-negative staphylococci may hide within the slime they create on prosthetic joint surfaces and not produce significant apparent disease.

The Gram stain has been used by some surgeons as an indicator of infection but prior studies, and this one, point out it is a poor and unreliable one. The use of histopathology to make a diagnosis of a prosthetic joint infection may provide a measure of accuracy and standardization, but it is not a timely one and also has limitations in that only 65% of cultures are positive, despite meeting histopathology criteria. Even with two or three positive cultures for the same organism, the histology was not always positive.

Atkins et al allude to the possible value of the specific bacteria in making a diagnosis of infection but do not provide clinical data. Certainly, the recovery of a *S. aureus* would make a serious infection more likely than a *Propionibacterium*. It would be nice to know if the culture or histopathology results correlate with outcomes of the infections.

This study suggests surgeons should use a protocol to take at least three careful cultures (one joint fluid and one tissue) at surgery and that they be separately processed. This would be helpful in many cases although the cost of the cultures should be considered.

The problem still remains as to whether to put in a new joint at the time of surgery, especially if there is some suspicion of infection. Some cases are obviously clinically infected. A Gram stain may be useful if pus is present but may not be helpful otherwise. Histopathology studies for inflammatory cells and cultures are not timely. The best approach may be a careful evaluation before surgery with blood studies (ESR, C-reactive protein) and cultures of joint fluid. There may also be benefit to aspirates or biopsies of abnormal areas on radiographic studies or where the ends of the prosthesis may be loose or particularly painful. ❖

The best method of diagnosing a prosthetic joint infection is:

a. clinical evaluation.
b. Gram stain taken in the operating room.
c. a positive culture at surgery.
d. histopathology showing at least five polymorphonuclear leukocytes per high power field.

Coagulase-negative staphylococci are:

a. the most frequent contaminants of prosthetic joint cultures.
b. the most frequent cause of prosthetic joint infections.
c. not significant if recovered from only one of four cultures.
d. all of the above

Ivermectin vs. Albendazole for Cutaneous Larva Migrans

CASE REPORT

A classic textbook case of cutaneous larva migrans (CLM) presented to our office two weeks ago. A 57-year-old woman had just returned from a one-week vacation in Jamaica, where she and her husband spent lots of time walking on the beach. Within two to three days of arriving in Jamaica, she developed increasingly itchy feet, which eventually precluded sleep. By the time she arrived back in the United States, her feet were red, hot, and markedly swollen. She was diagnosed with dermatitis and given a steroid injection, and within 24 hours had evidence of at least 30-40 serpiginous tracts on each foot, which quickly extended to the ankles.

She was seen in a local urgent care center and prescribed orally administered thiabendazole, which resulted in intractable nausea and vomiting for two days. In desperation, with progression of her creeping eruption, and unable to keep the medication down, she contacted our office and was given albendazole for five days. Remarkably, her husband showed no initial signs of infection, but within two days noticed involvement of two toes on the right foot, and was also given albendazole for five days. Both husband and wife rapidly responded without evidence of relapse at one month.

COMMENT BY CAROL A. KEMPER, MD

CLM is caused by any number of skin-penetrating roundworm larvae but are usually caused by dog or cat hookworms (*Ancylostoma*). Within days of infection, an often markedly pruritic dermatitis develops, followed by the appearance of serpiginous tracts revealing the nematodes aimless wandering. Three-fourths of the infections occur on the lower extremities, while 12% occur on the buttocks and anogenital area and 7% on the upper extremities.[1]

Various therapeutic approaches have been used for this condition, including cryotherapy, topical administration of thiabendazole, and systemic administration of thiabendazole, albendazole, and ivermectin. Cryotherapy is often destructive and ineffective, especially in cases of more severe infection (you have to hit the larvae approximately 1-2 cm ahead of its track). System thiabendazole is typically noxious, as my patient discovered, and topical thiabendazole was not readily available.

Both systemically administered ivermectin and albendazole are effective in the treatment of CLM, although ivermectin appears superior and has the convenience of a single-dose regimen. In one recent report, ivermectin, administered as a single oral dose of 12 mg, was curative in 49 of 50 patients (two patients relapsed and were successfully retreated).[2] The remaining patient, who was concurrently receiving corticosteroids and azathioprine for Crohn's disease, failed multiple courses of therapy. In another report, albendazole, 400 mg once daily for seven days, was curative in all 11 patients with extensive disease.[3] While shorter courses of albendazole (e.g., 3-5 days) may also be effective, data are lacking.

On the other hand, single-dose albendazole was an abysmal failure. Twenty-one patients were randomized to receive orally administered ivermectin (12 mg) or albendazole (400 mg) as a single dose. All 10 patients receiving ivermectin were completely cured of their infection, compared with one of 11 patients who failed albendazole and five who subsequently relapsed.[4]

On a slightly related note, SmithKline Beecham has signed a memorandum of understanding whereby SKB will donate albendazole to the WHO's efforts to eliminate lymphatic filiarisis in third-world countries over the next 20 years. The Albendazole Donation Program complements Merck's Ivermectin Donation Program for the WHO's Onchocerciasis Control Program. ❖

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Which of the following is correct with regard to cutaneous larva migrans?

a. It is commonly caused by dog and cat hookworms.
b. Mebendazole is the treatment of choice.
c. Single-dose therapy with albendazole is highly effective treatment.
d. Single-dose therapy with ivermectin has a high failure rate.

In Future Issues:

Understanding Guillain-Barré Syndrome

UPDATES

By Carol A. Kemper, MD

Spanish Sandfly Fever

Source: Mendoza-Montero J, et al. *Clin Infect Dis* 1998;27:434-436.

Toscana virus is a well-recognized cause of acute aseptic meningitis and encephalitis in central Italy, where it causes up to 80% of the viral CNS infections in children during the summer months (*Infect Dis Alert* 1998;17[15]:120). Cases have been recognized throughout the Mediterranean, but viral isolation has been accomplished only in Italy and Portugal. In contrast to Toscana virus, other causes of human sandfly fever, such as Sicilian virus and Naples virus, are not known to be neurotropic. Tocsana virus is believed to be transmitted by a sandfly, *Phlebotomus perniciosus* (also the vector for leishmaniasis), which is distributed throughout the Mediterranean, and is typically small enough to sneak through most window screens.

The authors identified 15 strains of Toscana virus isolated from the cerebrospinal fluid of 15 of 184 patients presenting with acute aseptic meningitis in Granada, Spain, between 1988 and 1998. Most of the patients were adults (median age, 27 years) and presented with abrupt onset of headache, vomiting, fever, and, less commonly, nuchal rigidity. All of the infections were self-limited.

Seroepidemiological studies, using indirect immunoflourescence, were performed in a total of 1268 serum specimens from nine different regions of Spain. Remarkably, 26.2% of specimens were positive for Toscana virus. Antibody titers first appeared in the second decade of life, and peaked in patients aged 60 or older. The highest rate of infection occurred in Palma de Mallorca (61%), a popular tourist destination on the Mediterranean Coast. These data suggest that Toscana virus is endemic throughout Spain, especially along the Mediterranean Coast. ■

Vampirism: Just Another Zoonosis?

Source: Gomez-Alonso J. *Neurology* 1998;51:856-859.

Gomez-alonso provides a tantalizing story for the possible association of rabies and the vampire legend. The earliest reports of vampirism date to the Balkans in the late 17th century, but vampires progressively vanished, except from the literary world, by the second half of the 18th century. Vampires were usually male, from poor or rural areas, and were described as pale or waxen in appearance, with prominent teeth, tongues, necks, and genitalia, with bloody fluid flowing out of the mouth. They were restless, wandered the earth, especially at night, and were feared for their ruthless attacks on people or animals, as well as their sexual proclivities. A person became a vampire through a bite from another vampire, or by eating the flesh of an animal killed by a vampire.

Any of this sound familiar? Rabies is seven times more common in males, prevails in rural areas, and commonly causes an encephalitic form of the disease with a predilection for the limbic system, resulting in restlessness, a wandering tendency, insomnia, and aggression toward others. "The rabid patient rushes at those who approach him, biting and tearing them as if he was a wild beast." Rabies can also cause persistent penile erections and hypersexuality, including reports of violent rapes. Laryngeal and facial spasms commonly result in an appearance of clenched teeth and retracted lips, which progresses to an inability to swallow secretions and frothing at the mouth.

It might also be mentioned that, in contrast to "furious rabies," paralytic rabies, which results in a progressive flacid paralysis, occurs in about 20% of those afflicted. Balkan legend holds that the "lying vampire" was "undead," whereas the "wandering vampire" was to be feared. And, as we all know, the vampire legend is tightly interwoven with bats, common carriers of rabies, as well as wolves and dogs (e.g., werewolves), which were both commonly affected during the rabies epidemics in 18th century central Europe. Now all we need is a skin snip from the nape of a vampire's neck to prove the theory correct. ■

Life in an Urban Wilderness

Source: California Disease Brief, October 1998;CDBRIEF@CAHWNET.GOV.

Having just spent considerable effort dissuading a family of raccoons from making a home in my attic, my attention was drawn to a recent California Communicable Disease Control Brief reporting a case of meningoencephalitis due to *Baylisascaris procyonis* in a one-year-old child in Monterey county. *B. procyonis* is an intestinal roundworm of raccoons in the United States, which rarely causes visceral larva migrans (VLM) and eosinophilic meningoencephalitis in humans. Although infection is apparently common in raccoons, only about 10 cases have been described in humans—most of whom were infants or small children (presumably as a result of their propensity to eat dirt).

Because their larvae are larger and have a greater tendency to migrate to the central nervous system than do feline or canine roundworms, infection with *B. procyonis* is often fatal or results in severe neurological sequelae. VLM should be considered in any small child with eosinophilic meningitis/encephalitis residing in an "urban wilderness." Because of the increasing migration of families to wooded areas on the fringe of large urban centers, we may start seeing more of these unusual zoonosis. ■