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Undetected Extended-Spectrum Beta-Lactamase and Failure of Cephalosporin Therapy

ABSTRACT & COMMENTARY

Synopsis: *Failure of antibiotic therapy may result from lack of laboratory detection of ESBL-producing Enterobacteriaceae.*

Source: Paterson DL, et al. Outcome of cephalosporin treatment for serious infections due to apparently susceptible organisms producing extended-spectrum B-lactamases: Implications for the clinical microbiology laboratory. *J Clin Microbiol.* 2001;39:2206-2212.

In the course of a multicenter observational study of *Klebsiella pneumoniae* bacteremia, Paterson and colleagues identified 85 organisms that produced extended-spectrum β-lactamases (ESBLs). Standard antibiotic susceptibility testing, however, had often failed to identify these organisms. The Table shows the actual proportion of isolates susceptible, intermediate, and resistant to cephalosporins (*see Table*).

Six patients with ESBL-producing strains were treated with a cephalosporin active according to routine in vitro testing (MIC ≤ 8 μg/mL). Two of these patients died of infection, and a third had clinical failure requiring a switch to meropenem. Three additional patients were treated with a cephalosporin to which the isolate showed intermediate susceptibility (MIC 16-32 μg/mL). One died, and the other 2 required alteration in therapy due to lack of clinical response.

Paterson et al identified a total of 32 patients with serious infections due to ESBL-producing *Klebsiella* species or *Escherichia coli* who received cephalosporin treatment, including 10 from centers participating in the bacteremia study and 22 reported in the literature. Eighty-three percent of patients were bacteremic. Fifteen of 28 patients (54%) had clinical failure when treated with a cephalosporin to which the infecting isolate was reported to be susceptible, as did all (4 of 4) of those treated with a cephalosporin to which the isolated showed intermediate susceptibility. Failure rates

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were significantly correlated with MIC: 100% (6 of 6) when the organism had an MIC of 8 µg/mL, compared with 27% when the MIC was < 2 µg/mL.

COMMENT BY ROBERT MUDER, MD

ESBLs produced by gram-negative bacilli have the ability to hydrolyze third-generation cephalosporins and aztreonam.[1] They are distinct from the chromosomal β-lactamases of *Enterobacter* and *Serratia*. ESBL-producing organisms are typically, but not universally, susceptible to cephamycins (ceftoxin, cefotetan), which are more resistant to ESBL-mediated hydrolysis than are cephalosporins. Resistance to carbapenems (imipenem, meropenem) is extrememly rare. ESBLs are located on plasmids, most frequently carried by *K pneumoniae*, although increasingly found in other Enterobacteriaceae as well. The widespread dissemination of ESBL-carrying gram-negative bacilli has paralleled the widespread use of cephalosporins.

A major issue with ESBLs is that susceptibility tests in routine clinical use often incorrectly report these organisms as susceptible to cephalosporins. In an attempt to improve identification of ESBL-producing organisms, the NCCLS recently established new guidelines for suscptibility testing of *K pneumoniae*, *K oxytoca*, and *E coli*.[2] These state that clinical laboratories should screen isolates with several third-generation cephalosporins. Isolates that show reduced zone diameter on disk susceptibility testing, or an MIC of > 1 µg/mL on broth dilution testing should undergo confirmatory testing. Isolates that show a greater than 4-fold reduction in MIC to a third-generation cephalosporin when clavulanate is added to the assay are confirmed as ESBL producers. The NCCLS recommends that these isolates be reported as resistant to all cephalosporins and penicillins, as well as to aztreonam.

These new recommendations are likely to lead to a considerable amount of additional work for most microbiology laboratories, as *Klebsiella* and *E coli* are extremely common organisms. Laboratories may be slow to adopt them citing cost concerns, and arguing that the data in the literature thus far does not definitively establish a relationship between ESBL production and clinical failure of cephalosporin therapy. I would argue that the data presented by Paterson et al represent fairly convincing observational evidence that cephalosporins are inadequate for treatment of serious infections caused by ESBL-producing organisms. Furthermore, outbreaks of nosocomial infection due to ESBL-producing Enterobactericeae are well documented.[3,4] Obviously, the resistant organisms must be identified before control measures can be implemented. Failure to do so may result in the establishment of endemic resistance in a facility, with adverse effects on patient outcomes and antibiotic costs. ❖

Table

Reported In Vitro Susceptibilities of ESBL-Producing *Klebsiella* Isolates

Antibiotic	Susceptible	Intermediate	Resistant
Cefepime	79%	4%	17%
Cefotaxime	49%	29%	22%
Ceftriaxone	36%	32%	32%
Ceftazidime	19%	8%	72%

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1. Paterson DL, Yu VL. Extended-spectrum B-lactamases: A call for improved detection and control. *Clin Infect Dis.* 1999;29:1419-1422.
2. NCCLS. Performance standards for antimicrobial susceptibility testin. Ninth informational supplement. Wayne, PA: National Committee for Clinical Laboratory Standards, 1999.

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3. Rice LB, et al. Ceftazidime-resistant *Klebsiella pneumoniae* isolates recovered at the Cleveland Department of Veterans Affairs Medical Center. *Clin Infect Dis.* 1996;23:118-124.
4. Lucet JC, et al. Control of a prolonged outbreak of extended-spectrum B-lactamase-producing enterobacteriaceae in a university hospital. *Clin Infect Dis.* 1999;29:1411-1418.

Do Antifungal Agents Provoke Bacteremia in Neutropenic Cancer Patients?

ABSTRACTS & COMMENTARY

Synopsis: *While this analysis of the EORTC trials database concludes, by multivariate analysis, that the administration of azole antifungal agents increases the risk of subsequent bacteremia in febrile neutropenic patients with malignancy, the validity of the results are questioned.*

Sources: Viscoli C, et al. Association between antifungal prophylaxis and rate of documented bacteremia in febrile neutropenic cancer patients. *Clin Infect Dis.* 2001;32:1532-1537; Wenzel RP, et al. Antifungal antibiotics and breakthrough bacteremias. *Clin Infect Dis.* 2001;32:1538-1539.

Viscoli and colleagues were intrigued by several reports that azole antifungal agents appeared to predispose neutropenic patients to developing bacteremia and by their own earlier observation that exposure to such agents was found to be an independent risk factor for bacteremia. Their position in the EORTC gave them access to a large uniform database containing 3080 records generated from similar trials that had been conducted during 1986 to 1994 to address the totally different question of which regimen was better for the empirical therapy of the febrile neutropenic patient. A diverse number of variables were included in the logistic regression model of the probability of detecting bacteremia with antifungal prophylaxis first being omitted and then included. This led to an improved model such that the odds ratio (OR) for receipt of absorbable antifungal agents for developing bacteremia was 1.41. Seven other factors gave higher ORs including shock, high temperature, and at least 1 day of granulocytopenia (*see Table*), while being older than 30 years of age yielded almost the same OR as absorbable antifungal agents. Factors that were less likely to be associated with bacteremia included hematological malignancies other than acute lymphoblastic leukemia (OR 0.64), granulocyte count < 0.1×10^9/L (OR 0.69), and antibacterial prophylaxis (OR 0.7). Hence, the results appear to support an association between the use of the absorbable azoles—ketoconazole, fluconazole, and itraconazole—and the occurrence of bacteremia suggesting that this may be clinically important.

The accompanying editorial by Wenzel and colleagues casts serious doubt upon this conclusion because of the failure to correct for confounding factors, the failure to estimate the risk for developing bacteremia that can be attributed to absorbable antifungal regimens, which turned out to be only 7% and, more importantly, the failure to offer any biologically plausible explanation for the phenomenon.

COMMENT BY J. PETER DONNELLY, PhD

Studies of this type are fashionable and it has become popular to try and distill evidence from large databases for or against an opinion, a long-held suspicion, an apparently common observation or, as in this case, an intriguing series of independent and unusual observations because PCs are ubiquitous, the necessary software is readily available, and it is relatively easy make use of existing databases. Granted, a professional statistician was intimately involved in Viscoli et al's study, but such an undertaking would have been just too time-consuming to do a decade ago to be considered worthwhile. That aside, what is the reader supposed to make of this and similar reports and how should they be placed in a proper context? Wenzel et al have done us a great ser-

Table
Factors Associated with Bacteremia Detection

Covariate	OR	95% CI	*P*
Shock	5.47	2.86-10.5	< 0.0001
Temperature ≥ 40°C	4.95	3.14-7.81	< 0.0001
> 15 days of granulocytopenia (< 0.5×10^9 cells/L)	2.63	1.52-4.57	< 0.0001
> 10 days in hospital	2.07	1.49-2.90	< 0.0001
Temperature 39.0-39.1°C	1.90	1.54-2.35	< 0.0001
Treatment for other than remission-induction	1.81	1.40-2.33	< 0.0001
1-15 days of granulocytopenia (< 0.5×10^9 cells/L)	1.64	1.02-2.61	0.04
Acute lymphoblastic leukemia	1.51	1.12-2.02	0.005
Absorbable antifungal agent	1.41	1.07-1.88	0.01
> 30 years of age	1.37	1.10-1.69	0.004

vice in critically appraising this study from an epidemiological standpoint. Their highlighting of the inadequate correction of confounding variables and their estimation of attributable risk help in this regard. However, even without their guidance, an amateur epidemiologist like myself would have had serious intuitive reservations since it is indeed hard to even begin to advance a biological explanation for the observation. Viscoli et al did admit to recognizing that the use of antifungal prophylaxis might be a marker for another factor but did not venture to suggest any. Might it not be that the drugs in question were only given to those patients likely to be at greater risk of developing bacteremia anyway because the intense treatment they received induced more mucosal damage which is associated with certain types of bacteremia? We were also not informed which bacteria were involved in bacteraemia, but one would guess that the Gram-positive cocci predominated over the Gram-negative bacilli given the fact that half the patients had been given antibacterial prophylaxis and, further, that the viridans streptococci, which are known to be associated with oral mucositis, would have been among the most frequent isolates. Indeed, had mucositis been included in the model we might have seen that this rather than antifungal prophylaxis was a risk factor. There is just no substitute for there being a biologically plausible basis for any association found between variables no matter how statistically significant. The temptation to think otherwise should be firmly resisted. ❖

Bone Cultures May be Helpful in Treating Osteomyelitis

ABSTRACT & COMMENTARY

Synopsis: *The results of underlying bone culture were not accurately predicted by those of overlying open wounds. While bone culture affected physician's choice of antimicrobial therapy, whether it affected outcomes was not studied.*

Source: Khatri G, et al. Effect of bone biopsy in guiding antimicrobial therapy of osteomyelitis complicating open wounds. *Am J Med Sci.* 2001;321:367-371.

The microbial ecology of infected human bone is complex, yet bone biopsy well performed can often guide what is otherwise purely empiric therapy. In this article, Khatri and colleagues attempt to address the microbial ecology of bone infections associated with open wounds.

Their approach was to review charts of patients who had bone cultures done during debridement. Khatri et al wanted to determine the usefulness of bone cultures in directing antimicrobial therapy. No attempt was made to study outcome.

Cases from 1994-1998 were reviewed. Osteomyelitis was determined to be present clinically if the physicians caring for the patient and/or the infectious diseases consultants made that diagnosis. In all, 44 biopsies were done: 22 in paraplegics, 5 in peripheral vascular disease, 1 in diabetes, and 18 had no reported diagnosis. Quantitative cultures were not performed but the bone to be biopsied was carefully cleaned to avoid contamination.

Biopsies yielded 53 isolates, 36 Gram-positive aerobes, 12 Gram-negative aerobes, and 5 anaerobes. A total of 31 isolates were found in bone but not in wound cultures. Only 13 isolates were found in bone that were-also isolated in wounds. *Staphylococcus aureus* was the most common isolate in bone and its presence in bone tended to reflect wound cultures. Yet in 6 cases, *S aureus* was present in bone and not in wound, 3 with MSSA and 3 with MRSA. Other species found in bone and not in wound included diphtheroids (8), *Pseudomonas* species (4), enterococci (3), *Bacterioides* species (3), *Acinetobacter* species (2), coagulase-negative staphylococci (2), and the MSSA and MRSA isolates mentioned.

In the 44 patients reviewed, bone biopsy cultures prompted a change in antibiotic therapy in 14 patients, antibiotics were discontinued in 6, coverage was in place to cover bone organisms in 10, and bone culture results were ignored in 14.

Bone cultures were negative in 11 cases, 5 of whom had antibiotics discontinued, 2 of whom had additional antibiotics added, and 3 of whom had the same agents continued. One patient was not on antibiotics at the time of the negative culture.

COMMENT BY JOSEPH F. JOHN, MD

Osteomyelitis is a difficult disease to study. Many of the published studies are flawed due to methodologic confounders. Yet due to the scarcity of data over the years, articles on osteomyelitis—though flawed—are readily published and often in good journals. Khatri et al have given us a focused study of an important subset of patients prone to osteomyelitis, albeit with some flaws. This study would have been strengthened if quantitative bone cultures had been performed. Bacteria that grew from thioglycollate broth—that we would assume were present in small quantities—were included in the study although were are not told how many organisms grew

from "thio" and were considered pathogens. Nevertheless, we may assume that organisms enumerated from bone were likely real since there was care taken during the biopsy to avoid contamination.

How does this study help us practitioners caring for these difficult patients? First it raises an old issue of the lack of value of overlying wound cultures. At the best, we can infer that if *S aureus* is part of the overlying flora, we probably should cover for that organism, paying attention to whether it is an MSSA and/or MRSA. However, up to 9-17% of *S aureus* isolates in wound will not be found in bone! Other organisms in wound culture matched bone isolates even more poorly, therein the strength of the study's findings. Disturbingly, there was an unduly large percentage of diphtheroids isolated from bone. Future studies will need to be done to determine if these Gram-positive rods of low virulence are emerging pathogens in contiguous osteomyelitis (the focus of this study) or only an aberration of the study population in question and culture techniques.

Many of the practitioners (we are not told the total of prescribers) in this study apparently believe the bone cultures as 20 of 44 resulted in discontinued or altered therapy and 10 of 44 in continuing the same therapy. Khatri et al point out that the bone cultures in this study were usually obtained at the time of a therapeutic debridement. For that reason, Khatri et al suggest encouraging the surgeon to perform cultures, as that may alter therapy in many cases.

Some ID physicians favor biopsying bone through unaffected tissue. A simple procedure popularized by Dr. Ben Lipsky in Seattle allows the physician to consider doing the biopsy using a small trephene biopsy needle.[1] Many a time in the last several years I wish I had skill of this procedure and could proceed to biopsy certain patients, particularly those with diabetic foot infections. On the other hand, many surgeons still are reluctant to biopsy bone through intact skin so patients with contiguous osteomyelitis still have to be managed in an individualized fashion. The work by Mader and colleagues emphasizes that nothing ensures success more than a good working relationship with a surgeon who will work closely with the infectious disease consultants.[2] Even more important than a correlation of wound bone cultures and its effect on antimicrobial prescribing would be a study that determined the effect of bone biopsy culture and clinical outcome. ❖

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1. Lipsky BA. Osteomyelitis of the foot in diabetic patients. *Clin Infect Dis.* 1997;25:1318-1326.
2. Mader JT, et al. A practical guide to the diagnosis and management of bone and joint infections. *Drugs.* 1997; 54:253-264.

Recombinant Granulocyte Colony-Stimulating Factor (rG-CSF) for Early-Onset Neonatal Sepsis

ABSTRACT & COMMENTARY

Synopsis: *A meta-analysis of clinical trials suggests that, while the routine use of rG-CSF cannot be currently recommended for all neonates with early onset sepsis, its use appears promising in the management of septic, low birth weight, and/or neutropenic neonates.*

Source: Bernstein HM, et al. Administration of recombinant granulocyte colony-stimulating factor to neonates with septicemia: A meta-analysis. *J Pediatr.* 2001;138:917-920.

A literature review of rg-csf for neonatal sepsis identified 5 studies (n = 20 to 44) deemed acceptable for inclusion in a meta-analysis to assess the effect of rG-CSF on mortality. Three studies were randomized and placebo-controlled, and 2 studies used historic controls. Two studies enrolled only patients weighing ≤ 1000 g, and 3 studies had no weight criterion. Four studies required neutropenia. The definition of early-onset sepsis was onset within 72 hours of birth in 3 studies and within 96 hours in 2 studies. None of the studies required a positive blood culture for diagnosis of sepsis. Among 73 rG-CSF recipients and 82 control subjects, mortality was lower among the rG-CSF recipients (odds ratio, 0.17; 95% CI, 0.03-0.70; $P < .05$). For subgroups of newborns < 2000 g or with neutropenia, the P value was .02. However, when the nonrandomized studies were excluded, the overall P value was .13.

COMMENT BY HAL B. JENSON, MD, FAAP

Several small studies of rG-CSF for neonatal sepsis have been reported, which have varied by use of placebo controls or historic controls, birth weights and gestational ages of subjects, and severity of illness at study entry. These factors may confound the ability to perform post hoc meta-analysis. Perhaps the most significant shortcoming of these original studies, and subsequently this meta-analysis, is that a positive blood culture was not required for diagnosis of sepsis. The diagnosis of early-

onset sepsis is often considered, especially in premature newborns, but infrequently confirmed by blood culture. It is likely that many cases of apparent sepsis in low-birth-weight premature newborns are the result of prematurity and may not result from bacterial infection. Also, this meta-analysis used an objective but crude outcome, of mortality, which might miss benefit of rG-CSF on reduced morbidity.

All 5 studies showed that rG-CSF was associated with at least a trend toward lower mortality, which persisted with meta-analysis of the 3 randomized, placebo-controlled studies. However, the low confidence interval (95% CI, 0.14-1.23) and the *P* value (*P* = .13) of meta-analysis of only these 3 studies suggest a low level of confidence in concluding benefit of rG-CSF in reducing mortality. Including the 2 studies with historic controls did show a significant reduction in mortality, but the inclusion of historic controls may bias the results and precludes routinely recommending rG-CSF for presumed early-onset neonatal sepsis at this time. Newborns with birth weight < 2000 g or with neutropenia appeared to benefit the most from rG-CSF. Additional studies or rG-CSF should incorporate these criteria into their design. ❖

Antibiotic Rotation—Worthwhile or Not?

ABSTRACT & COMMENTARY

Synopsis: *The value of planned antibiotic cycling in the reduction of antibiotic resistance remains unproved, but is the subject of a CDC-sponsored 3-center trial.*

Source: Vecchione A. Antibiotic rotation theory is still questionable. *Hospital Pharmacist Report.* 2001;6:31-32.

This special report reviews the concept of antibiotic rotation (also known as antibiotic cycling) and its role in reducing antibiotic resistance. The theory is that by restricting certain antibiotics for preset periods of time, the lessened exposure of microbes to those antibiotics should lessen the likelihood of resistance. Unfortunately, there is little support for this concept in the literature, and few hospitals have actually implemented antibiotic rotation programs.

Of the few studies performed, one of the largest that looked at antibiotic rotation was in the 1980s at the Veterans Administration Medical Center in Minnesota. Due to a problem they were having with gentamicin resistant organisms, they switched from gentamicin to another agent and the gentamicin resistance disappeared.

In order to shed some light on this concept, the Centers for Disease Control and Prevention (CDC) have initiated a 3-year study with 3 academic medical centers to evaluate the efficacy of a scheduled rotation of antibiotics in the intensive care unit. Participating in the study are the Washington University in St. Louis, Mo, the University of Virginia in Charlottesville, and the Rush-Presbyterian-St. Luke's Medical Center in Chicago, Ill. In this study, certain antibiotics will be rotated every 3-4 months. One of the key elements of this study will be to insure that patient care is not compromised as a result of antibiotic cycling. As a result, patient outcomes will be closely monitored to insure that length of stay and mortality do not trend in a negative direction. Other elements being studied are the cost factors associated with the cyclic rotation of antibiotics.

COMMENT BY THOMAS G. SCHLEIS, MS, RPh

Antibiotic cycling has always been an interesting concept, but no one has actually investigated it in enough detail to garner any wide-range support. That is why the CDC study is desperately needed to help answer many of these questions.

Antibiotic formularies at most hospitals are driven by acquisition cost, with the primary goal being to lower overall antibiotic expenditures. Often I have heard the term "antibiotic cycling" as an enticement to change formulary items to a less expensive antibiotic. Unfortunately, there is no really good science at this time to support this. In fact, should antibiotic rotation be recommended, I feel most hospital pharmacists would be concerned over the potential formulary cost increases. Cost increases would result when more expensive antibiotics are used in the "rotation," the loss of contract pricing because of lack of ability to commit to volume and market share, and the increased personnel time needed to implement rotations and provide educational support. Pharmacists will need to look "outside the box" to evaluate the overall cost of patient care—the cost of antibiotic rotation and the cost of antibiotic resistance—in order to decide whether implementation of such a program at their institution is warranted.

While most experts agree that antibiotic rotation may not be the complete solution to the resistance problem, they support studies such as the one being conducted by the CDC. It is hoped that this study will help determine if antibiotic rotation has merit and when and where it should be performed. (*Editor's*

Note: As this issue went to press, Puzniak and colleagues reported failure of scheduled antibiotic rotation to reduce the rate of acquisition of enteric vancomycin-resistant enterococci in an ICU [Puzniak LA, et al. Clin Infect Dis. 2001;33:151-157.]) ❖

CME Questions

1. **Which statement is true about the microbiology of contiguous osteomyelitis?**
   a. A superficial wound culture will reflect the underlying pathogens in bone.
   b. Bone cultures are usually sterile.
   c. Bone cultures often grow pathogens not seen in superficial cultures.
   d. The infection is nearly always polymicrobial and so the culture is of no use.

2. **A patient is admitted to the intensive care unit with nosocomial pneumonia after elective surgery. The patient is intubated and requires pressor support. Sputum and blood cultures yield *Klebsiella pneumonia* with the following MICs: ceftazidime, 16 µg/mL; ceftriaxone, 8 µg/mL; cefotaxime, 4 µg/mL; aztreonam, 4 µg/mL. Which of the following statements is most likely to be true?**
   a. The isolate produces an extended-spectrum β-lactamase (ESBL) and is likely to be susceptible to a penicillin/beta-lactamase inhibitor combination such as ampicillin/sulbactam.
   b. The isolate produces an ESBL but is fully susceptible to cefotaxime based on the results of in vitro susceptibility testing.
   c. The isolate is susceptible to meropenem.
   d. The isolate produces an ESBL but is fully susceptible to aztreonam based on the results of in vitro susceptibility testing.

3. **Which of the following is true?**
   a. Antibiotic rotation programs are proven to reduce antibiotic resistance.
   b. Antibiotic rotation programs have been investigated at most hospitals.
   c. Antibiotic rotation programs have been shown to reduce overall costs of patient care.
   d. Antibiotic rotation programs may increase antibiotic acquisition costs.

4. **Which of the following is correct?**
   a. The administration of rG-CSF is indicated in the management of all neonates with fever or other signs of sepsis.
   b. Low birth weight or neutropenic septic neonates appear most likely to benefit from receipt of rG-CSF.
   c. While the presence of cats may be considered a plague, feral felines are not a source of infection with the plague bacillus.
   d. Feline buboes constitute cat scratch disease.

In Future Issues:

A Wake-Up Call:
African Trypanosomiasis Strikes Back

UPDATES

By Carol A. Kemper, MD, FACP

Show-and-Tell: Look! My Dog has Rabies!

Source: ProMED-mail, March 2 and 5, 2001. Promed@promedmail.org.

A 9-week-old border collie subsequently diagnosed with rabies exposed more than 50 adults and small children in Mecklenburg County, North Carolina, this spring, many of whom required postexposure prophylaxis. The puppy was adopted by a couple with 2 small children in early February, and then attended 2 birthday parties and visited a local preschool for show-and-tell. Four days later, the puppy began showing increasing signs of illness and was euthanized. In retrospect, the puppy's behavior at the preschool was erratic—he had snapped and snarled at a couple of kids and then would run and hide—not exactly puppy behavior. DFA confirmed rabies; the strain appeared to be raccoon in origin.

Parents of 26 children at the preschool and the preschool staff, as well as 25 people from the birthday parties were requesting postexposure prophylaxis. Neither the breeder nor the family recalled seeing the puppy in association with wild animals or bats, and all of the other puppies in the litter were apparently without disease.

While cases of rabies in domestic animals have significantly decreased in past years, rabies among wild animals, especially raccoons, has increased ~20% since 1996 (Kuritzky L. *Infectious Disease Alert.* 2000;20:8). The only case of rabies in a domestic animal in the Bay Area in recent years occurred in an adopted stray cat, which unfortunately bit the family's 2-year-old child—the cat had likely been exposed to a rabid raccoon or skunk. Even in our neighborhood only 4 miles down the road from Stanford, raccoons and skunks make their nightly foray across the back deck, the coyotes are howling down in the canyon—and the cats are in and out all day—a perfect scenario for rabies transmission. Fortunately, rabies in domestic animals remains uncommon. ■

Kids Pick Up *Salmonella* from Owl Droppings

Source: http://www.salon.com/mwt/wire/2001/06/07/salmonella_outbreak. June 7, 2001.

Dozens of elementary school children in Washington County, Minnesota, developed salmonellosis after participating in a school project to learn what an owl eats. Apparently dissecting owl "pellets"—regurgitated food—is a great way for kids to learn more about owls and their prey. Owls typically dine on small rodents and mammals such as mice, voles, and shrews, although occasionally they will eat other animals like squirrels, snakes, frogs, birds, and skunks. A hungry owl will often swallow his prey whole. While the soft tissues are dissolved by gastric juices, the indigestible parts are packaged together as pellets and regurgitated several hours later. If you find an owl roost, you can often find the characteristic pellets on the ground beneath. The pellets typically contain bones, fur, and feathers and—often—whole skulls (http://www.conservation.state.mo.us/conmag/1998).

Like small detectives armed with zoology texts, kids can identify which animal met its fate by dissecting the pellets. This outbreak of salmonellosis was traced to an owl at a local nature center that provided droppings for the class project. One dissection apparently occurred in the cafeteria just before lunch—and the lunch table had not been immediately disinfected. Molecular studies subsequently confirmed that the salmonella isolated from the children matched an isolate obtained from the owl. ■

Feral Cats Transmit Plague

Source: ProMED-mail, June 26-28, 2001. Promed@promedmail.org.

Similar to other wild animals such as foxes and coyotes, cats and dogs are vulnerable to *Yersinia pestis* infection, which may be transmitted to humans. Once thought to be unusual, New Mexico, for example, has identified 294 cases of feline plague since 1977. The disease can be overlooked in cats as the swollen and draining buboes can easily be mistaken for typical cat-bite abscesses (Kemper CA. *Infectious Disease Alert.* 2000;19:176).

After identification of 2 feral cats with plague, Clark County Health District officials in Nevada have issued an alert to visitors and residents in the area (where 4 foxes and a coyote developed plague last year). And, authorities in Santa Fe County, New Mexico, where 3 cats with plague have been identified thus far this year, confirmed that a 21-year-old man is the first person to contract plague in the state this year. It is not clear if the man had contact with any infected cats.

Cats have been identified as the source of at least 15 cases of human plague infection in the United States. *Y pestis* can be transmitted to humans through the bite of an infected flea, the bite of an infected animal, or contact with draining buboes or inhalation of droplets from an infected animal (Gage K, et al. *Clin Infect Dis.* 2000;30:893-900). Transmission risk can be reduced by keeping your cats indoors, limiting their hunting of rodents, and good flea control. ■