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INFECTIOUS DISEASE ALERT®

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Physician-to-Patient HIV-1 Transmission

ABSTRACT & COMMENTARY

Source: Lot F, et al. *Ann Intern Med* 1999;130:1-6.

Reasonable evidence of possible transmission of hiv from medical personnel to patients has been limited to one well-publicized cluster of cases involving a dentist in Florida. Following the recognition of HIV infection in a 53-year-old orthopedic surgeon practicing in a Parisian suburb who presented with HIV encephalopathy in 1994, Lot and colleagues from France began attempts to contact 3004 former patients. It was believed that the surgeon had likely been infected while performing surgery 12 years earlier, and his CD4+ cell count on presentation was 46/mm^3. A total of 983 patients responded to letters requesting information regarding their HIV status or were referred for HIV testing.

Attempts to contact nonresponders were made by obtaining current addresses through the hospital registry or the French National Health Insurance Registry. In addition, with the agreement of the French Committee on Information and Privacy, all untested patients were "matched" to the National AIDS case registry.

Only one (0.1%) person with HIV infection was identified—a 67-year-old woman who had undergone a difficult 10-hour hip replacement in 1992 whose retroviral infection was recognized during a preoperative screen in 1994. Phylogenetic analysis revealed that the *env* sequences of the HIV from the patient and surgeon were similar and probably belonged to a unique and as-yet unidentified HIV-1 subtype.

On in-depth questioning, the surgeon reported frequent cutaneous blood exposures and almost weekly percutaneous injuries. His orthopedic surgical colleagues reported a similar frequency of percutaneous injuries, especially while suturing in a blind cavity or while placing metal wires or pins. Few, if any, of these exposures were reported. This remarkably high frequency of high-risk exposures was common to orthopedic surgeons and was not shared by other surgical subspecialties.

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INSIDE

COMMENT BY CAROL A. KEMPER, MD

Despite having performed thousands of surgical procedures, many of them high risk, during a period of time when he was probably viremic, only 0.1% of this surgeon's patients may have acquired HIV. It's reassuring to note that no other cases of HIV as the result of transmission from health care provider to patient have been documented to date. Nevertheless, these data suggest that physicians in specialties with frequent blood exposures should be aware of their HIV status and should take extra precautions to prevent transmission whenever possible. Improved reporting of percutaneous blood exposures should be encouraged.

A possibly more disturbing aspect of this story was the use of the French National Health Insurance system to track patients, especially those who had changed address or phone numbers or those who did not respond to the first direct mailing. Furthermore, the French National Committee on Information and Privacy gave Lot et al permission to examine the mandated National AIDS case registry in an attempt to match AIDS cases with the surgeon's list of patients who had not voluntarily reported for testing.

Not a single additional patient was identified through these measures. The ethical and scientific merits for the use of these patient databases in this instance should be carefully examined as we, in the United States, contemplate similar (supposedly, confidential) systems. One could argue that patients would want to know their potential risk and that the availability of successful therapeutic intervention provides a rationale for early case identification. However, based on the lack of documentation of any similar cases of HIV-1 transmission, despite thousands of surgeries and invasive procedures having been performed since the beginning of the HIV epidemic, the justification for the invasiveness of this investigation does not seem warranted. On the other hand, when is the sacrifice of civil liberties justified? How many lives is it worth? And who decides? I ask myself if I would have seen this article in a different light if, for example, 30 patients had been discovered, none of whom knew they were HIV infected. ❖

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Role of Streptococcal Infection in Tourette Syndrome and Other Neuropsychiatric Disease

ABSTRACTS & COMMENTARY

Synopsis: *PANDAS describes a group of neurologic disorders that appear to occur consequent to infection with streptococcus pyogenes.*

Sources: Singer HS, et al. *Neurology* 1998;50:1618-1624; Kurlan R. *Neurology* 1998;50:1530-1534; Garvey MA, et al. *J Child Neurol* 1998;13:413-423; Hall MC, et al. *J Child Neurol* 1998;13:354-356; DiFazio MP, et al. *J Child Neurol* 1998; 13:516-518; Sanberg PR, et al. *Lancet* 1998;352:705-706.

Since the original description of sydenham's chorea (SC) many decades ago, a growing appreciation has emerged of the complexity of neurologic disease that may be related to streptococcal infection. The acronym PANDAS (pediatric autoimmune neuropsychiatric disorders associated with streptococcal infection) is a relatively new diagnostic construct to describe this spectrum of disease.

Several investigators have presented converging lines of evidence for a role of streptococcal infection in triggering Tourette syndrome (TS), obsessive-compulsive disorder (OCD), and other neuropsychiatric disease. Using standard ELISA and Western blot techniques, Singer and colleagues tested serum from 41 patients with TS (33 boys, 8 girls; mean age 11.3 years) and 39 controls (22 boys, 17 girls; mean age 12.1 years) for

immune reactivity against human caudate, putamen, and globus pallidus. TS patients generated a significant increase in antineuronal antibodies, largely against putamen and caudate, compared to controls. Markers for streptococcal infection such as antistreptolysin O (ASO) titers were often equivocal.

DiFazio and colleagues reported three male patients, ages 5, 10, and 12 years, who developed a variety of myoclonic movement disorders associated with occult streptococcal infection. Only one patient was culture positive, but all had high ASO and anti-DNAase B titers. The myoclonus was effectively treated with erythromycin or penicillin, and recurred with subsequent reinfection with streptococcus. Similarly, Hall et al reported a case of an 11-year-old boy who, one week following group A beta-hemolytic streptococcal pharyngitis, developed paraparesis with a post-infectious encephalomyelitis. The patient responded well to antibiotics and corticosteroids.

Sanberg et al reported a retrospective case series of 13 Tourette's patients treated with the nicotinic antagonist mecamylamine 2.5-5 mg/d, alone or in combination with haloperidol or sertraline. Four were adults (one female; mean age 34 years) and nine were children (one female; mean age 14 years). Eleven of the 13 improved significantly in motor and vocal tics, as well as behavioral complaints such as irritability and aggression.

COMMENT BY BRIAN R. APATOFF, MD, PhD

Garvey et al and Kurlan provide excellent reviews of TS, tic disorders, and associated behavioral disturbance such as OCD that appear to arise from post-infectious autoimmune mechanisms. Thus, in addition to genetic factors that may determine a predisposition to TS, there appear to be important environmental triggers. An immune response generated against streptococcal antigens may crossreact with neuronal epitopes in the basal ganglia to cause neurological dysfunction. Trifiletti and colleagues at Cornell University Medical College have preliminarily identified a 83-kd brain protein by immunoblot analysis that seems to be recognized by antibodies in the serum of TS and OCD patients.[1]

The clinical therapeutic significance of these findings is important. Physicians now recognize the importance of penicillin prophylaxis for group A beta-hemolytic streptococcal infections in avoiding neurologic as well as cardiac complications. Undiagnosed streptococcal infection should always be considered in young patients presenting with new TS, OCD, SC, or other unusual movement disorders. Rather than using harsh neuroleptics for symptomatic management of TS or OCD, investigators are using immunomodulatory therapies such as corticosteroids, IVIG, and plasmapheresis with suggestion of benefit in small uncontrolled trials. Larger numbers of patients in carefully conducted studies will be required to assess the efficacy of these immune approaches that carry significant risks. Until then, pharmacologic agents such as the nicotinic drug mecamylamine may provide better symptomatic control. *(Dr. Apatoff is Assistant Professor of Neurology, New York Presbyterian Hospital-Cornell Campus.)* ❖

Reference

1. Trifiletti RR, et al. *Ann Neurol* 1998;44:561.

Intradermal Rabies Vaccination

ABSTRACT & COMMENTARY

Synopsis: *Children who received intradermal vaccination had lower rabies-neutralizing antibody levels than children intramuscularly immunized.*

Source: Sabchareon A, et al. *Pediatr Infect Dis J* 1998; 17:1001-1007.

Concerned about the high cost of intramuscular rabies vaccine in developing countries, researchers in Thailand compared intradermal (lower volume and, hence, lower cost) and intramuscular use of purified Vero cell rabies vaccine as pre-exposure prophylaxis in children. Three doses of vaccine were given during a 28-day period to each of 190 children, and a booster dose was given a year later. Follow-up data were available from 82% of children one year after the primary series and from 62% of children two years following the booster dose. Children who received intradermal vaccination had lower rabies-neutralizing antibody levels than children intramuscularly immunized. Nonetheless, "adequate" protective titers were achieved in nearly all (94-100% at the different times tested) children whether they received intradermal or intramuscular vaccine. Side effects were generally minor and were similar in each treatment group.

COMMENT BY PHILIP R. FISCHER, MD

Rabies is still a uniformly fatal illness, and there are more than 50,000 human deaths due to rabies each year. Most fatalities occur in children in Asia, South America, and Africa, and exposure to rabid dogs is responsible for more than 99% of human rabies deaths worldwide. Human rabies is almost always associated with an actual bite wound, though other more subtle exposures have

been reported. Control of animal rabies depends on vaccination of domestic dogs and elimination of stray dogs. Sadly, however, such control programs require heavy, ongoing expenditures.

Effective rabies vaccines are available. Pre-exposure vaccination provides significant protection and simplifies the post-exposure therapy by obviating the need for rabies immune globulin following exposure to rabies and by decreasing the number of needed post-exposure vaccine doses to two.

There are still, however, several controversial issues in regard to rabies vaccination. Who should be vaccinated? Which vaccine should be used? By which route should vaccine be administered? Cost is a significant factor in determining responses to these questions, and this study from Thailand is, therefore, helpful in identifying a lower cost means of effectively administering rabies vaccine to masses of children at risk of rabies in areas of limited financial resources.

The decision about whether to vaccinate a traveler depends on several individualized factors: age (more risk in children), planned activity (more risk in veterinary workers and spelunkers), destination (most risk in Latin America and Asia, only a few countries risk-free), duration of travel, access during travel to emergent administration of rabies immune globulin, and financial resources (as well as local cost of the pre-exposure vaccine that varies markedly from place to place). Whether immunized before the exposure, additional treatment is necessary following actual or presumed rabies exposure.

Until recently, there were two rabies vaccines available in the United States. Imovax is a human diploid cell rabies vaccine manufactured by Pasteur Merieux Connaught and has forms approved for intradermal and intramuscular use. Rabies Vaccine Adsorbed, produced by SmithKline Beecham, is available for intramuscular use. The FDA recently approved for marketing a new inactivated rabies vaccine (RabAvert, Chiron Corp.) that is grown in primary cultures of chicken fibroblasts. It is the first new vaccine against rabies to be introduced in almost 10 years and has been approved for both pre-exposure prophylaxis and post-exposure vaccination . A purified Vero cell rabies vaccine from Pasteur Merieux Connaught was used in the Thai study but is not currently available in the United States.

What antibody level is "protective" against rabies? The CDC and the WHO consider the lower limit of "protective" to be at different levels. By the higher WHO minimum protective titer, fewer Thai children achieved "adequate" levels, and the intramuscularly treated children were more likely to have "adequate" protection. By the CDC criterion, "protection" was almost always achieved, and there was no difference in efficacy between the two routes of administration. The Thai study provides evidence that the intradermal route will be widely effective and could find generalized use in developing country areas with limited financial resources. It is doubtful, however, that wealthier travelers would choose a route of administration that clearly prompts lower antibody levels that are not uniformly considered to be protective. If cost factors lead travelers to consider the intradermal route of this purified Vero cell rabies vaccine when it becomes available, travel medicine practitioners might, nonetheless, advise intramuscular use in travelers at risk of blunted anti-rabies immune responses (immunosuppressed individuals and individuals who must take chloroquine or similar antimalarials during the course of the rabies vaccination).

Children in the Thai study responded well to a booster dose regardless of their pre-booster antibody titer, and side effects were more common after the booster doses. It could be, as Sabchareon and colleagues point out, that repeated pre-exposure booster doses will not be needed in individuals who can have reasonable access to the two-dose post-exposure vaccination in the event of an animal bite.

This report is useful in leading the way to more affordable rabies prevention in financially challenged areas of the world. *(Dr. Fischer is Associate Professor of Pediatrics, Department of Pediatric & Adolescent Medicine, Mayo Clinic, Rochester, MN.)* ❖

Outcome of Children with Pneumonia in the Era of Penicillin-Resistant *Streptococcus pneumoniae*

ABSTRACT & COMMENTARY

Synopsis: *There was no apparent difference in outcomes of children with pneumonia due to either penicillin-susceptible or penicillin-resistant pneumococci.*

Source: Tan TQ, et al. *Pediatrics* 1998;102:1369-1375.

In this study, the "united states pediatric multicenter Pneumococcal Surveillance Study Group" reported on the clinical characteristics, treatment, and outcome of pediatric patients with pneumonia caused by penicillin susceptible and penicillin-nonsusceptible

Streptococcus pneumoniae. Eight pediatric hospitals from around the country prospectively identified 254 patients with pneumococcal pneumonia between September 1993 and August 1996. Pneumococcal pneumonia was diagnosed based on chest x-ray findings and a positive blood or pleural fluid culture. Of the 254 patients, 189 (74%) were hospitalized. The hospitalized patients were more likely to have underlying illnesses, multiple lobe involvement, and pleural effusions.

Of the 257 *S. pneumoniae* isolates, 14% were nonsusceptible to penicillin (8% intermediately resistant and 6% resistant), and 5% were nonsusceptible to cefriaxone. There were no significant differences for duration of fever, oxygen requirement, WBC count, underlying disease, x-ray findings, or hospitalization rates between the penicillin-susceptible and penicillin-nonsusceptible groups.

There was also no significant difference in outcome between the penicillin-susceptible and penicillin-nonsusceptible groups. Ninety-eight percent of the 254 patients had a good response to therapy. All six children with poor outcomes had underlying illnesses (1 had a penicillin-resistant isolate).

COMMENT BY LEONARD FRIEDLAND, MD

The increasing prevalence of isolates of *S. pneumoniae* that are resistant to penicillin and other antibiotics affect our current treatment of common bacterial diseases caused by *S. pneumoniae*, such as otitis media and community-acquired pneumonia. In this recent study from sites throughout the United States, clinical characteristics and patient outcome did not differ between children with pneumonia attributable to penicillin-susceptible and penicillin-nonsusceptible *S. pneumoniae*.

What antibiotic regimen should be used for the treatment of infections caused by penicillin-resistant *S. pneumoniae*? The specific doses of antimicrobial agents used in study patients are not presented. However, we are told that in the group treated as outpatients, 80% received a dose of parenteral second- or third-generation cephalosporin followed by a course of oral antibiotic, 17% were treated with oral beta-lactam antibiotic alone, and 3% with oral nonbeta-lactam antibiotic alone. In the group hospitalized, 48% received a dose of parenteral second- or third-generation cephalosporin followed by a course of oral antibiotic. All the children without underlying illnesses responded well to what appears to be standard antimicrobial therapy.

Information I have gleaned from the literature and attending conferences indicates that standard doses of amoxicillin, amoxicillin with clavulinic acid, and cephalosporins can exceed the MIC of resistant strains of *S. pneumoniae*. Despite this, many infectious disease experts now recommend that high doses of oral antibiotics be used to treat *S. pneumoniae* infections (e.g., treating an episode of acute otitis media with 80 mg/kg/d of amoxicillin). The rationale behind this recommendation is to clearly exceed the MIC of the resistant strain. I expect to report again on this topic as the prevalence of *S. pneumoniae* antibiotic resistance continues to increase. *(Dr. Friedland is Associate Professor of Pediatrics and Medicine, Temple University School of Medicine, Director of Pediatric Emergency Medicine, Temple University Children's Medical Center, Philadelphia, PA.)* ❖

Salmonella bacteremia in Southern Viet Nam

ABSTRACT & COMMENTARY

Synopsis: *Multidrug-resistant Salmonella typhi is a frequent cause of community-acquired septicemia in southern Viet Nam. As tourism to this part of southeast Asia increases, typhoid fever should be carefully considered in the differential diagnosis of febrile patients returning from the area. Multidrug resistant strains and potentially high mortality rates associated with them should be of concern to travel medicine practitioners.*

Source: Hoa NTT, et al. *Trans Royal Soc Trop Med Hyg* 1998;92:503-508.

A prospective study of community-acquired bacteremia was conducted from mid-1993 to 1994 in southern Viet Nam. Patients were evaluated at the Centre for Tropical Diseases, Cho Quan Hospital, in Ho Chi Minh City. The microbiology, clinical features, and outcome were compared with studies from other developing countries. During this one-year study period, 3783 blood culture sets were obtained from 3365 patients. Five hundred eighteen had positive cultures (15.3%) and the isolate was considered a community-acquired, clinically significant non-contaminant in 437 patients (13%). Anaerobic blood cultures were not performed as a part of this study. The incidence of bacteremia detected was 20.4 episodes per 1000 admissions. Gram-negative aerobes (facultative organisms) accounted for 90% of all isolates in documented cases of bacteremia. *Salmonella typhi* caused 67% (309 cases) and *Salmonella paratyphi* A accounted for 3%. Seventy percent of *S. typhi* were multidrug-resistant (MDR-resistant to chloramphenicol, co-trimoxazole, ampicillin, and tetracycline), and 4%

were resistant to nalidixic acid. Three patients were co-infected with both *S. typhi* and *Plasmodium falciparum*.

The clinical features and outcomes for those patients with *Salmonella*-associated enteric fever were compared with those of patients with other types of bacteremia. The patients with enteric fever were younger than patients with nonenteric fever (median age of 16 years vs 43 years). The median duration of illness before admission was 10 days for enteric fevers, which was longer than the duration of illness for other types of Gram-negative and Gram-positive bacteremia (4-5 days). Thirty-five percent of patients with enteric fever had diarrhea. Severe disease (with shock, impaired consciousness, gastrointestinal bleeding, intestinal perforation, renal failure, or jaundice) developed in 9% of the patients with enteric fever. However, severely ill patients were often admitted to other hospitals in the city. The mortality rate was lower in the patients with enteric fever than the patients with other forms of bacteremia (0.3% vs 23%).

The proportion of community-acquired bacteremia due to *Salmonella* sp. was compared with studies from other developing countries. *Salmonella* sp. caused an unusually high (72%) proportion of bacteremia in Viet Nam. In contrast to the current study, Hoa and associates cited a report on enteric fever in Thai children that had shown a decline of typhoid fever. This trend was attributed to improved hygiene and sanitation as well as the parenteral typhoid vaccination program for children that began in Thailand in 1977.[1]

COMMENT BY LIN H. CHEN, MD

Enteric fever is a major health problem in many developing countries and refers to both typhoid fever and paratyphoid fever. The current study of mostly urban patients from southern Viet Nam shows a strikingly high proportion of *Salmonella sp.*, especially *S. typhi*, causing community-acquired bacteremia. By comparison, a report from Hong Kong showed *Salmonella sp.* caused 27% of community-acquired bacteremia in children, and *S. typhi* accounted for only one-third of these infections.[2] Travelers to southern Viet Nam appear to have a significant risk of potentially returning with typhoid fever, particularly given the median duration of illness of 10 days ensuing prior to admission. This is an area of the world where HIV is just beginning to emerge and the proportion of Salmonella-associated bacteremia due to nontyphoidal strains may increase as it has in Africa with the AIDS pandemic.

Epidemics of MDR *S. typhi* have been reported from numerous countries.[3,4] MDR *S. typhi* has unfortunately been associated with a higher mortality than infection with susceptible strains,[3] and it is alarming that a majority of the strains in the current report (70%) were MDR strains. It is also of concern that nalidixic acid-resistance is emerging, since the quinolone antibiotics have been widely and effectively used to treat multidrug-resistant typhoid fever.[5]

Given the high proportion of bacteremia caused by *S. typhi*, the high percentage of MDR strains, and the emergence of quinolone resistance, travelers to southern Viet Nam should be particularly cautious regarding typhoid fever. Although food and water precautions are the most important preventive measures, an aggressive approach toward typhoid vaccination appears to be warranted for travelers to southern Viet Nam. Unfortunately, a large inoculum of *S. typhi* can overcome the protective effects of typhoid vaccines, and typhoid fever should remain high in the differential diagnosis of febrile travelers returning from Viet Nam, even if they have received typhoid vaccine. *(Dr. Chen is Clinical Instructor, Harvard Medical School and Travel/Tropical Medicine Clinic, Lahey Hitchcock Medical Center.)* ❖

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3. Bhutta ZA, et al. *Rev Infect Dis* 1991;13:832-836.
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5. Wain J, et al. *Clin Infect Dis* 1997;25:1404-1410.

Brief Report

Tuberculin Skin Test Screening in College Students

Source: Hennessey KA, et al. *JAMA* 1998;280:2008-2012.

Concerns about the spread of tuberculosis on college campuses because of the prolonged close contact college students have with each other have prompted some schools to require skin testing of their students before matriculation. However, little is known about the extent of tuberculin testing at American colleges and universities. Hennessey and colleagues at the Centers for Disease Control and Prevention in Atlanta conducted a national survey of tuberculin skin testing procedures and results of screening in colleges and universities in the United States in 1992-1996. A stratified, randomized sample of 624 U.S. two- and four-year col-

leges responded to a self-administered mail and telephone questionnaire concerning whether tuberculin testing was required, the type of skin test, and the number and rate of students with positive skin test results and/or diagnosed as having tuberculosis.

Overall, 378 of 624 (61%) schools required tuberculin testing. It was required for all new students (both U.S. and international students) in 26% of schools; and all new international but not new U.S. residents in 8% of schools. Forty-seven percent of schools required tuberculin testing for students enrolled in specific academic programs such as health care, education, and social work. Tuberculin testing requirements were more likely in four-year compared to two-year schools, and in schools that had a student health clinic. Exemptions from required testing were permitted in 85% of schools for reasons such as reports of prior positive skin test results, a history of BCG vaccination, or religious reasons. Tine or multiple puncture tests were accepted in 25% of schools.

Analysis of screening results was limited to 168 schools that required screening, accepted the Mantoux skin test only, and reported results of their screening programs. A total of 348,368 students were screened and 3.1% of these had a positive test result. The skin positivity rate for U.S. residents was 1.1 per 100,000 students screened; the rate for international students was 35.2 per 100,000 students screened. During the four-year period of the study, 114 cases of active tuberculosis were reported from 68 (11%) of the 624 schools surveyed. Of these 114 cases, only 32 cases were identified as a result of required tuberculin screening and 26% of these cases were in foreign-born students.

Hennessey et al conclude that universal screening of the general American college student population should not be done. Instead, students at higher risk, such as international or foreign-born students from countries with high rates of tuberculosis, students working in health care settings, and immunocompromised students, should be tested. Further, only the Mantoux method of skin testing should be used. Because tuberculin reactivity as a result of receiving BCG wanes over time and rarely persists more than 10 years after vaccination,[1] students with a history of BCG vaccination, most of whom come from high-risk areas of the world, should be included in any tuberculin skin test screening requirements. *(Dr. Louis M. Bell is Associate Professor of Pediatrics, Infectious Diseases, University of Pennsylvania School of Medicine, Philadelphia, PA.)* ❖

Reference

1. Centers for Disease Control and Prevention. *MMWR Morb Mortal Wkly Rep* 1996;45(RR-4):1-18.

CME Questions

9. Recent investigations have demonstrated a relationship between streptococcal infection and auto-immune-precipitated neurological disease in children. Which of the following disorders has *not* been verified in this respect?

a. Chorea
b. Recurrent myoclonus
c. Tourette syndrome
d. Generalized epilepsy
e. Myelitis

10. Effective pre-exposure rabies vaccination:

a. is currently available by both intradermal and intramuscular routes.
b. obviates the need for post-exposure rabies vaccination.
c. may be given by either intradermal or intramuscular routes using each of the vaccine preparations available in the United States.
d. is routinely given to children in developing countries.

11. All of the following statements comparing the children with pneumonia attributable to penicillin-susceptible and penicillin-nonsusceptible *Streptococcus pneumoniae* are true *except*:

a. Clinical characteristics did not differ.
b. Patient outcome did not differ.
c. Hospitalization rates did differ.
d. Chest x-ray findings did not differ.

12. Which one of the following statements is correct?

a. *Salmonella typhi* is still universally susceptible to fluoroquinolone antibiotics.
b. Vaccination programs and improved hygiene have decreased the incidence of typhoid fever in some developing countries.
c. Fluoroquinolones should be used to treat multidrug-resistant and nalidixic acid-resistant *Salmonella typhi* infections.
d. Typhoid vaccines would generally eliminate all possibility of clinical infections associated with *Salmonella typhi*.
e. The prevalence of *Salmonella typhi*, as opposed to non-typhoidal *Salmonella*, infections increases in association with HIV-incidence.

13. Tuberculin testing of students at American colleges and universities:

a. is mandatory in more than half of institutions.
b. usually uses tine or multiple puncture tests.
c. usually reveals positive results in students who received BCG in infancy.
d. reveals a lower rate of positivity in international as opposed to native-born students.

In Future Issues:

Summaries of the 6th Conference on Retroviruses and Opportunistic Infections

UPDATES

By Carol A. Kemper, MD

False-Positive HIV-1 RNA Results

Source: Rich JD, et al. *Ann Intern Med* 1999;130:37-39.

Rich and colleagues describe three probable cases of falsely-positive HIV RNA test results. Levels of plasma HIV-1 were low in all cases, ranging from 1254-1574 copies/mL. Case 1 was a healthy 12-year-old boy who had previously tested HIV-negative on multiple occasions following perinatal exposure to HIV. Following an episode of herpes zoster, a single positive HIV-1 RNA (using the BDNA assay) was obtained, but all further studies and repeat RNAs were negative. Case 2 was a healthy 40-year-old woman who had a positive HIV RNA test result (using BDNA) following unprotected sex with an HIV-positive male partner. All other studies remained negative and three subsequent HIV-RNA tests were negative. Case 3 was a bit more complex—a 20-year-old woman whose only risk factor was heterosexual sex, had positive HIV ELISA and indeterminate western blot test results on at least two occasions. Repeat studies five months later were negative, but a single HIV-RNA was positive (using RT PCR). Repeat studies remained negative six months later.

None of these patients were believed to be HIV-infected, although there were no further attempts to investigate this possibility. Rich et al argue that only one of these patients had recent significant HIV risk factors and each had only one RNA test result that was positive, raising the possibility of laboratory error or specimen mix-up. In addition, low viral test results are inconsistent with those typically observed in primary HIV infection or in long-standing disease.

On the other hand, consideration should be given to the possibility that these patients may have had transient viremia. Six patients were recently described with HIV-1 viremia despite persistent seronegativity (Sixth Retrovirus Conference. Chicago, IL. *Abstract #52*). Peripheral blood mononuclear cells from all six patients failed to produce antibodies to HIV-1 in vitro.

While it may be tempting to use HIV RNA as a "screening" tool, and there are certainly instances when it may seem desirable, consideration of the pre-test probability and a certain degree of circumspection is required when evaluating discrepant test results. ■

Infected Bite Wounds

Source: Talan DA, et al. *N Engl J Med* 1999;340:84-92.

A surgeon friend was recently bit on the right hand by a small (but territorial) dachshund, and wondered if he should take prophylactic antibiotics. He sustained only three small but relatively deep puncture wounds, which were promptly washed with soap and water. Should he have been given antibiotics preemptively and, if so, with what?

Talan and colleagues describe an amazing constellation of bacteria found in infected bites wounds inflicted by cats and dogs. Fifty patients with dog bites and 57 patients with cat bites were evaluated by 18 different emergency rooms throughout the United States. More than one-half of the bites occurred on the hands. About two-thirds were puncture wounds, 3% were lacerations, and the remainder were both. Tendon involvement occurred in 19% and one infection involved the finger joint. Lymphangitis was present in 44%, and nearly one-half of the wounds required incision and drainage and/or debridement. One-third of the patients were initially hospitalized for parenteral antibiotics.

Mixed aerobic and anaerobic infections were found in 63% of cat wounds and 48% of dog bites, with an average of five different organisms found in each wound. Even nonpurulent dog wounds grew an average of two different organisms (range, 0-9), and nonpurulent cat wounds grew five (range, 0-12). Only 7% of the cultures had no growth. *Pasteurella* species were the most frequently identified isolates from both dog (50%) and cat bites (75%). Common aerobic species found in 10% or more of wounds included various *Streptococcus*, *Staphylococcus*, *Neisseria*, and *Moraxella* species. *Fusobacterium*, *Bacteroides*, *Porphyromonas*, *Prevotella*, and *Propionibacterium* were common anaerobic isolates (> 10%). *Capnocytophaga* was isolated from 7% of cat bites and 2% of dog bites. A number of organisms not previously associated with bites or human infection were identified, including *Reimerellea anatipestifer*—a pathogen related to weeksella and *Capnocytophaga* which causes sepsis in birds (one can only imagine what the bird looked like).

The reference laboratory was much more successful than local laboratories at isolating organisms: while the reference lab was able to isolate a median of five organisms per wound, the local laboratories cultured an average of only one and negative cultures were twice as frequent.

All but four patients improved with antimicrobial therapy, each of whom initially received a first-generation cephalosporin. The most successful regimens included a beta-lactam plus a beta-lactamase inhibitor, a combination of penicillin plus a first-generation cephalosporin, or clindamycin plus a flouroquinolone. Although the microbial flora of bite wounds is much more varied and complex than previously understood, appropriate antibiotics such as augmentin or trovafloxacin coupled with aggressive debridement as needed, are adequate for most infected dog and cat bites. We are also reminded that prophylactic antibiotics are recommended for any high-risk wounds (especially deep puncture wounds from cat bites) or wounds that require surgical repair—or those that involve the hands! ■