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Outpatient Parenteral Antibiotic Therapy—What's the Risk?

ABSTRACT & COMMENTARY

Source: Hoffman-Terry ML, et al. Adverse effects of outpatient parenteral antibiotic therapy. *Am J Med* 1999;106:44-49.

Hoffman-terry and colleagues report a series of 269 patients who received 291 courses of outpatient parenteral antimicrobial therapy (OPAT) over two years. This was a retrospective study of patients treated through the Thomas Jefferson University Hospital Home Infusion Program in Philadelphia during 1992 and 1993. Their model was self-administration through a hospital-based OPAT program. All patients were initially hospitalized. Patients were seen two or three times per week by nurses of the infusion service and by the prescribing doctor as deemed necessary. Blood monitoring specimens were drawn at least weekly in the home. Medications were delivered on a weekly basis.

The average age was 49 years, although ages ranged from newborn to 86 years of age. Most patients had complicating medical illnesses (81%). The mean duration of therapy was 40 days with a median of 42 and a range from three to 141 days. The majority of patients were treated for bone and joint infections (59%), followed by endovascular infections (16%), and abscesses (9%). Patients with HIV were excluded. Nearly half of the patients received more than one intravenous antibiotic. Vancomycin was the most frequently prescribed antibiotic, with beta-lactams second.

Hoffman-Terry et al did a detailed chart review with careful assessment of a number of factors that were linked to adverse effects. They defined "leukopenia" as a total leukocyte count of 4000 per mm^3 or less, "neutropenia" as an absolute neutrophil count of 1500 per mm^3 or less, and "eosinophilia" as an absolute eosinophil count of 500 per mm^3 or more. "Thrombocytopenia" was defined as a total platelet count of 140,000 mcg or less. Nephrotoxicity was defined as an increase in creatinine concentration of 1 mg/dL or more if the baseline serum creatinine was less than 3 mg/dL or an increase of 0.5 mg/dL or more if the creatinine was more than 3 mg/dL.

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Hoffman-Terry et al found a surprisingly high incidence of adverse effects and problems during the OPAT program. The most frequent problems were leukopenia and eosinophilia—which occurred in 16% and 12% of cases, respectively. Venous access was a problem in 31 (11%) cases, with 12 patients requiring hospitalization. The fourth most frequent problem was nephrotoxicity, which occurred in 8%, followed by diarrhea, which was noted in 7% of patients.

Twenty-two patients required rehospitalization, 12 for venous access-related problems. Four patients died during therapy, but in no case were the deaths attributed to complications of infusion therapy.

COMMENT BY ALAN D. TICE, MD

This study reinforces the concern that OPAT has as many or more associated adverse effects as intravenous antibiotic therapy in the hospital. Complications and problems of OPAT have been reported previously but investigations have not been as detailed as this one.[1,2]

Of concern is the finding that many of the adverse effects occurred well into the course of therapy. The mean time until leukopenia and eosinophilia were found was 30 days. Even the rashes appeared after an average of 29 days. Diarrhea and vomiting did not become a problem until 18 and 19 days, respectively. This points out the need for increased vigilance and close physician monitoring late in the course of therapy—even though the patient may be improving from an infection standpoint.[3]

Blood was drawn weekly to monitor for toxicity. This is the minimum frequency recommended by the guidelines of the Infectious Diseases Society of America (IDSA).[4] It is also of concern that there were no standards for physician follow-up visits. The IDSA guidelines recommend these visits should be at least weekly as well.

Hoffman-Terry et al also recognized the problems with vascular access with complications in 11% of 180 permanent indwelling catheters. Thirteen of them had to be removed. Peripherally inserted central catheters (PICCs) had a lower complication rate (9 of 99), seven required removal. Five percent of permanent in-dwelling catheters and 3% of PICCs had complications that required rehospitalization.

This study points out the relatively high incidence of side effects and problems with intravenous therapy. While they may be no greater than in the hospitalized patient, the ability to evaluate and control them outside the hospital is considerably less—particularly if there is not close follow-up by a knowledgeable physician. In addition to the usual side effects of antibiotics, vascular access is a significant problem and may cause life-threatening complications, such as sepsis and central vein thrombosis. It is notable that approximately 4% of the patients were rehospitalized because of vascular access problems and complications. This poses a significant risk to patients who are not seen by a physician on a regular basis and who may be receiving potentially toxic medications. As the financial incentive to send people home on OPAT increases, the concerns about the quality of care and monitoring for even the expected problems may become lax.

As for infectious disease specialists, this article raises further concerns about who is to manage OPAT and what the role of the physician should be. On the one hand, infectious disease physicians are sought for responsibility and liability for OPAT but they are often not compensated for their efforts and risks. This points to the need to set and follow standards for monitoring in the infectious diseases community in regard to the care and quality assurance for these patients—particularly as the compensation for OPAT and patient care continue to decline. ❖

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STD Risk Reduction: One Size Doesn't Fit All

ABSTRACT & COMMENTARY

Synopsis: *Behavioral intervention with high-risk populations of women of color, in which cultural and gender-specific issues were considered, proved to significantly decrease the rate of STD infection and/or reinfection by almost 40%.*

Source: Shain RN, et al. A randomized, controlled trial of a behavioral intervention to prevent sexually transmitted disease among minority women. *N Engl J Med* 1999;340:93-100.

Growing numbers of african-american and latina patients are becoming infected with STDs such as chlamydia, gonorrhea, syphilis, trichomoniasis, and HIV. In an effort to reduce infection rates among high-risk populations of women of color, Shain and colleagues designed and implemented a behavioral intervention adapted from the AIDS Reduction Model. This model is based on the integration of several social and psychological theories (e.g., the Health Belief Model,[1] self-efficacy theory,[2] decision-making models,[3] and diffusion theory[4]). For this study, the AIDS Reduction Model was further modified with extensive ethnographic data on the study's target population—English-speaking, African-American, and Mexican-American females with a nonviral STD. Ethnographic data were collected over a period of approximately 18 months through 25 focus-group interviews and 102 in-depth interviews. Extensive observations of the communities were also conducted.

In all, 424 Mexican-American and 193 African-American female participants were enrolled in the study. Of the 617 participants, 304 women were randomly assigned to the control group and 313 women to the intervention group. Overall, 71% of the women were 24 years old or younger (range, 14-45 years of age) and most had low levels of formal education and income.

The women in the control group received standard individual counseling (a one-on-one counseling session usually lasting 15 minutes), with an invitation to participate in the group intervention at the completion of the study.

Women in the intervention group attended three group sessions that addressed recognition of their own risk, a commitment to change their behavior, and acquisition of new skills. The average group size was five or six women (range, 3-12) and they met once a week for three or four hours over a three-week period. Each group was led by a female facilitator. The facilitator and participants in each group were the same ethnicity.

Activities in the sessions consisted of group discussions, role playing, watching videos, and modeling changes in behavior. Each of these activities was further modified and enhanced by the ethnographic information that had been gathered, allowing the session leaders to include cultural- and gender-specific issues in the intervention. For example, in the groups for Mexican-American women, the concept of "machismo" was discussed, as was recognition that sexual enjoyment is appropriate for women. In the African-American groups, the belief that the HIV virus was purposefully introduced into the African-American community was discussed. And all of the groups discussed what women want from relationships, what they derive, and why they may tolerate poor behavior from their partners. Triggers for unsafe sex were identified and discussed. All participants were screened for chlamydia, gonorrhea, trichomoniasis, and syphilis at baseline and at 6 and 12 months, as well as in the event of any gynecological symptoms, to assess the success of the intervention. HIV testing was offered at each visit.

Retention rates in both the study group and the control group were high (more than 80%) at both the six-month and 12-month follow-up visits. The intervention ultimately proved to be effective and long lasting. At the six-month follow-up, the infection rate of the intervention group was 34% less than that of the control group (11.3% vs 17.2%; P = 0.05); at 12 months, it was 49% less (9.1% vs 17.7%; P = 0.008); and overall, the intervention group's rate of infection was 38% less than that of the control group. Furthermore, women in the intervention group were less likely to have multiple sex partners and/or to engage in high-risk sex.

COMMENT BY SAMANTHA BROUN, EdM

The findings of this study are important for a number of reasons. First, while changes in sexual behavior are imperative in reducing the rate of infection and reinfection, most behavioral interventions do little more than

give participants concrete facts about risky behavior and possible alternatives. Information alone rarely results in changes in behavior. This intervention, however, provided participants with group support, opportunities to participate in discussions, and exercises that allowed them to practice newly gained skills. In addition, although the goal of this study was to reduce the risk of repeated STD infection, its results may provide insight into effective interventions for also reducing the risk of infection with HIV.

Secondly, surprisingly few behavioral studies incorporate clinical end points to assess their success in changing sexual behaviors. The effectiveness of this study was not only measured by reported changes in behavior, but by actual reduction in STDs. In this way, reported changes in behavior could be more accurately compared to actual clinical outcomes.

And third, this intervention is important for the mere fact that not only does it acknowledge the importance of *what* disease the patient is dealing with but also *who* the patient is. Ethnographic information increases the sense of understanding between practitioners and their patients and may provide practitioners insight into the specific cultural and social roots of certain behaviors. What may have previously been seen as an irrational risk-taking behavior may make more sense given its proper cultural context. And, by incorporating gender-specific and culturally relevant issues into interventions, participants may identify more closely with intervention curriculums and feel less resistant and more supported in making changes.

Hines and Caetano take this notion a step further. In their study on Latino men and women and the effects alcohol may have on risky sexual behavior, they suggest that perception of risk and engagement in risk-taking behavior are related to levels of acculturation[5] (i.e., the varying degree of change in cultural orientation of Latinos as they adapt to American culture). Furthermore, levels of acculturation affect men and women differently. In some cases, greater levels of acculturation mean greater risk-taking behaviors. For example, research has shown that there is an increase in the number of sexual partners for both Latino men and women the more acculturated they are to U.S. culture. Therefore, Hines and Caetano suggest that the design and focus of intervention and prevention programs should vary according to the gender, ethnicity, and the level of acculturation of its participants.

The keys to the success of Shain and colleagues' intervention were: 1) its format—group sessions with all the participants of the same gender and ethnic group; 2) repeated group session interventions over time; and, perhaps most importantly, 3) the intervention was based on specific qualitative and ethnographic data of the target population. Ultimately, using ethnographic data can only contribute to creating a more holistic, healthy, and responsive health care system. (*Samantha Broun is Study Coordinator and Research Assistant, Positive PACE Clinic, Santa Clara Valley Medical Center, San Jose, CA.*) ❖

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Update on Otitis Media Treatment

ABSTRACT & COMMENTARY

Synopsis: *An expert group convened by the Centers for Disease Control and Prevention addressed key questions related to treatment of otitis media in the current circumstances of increasing drug-resistant Streptococcus pneumoniae.*

Source: Dowell SF, et al. Acute otitis media: Management and surveillance in an era of pneumococcal resistance—A report from the drug-resistant *Streptococcus pneumoniae* Therapeutic Working Group. *Pediatr Infect Dis J* 1999;18:1-9.

Published and unpublished data summarized from the scientific literature and from the experience of more than 30 experts provided consensus opinion on the following questions: 1) Which is the best initial agent for treatment of acute otitis media (AOM)? Amoxicillin should remain the first-line antimicrobial agent for treating AOM, at doses of 80-90 mg/kg/d; 2) What are suitable alternatives if amoxicillin fails? For patients with clinically defined treatment failure after three days of therapy, alternative agents include oral amoxicillin-

clavulanate, cefuroxime axetil, and intramuscular ceftriaxone; 3) Should empirical treatment of AOM vary by geographic region? Local surveillance data of pneumococcal resistance that are relevant for the clinical management of AOM are not available from most areas in the United States.

COMMENT BY HAL B. JENSON, MD, FAAP

The management of otitis media has entered a new era with the increasing prevalence of drug-resistant *Streptococcus pneumoniae*. This organism causes 40-50% of all cases of AOM, with reduced susceptibility to penicillin in 8-35% (2-4% highly resistant) of isolates and reduced susceptibility to third-generation cephalosporins in 10% of isolates (about 4% highly resistant); the reduced antibiotic susceptibilities occur independently. The recommendations of this group provide a framework for appropriate management of AOM in 1999.

There is no single oral antimicrobial that eradicates all AOM pathogens. Amoxicillin at higher doses of 80-90 mg/kg/day, which achieves the higher middle ear fluid concentrations necessary to treat resistant *S. pneumoniae*, is effective as a first choice. There are surprisingly (at least to me) few adverse events even at these higher doses, and amoxicillin is inexpensive compared to many of the alternatives. There are compelling data for cefuroxime axetil (Ceftin) and amoxicillin-clavulanate (Augmentin) orally, and ceftriaxone (Rocephin) intramuscularly, as second-line drugs for treatment failure, which is defined as ear pain, fever, or bulging tympanic membrane or otorrhea after three days of therapy. (Persisting middle ear fluid is found in 70% of children at 10 days and, in the absence of specific evidence of ongoing infection, does not represent treatment failure.) However, many of the 13 other drugs approved by the Food and Drug Administration lack good evidence for efficacy against drug-resistant *S. pneumoniae*. There are promising but insufficient data at this time to recommend cefpodoxime (Vantin) and cefprozil (Cefzil), but many of the traditional second-line drugs should now be considered ineffective for AOM. These include trimethoprim-sulfamethoxazole and erythromycin-sulfisoxazole, which have traditionally been used for AOM, and the newer macrolides, clarithromycin and azithromycin, which initially showed promise. Some of these other drugs may be useful for selected cases based on susceptibility testing of middle ear fluid isolates obtained by tympanocentesis.

The increasing frequency of drug-resistant pneumococci further increases the urgency of the release of a conjugated pneumococcal vaccine that may be effective in preventing the 40% of infantile otitis media that are now caused by *S. pneumoniae*, especially drug-resistant strains. (*Dr. Jenson is Chief, Pediatric Infectious Diseases, University of Texas Health Science Center, San Antonio, TX.*) ❖

Summaries of the Sixth Conference on Retroviruses and Opportunistic Infections: Part III

CONFERENCE COVERAGE

Note: *The following summaries represent a selection of papers from those presented at the 6th Conference on Retroviruses and Opportunistic Infections held on Jan. 31-Feb. 4, 1999, in Chicago, IL. It is important to recognize that some of these summaries are extracted only from the published abstract and it is possible that some of the material presented at the conference may have differed. The abstracts and posters, as well as other information presented at the conference, are available on the internet at www.retroconference.org. —Stan Deresinski, MD, FACP*

Immunology

Evidence continues to accumulate confirming the crucial role of CD8+ T cells in the control of HIV replication. CD8+ T-cell depletion by administration of a monoclonal antibody is associated with a dramatic increase in viremia in SIV-infected macaques and rhesus monkeys. (*Abstracts 252, 253.*) The emergence of cytotoxic T lymphocytes coincides with clearance of virus during primary SIVmac infection in rhesus monkeys. (*Abstract 254.*) However, virus-specific CTL responses may select escape mutants in SIV-infected macaques. (*Abstract 255.*)

Two studies demonstrated that perforin expression by CD8+ T cells in lymphoid tissue is abnormally low. Although granzyme B levels are not impaired, the absence of perforin prevents the entry of this enzyme into target cells, thus, causing a significant defect in effector cytolytic T-lymphocyte (CTL) function. (*Abstracts 62, LB3B.*)

Using a fetal thymus organ culture system, it was found that progressors had lost 90% of their T-cell development capacity; long-term nonprogressors had lost only 68% of that capacity after eight years of infection. Sixty percent of patients had a more than two-fold

increase in T-cell development capacity after six months of therapy and there was a significant correlation between this increase and the number of naïve CD4+ and CD8+ T cells in peripheral blood. (*Abstract 22.*)

T-cell receptor excision circles (TREC) are a by-product of intra-thymic T-cell selection; they represent excised DNA that is not replicated at the time of cellular replication. As a consequence, cells containing TREC are progressively diluted out over time. As a consequence, the quantification of TREC-containing T cells serves as a marker for thymus-derived naïve T cells. Administration of HAART is associated with a sustained increase in TREC-positive cells in lymph nodes and blood, indicating effective thymic production of naïve cells—good news for hopes of successful immune reconstitution (Star TREC, the New Generation?) (*Abstract S42.*)

After controlling for virological responsiveness, the rate of CD4+ reconstitution in response to HAART is diminished in older patients. (*Abstract 335.*)

HAART therapy is associated with reversion of the cytokine profile to a Th1 pattern as well as partially improved neutrophil and monocyte function. (*Abstracts 333, 336.*) Sustained control of HIV replication is associated with a reversion of the CD8+ T-cell repertoire to a polyclonal configuration from one with oligoclonal proliferations. (*Abstract 342.*) In a study of children receiving HAART, the greatest rise in HIV-specific CTL frequency was observed in those with incomplete viral suppression but increasing CD4+ T-cell counts. (*Abstract 339.*)

Successful HAART therapy is not associated with restoration of HIV-1 specific CD4+ T-cell responses. (*Abstract 343.*)

Both saquinavir and ritonavir reduced spontaneous in vitro apoptosis of CD4+ and CD8+ T cells of peripheral blood mononuclear cells obtained from HIV-infected PI-naïve patients. Each inhibited Fas induced CD4+ and CD8+ T-cell apoptosis. Apoptosis of uninfected cells was not affected. NRTIs did not affect apoptosis. The effect of the PIs appeared to be independent of their ability to inhibit HIV replication. (*Abstract 349.*)

Both ritonavir and saquinavir inhibit the in vitro responses of peripheral blood mononuclear cells from HIV-seronegative donors. (*Abstract 345.*) Indinavir inhibits anti-CD3 induced T-cell activation in vitro. It also, however, blocks cells in G0/G1 phase and induces IL-16 production, activities that may inhibit HIV replication. (*Abstract 348.*)

Neutralizing antibody increased after institution of HAART. (*Abstract 352.*)

Viral Eradication

With the exception of a few reports in patients treated very early in their infection, the bulk of evidence continues to indicate that complete viral eradication, if possible, is likely to require extremely long periods of treatment.

Prior to the start of therapy, the level of viral DNA expressing cells was approximately 2 $\log_{10}$ higher than was that of cells expressing viral RNA. Initiation of HAART was associated with a 0.7 $\log_{10}$ reduction in cellular HIV viral DNA within the first 10 weeks, probably due to loss of labile preintegration complex DNA. However, between 12 and 36 weeks of therapy, no further reduction in HIV viral DNA was found, indicating stability of integrated viral DNA in the face of HAART. (*Abstract 158.*) All 42 patients with undetectable viral loads for six months still had detectable cellular proviral DNA. (*Abstract 397.*)

A reservoir of "latently" infected T cells persists despite prolonged viral suppression as a result of HAART. A careful examination of blood mononuclear cells of patients with or without apparent suppression of viral replication detected the presence in both groups of two distinct populations of infected cells with regard to HIV replication—inducible and transcriptionally active. Neither decreased with increased duration of viral suppression. (*Abstract 5.*)

Examination of lymph nodes after two years of viral suppression (plasma HIV RNA < 500 copies/mL for at least 72 months) with IDV/ZDV/3TC found persistence of HIV RNA at a level essentially unchanged from that seen after one year of therapy. This observation suggests that the decay in viral RNA may have reached a plateau in this compartment. HIV RNA was less than 50 copies/mL in CSF from 15 of 15 patients while viral RNA was detected in genital secretions of three of 23 subjects. (*Abstract 6.*)

Fifteen (88%) of 17 patients on HAART for more than three years and with plasma HIV RNA less than 400 copies/mL had detectable HIV RNA in mucosal tissue obtained rectosigmoid biopsy with an assay with sensitivity of 10 copies. (*Abstract 160.*) The decay half-life of the latent HIV reservoir in patients with prolonged (2-3 years) viral suppression was estimated to be approximately six months. Examination of PBMCs and gut-associated lymphoid tissue (GALT) from patients with viral loads less than 50 copies/mL for two to three years found frequent evidence of proviral DNA and sequencing studies found evidence of evolution in envelope sequences consistent with ongoing replication. (*Abstract 495.*)

Eight patients with CD4 more than 500 cells/mm^3 who had received d4T/3TC/ritonavir discontinued their

therapy. Prior to discontinuation, all had plasma viral load less than 20 copies/mL and five had less than 5 copies/mL; tonsillar tissue had less than 40 copies/mg in five of five. Nonetheless, plasma virus rebounded in all eight patients at days 2-27. In three patients, the plasma viral load reached more than 0.5 $\log_{10}$ than prior to initiation of therapy. Phenotypic lymphocyte studies appeared to recapitulate those reported during primary HIV infection. Plasma viral load dropped to less than 20 copies/mL in all patients after reinitiation of therapy. (*Abstract 629.*)

An update on a previously reported patient from Berlin whose plasma viral load has remained undetectable after two treatment interruptions, the last for two years, was provided. There continues to be evidence of low-level replication competent virus in his lymph nodes and no evidence of neutralizing antibody. There is, however, evidence of a vigorous CTL response directed at p24 antigen. (*Abstract LB6.*)

Four patients started on HAART within 90 days of HIV infection with decrease in viral load to less than 500 copies/mL had episodes of discontinuation of antiretroviral therapy. In two patients with repeat episodes of nonadherence who finally discontinued therapy, plasma HIV RNA fell to undetectable levels and remained there for 21 and 14 months. Their CTL precursor frequency, which had fallen to low levels during viral suppression, was boosted during short periods of drug discontinuation associated with viral rebound. With final discontinuation of therapy, broad and strong CTL responses remained high. The third patient contained viral replication for four months after drug discontinuation, but CTL faded and virus rebounded. The fourth patient had, after discontinuation, only a low frequency of HIV-specific CTL and had an immediate viral rebound. (*Abstract 256.*)

Three patients with stable viremia were treated with HAART regimens containing hydroxyurea for three weeks, followed by therapy interruption for one week, then two cycles of three months each followed by treatment interruption and reinitiation as soon as rebound to more than 5000 copies/mL occurred. Mean rebound-free intervals were extended from seven days to 14 days and then to 37 days. A similar approach in SIV-infected macaques with treatment begun 28 days after infection was associated with progressively lower steady state viral load during treatment-free intervals. (*Abstract LB5.*)

The frequency of resting CD4+ T cells in peripheral blood carrying replication competent HIV in patients receiving intermittent rhIL-2 plus HAART is significantly lower than that in patients receiving HAART alone. No evidence of latently infected CD4+ T cells could be detected in three of six patients without detectable plasma HIV RNA receiving the combination. Lymph node tissue was obtained from two of these patients and no virus was detected in these. These two patients discontinued therapy and, at three-week follow-up, plasma HIV RNA could not be detected in their plasma. (*Abstract 496.*) ❖

CME Questions

24. The most frequent adverse effect of OPAT leading to hospitalization is:

a. renal failure.
b. vascular complications.
c. leukopenia.
d. allergic reaction.

25. Initial antibiotic treatment of otitis media:

a. should use amoxicillin, 40 mg/kg/d.
b. should be changed if fever and pain are still present after three days.
c. should be guided by local surveillance data.
d. should be changed if middle ear fluid is still present after 10 days in an otherwise well child.

26. Which of the following is *not* correct?

a. CD8 + T cells play an important role in the control of HIV infection.
b. The cytolytic function of CD8+ T cells may be impaired in HIV infected patients.
c. HIV infected "progressors" have reduced T-cell development capacity.
d. Successful highly active antiretroviral therapy (HAART) is routinely associated with a restoration of HIV-1 specific CD4+ T cell responses.

27. Which of the following is correct?

a. HIV proviral DNA is usually eradicated from patients whose plasma viral load remains undetectable due to HAART for six months or more.
b. HIV RNA is almost always undetectable in gut-associated lymphoid tissue in patients who have had undetectable plasma viral load for more than six months.
c. Studies examining the presence of T-cell receptor excision circles (TREC) demonstrate that successful HAART is associated with effective production of naïve T cells by the thymus.
d. Complete eradication of HIV is likely to require 9-12 months of HAART.

In Future Issues:

Remedy or Panacea?

UPDATES

By Carol A. Kemper, MD

Encouraging Needlestick Reporting

Source: Haiduven DJ, et al. *Hosp Infect* 1999;41:151-154.

Failure to report needlestick injuries is remarkably common, especially among physicians and medical students (Donnelly JP. *Infect Dis Alert* 1999;18:81-82; Osborn EH, et al. *Ann Intern Med* 1999;130:45-51). Haiduven and colleagues distributed confidential surveys to healthcare personnel at a public teaching hospital in San Jose between 1992 and 1995. A total of 549 individuals responded to the survey, 83% of whom were nurses and 7% of whom were physicians. The remaining subjects included operating room technicians, dentists, and other hospital personnel.

About one-half of the nurses and physicians and 84% of the remaining personnel reported at least one percutaneous needlestick injury within the previous five years. However, 46% failed to report all of their injuries, including 80% of the physicians and 45% of registered nurses. Reasons for nonreporting included the perception that the stick was sterile or clean (39%), or represented no risk (26%), too busy (9%), and dissatisfaction with follow-up (8%).

While educational interventions regarding actual risk may enhance reporting behaviors, establishing user-friendly mechanisms by which needlestick injuries can be dealt with quickly and appropriately, as well as adequate follow-up, is essential. The use of the ER for after-hours injuries is, in my experience, inadequate in that patients are often required to wait longer than that recommended for the administration of post-exposure prophylaxis (< 1 hour), and the management is often inconsistent and occasionally incorrect. This is despite the availability of approved hospital protocols. A designated 24-hour hotline, such as the one established at the San Francisco General Hospital, (which, after-hours, usually rings a knowledgeable fellow or faculty member) appears to more consistently meet the needs of their hospital personnel. The hotline number is prominently posted in blazing colors throughout the hospital to encourage reporting. ■

Penile Chiggers in Kids

Source: Smith GA, et al. *Pediatr Emerg Care* 1998;14:116-118.

Chigger bites causing an acute penile hypersensitivity syndrome in boys in the summer months is apparently quite common and well known to emergency room physicians, although I had never heard of it. Chiggers are those nonhuman mites that are unable to burrow under human skin and suck blood like human scabies, but instead can only attach to the surface skin where they inject saliva and feed on tissue fluids. Like scabies, however, mite bites usually occur around the waist and groin where clothing is tighter, and the immune response is generally more marked in those sensitized by prior infestations. Hence, the resulting penile swelling and severe pruritis found in young males (typically 1-10 years of age). An additional 33% of patients may complain of dysuria. Although only half of the patients have an obvious papule or bite on the penis, bites may be found on other parts of the body. The symptoms usually last about two weeks and eventually respond to topical remedies, such as camphorated oil and baking soda, cold compresses, and antihistamines. Because the mites are usually long-gone, treatment with permethrin is not necessary, but consideration can be given to treating clothing in those with recurrent infestations. ■

Progression in a Nonprogressor

Source: Greenough TC, et al. *N Engl J Med* 1999;340:236-237.

An earlier report from greenough and colleagues documented the presence of HIV-infection in a long-term nonprogressor infected with only *nef*-deleted forms of HIV-1 (Kirchhoff F, et al. *N Engl J Med* 1995;332:228-232). *Nef*-deficient virus has been associated with decreased virulence and has, therefore, been proposed for possible use in an attenuated viral vaccine. Beginning in January 1997, however, the patient's CD4+ cell count began to mysteriously decline (from a peak of 713 to as low as 216/mm^3), although plasma levels of HIV remained undetectable (< 50 particles/mL). Despite repeated attempts, HIV was cultured from blood on only one occasion in 1994, and levels of viral DNA in peripheral blood mononuclear cells have remained low (20-164 copies/106 CD4+ cells).

Despite evidence of low-level infection, several findings in vitro suggest continued HIV-1 antigenic stimulation, including the presence of HIV-specific cytotoxic T-cell responses, increased levels of activated CD8+ cells, and strong CD4 T-lymphocyte proliferative responses to gag antigen. The pathogenetic basis for this patient's declining CD4+ cell count, despite barely detectable HIV replication, remains uncertain. But this individual case suggests that factors other than readily demonstrable viral replication, which have not yet been elucidated, may be responsible for declines in CD4+ count. ■