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Problems with Parasites and Praziquantel

CASE REPORT

Synopsis: *A consultation for tapeworm infestation leads to the discovery that praziquantel is only being supplied in limited quantities.*

A 42-year-old asian indian man was recently referred to me for evaluation of tapeworm infestation. He had immigrated to the United States from India in 1988, working—like almost everyone else in Silicon Valley these days—as a software engineer. He was diagnosed with chronic myelogenous leukemia in 1991, and underwent successful bone marrow transplantation. He had not been back to India for eight years. He had done extremely well until a few weeks earlier when he noticed a long white object in the toilet bowl. Fishing it out with a stick—and nearly giving his poor wife a heart attack in the process—he determined that it was about 5 feet in length, opaque-white, with numerous small segments. He then carefully placed it back in the bowl, and flushed it.

Upon contacting his internist, he was promptly referred to me for an Infectious Disease consultation. I thought this was going to be a slam-dunk. In fact, I thought it was an unnecessary consultation, assuming any good internist could treat a tapeworm.

When the patient came to my office several days later, he was armed with an exhaustive list of questions, including the age of the worm, its species, how it obtained nutrients, etc. By now, he'd had access to the internet, and knew more about tapeworms than I ever hope to. His major concern was autochtonous infection. Ninety minutes later, the patient was mostly satisfied, and I scribbled out a prescription for a single 600 mg dose of praziquantel (Biltricide, Bayer Pharmaceutical), ordered three stool O & P, and wished him well.

COMMENT BY CAROL A. KEMPER, MD, FACP

It was there that the trouble really began. Seldom has such a seemingly straightforward consultation been such a problem! A flur-

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ry of phone calls later, it was determined that not a single pharmacy in our area carried praziquantel tablets including Rite-AID, Walgreen's, Longs Drug, and two hospital pharmacies. We were repeatedly told that it was "unavailable." Further inquiry revealed that Bayer was no longer distributing praziquantel tablets. I finally located several tablets but they were a year out of date and the pharmacist refused to dispense them. What to do? According to the *Medical Letter*, praziquantel is considered the first-line agent for intestinal tapeworms. Albendazole does not have sufficient intraluminal activity and is not recommended. I quickly learned that niclosamide (nicloside), the alternate agent, was also unavailable.

Finally, much to my delight, the pharmacist at our HMO-based clinic got on the web and learned that biltricide compound, which is routinely used by veterinarians, was readily available, and downloaded a "recipe" for the appropriate dose. Several phone calls later, we convinced the patient that what works for cats and dogs would probably be sufficient for him.

If only this patient had presented a few weeks later. Bayer has announced that, effective Oct. 1, praziquantel tablets are available only through limited distribution (http://www.fda/gov/cder/drug/shortages). Health care professionals may obtain the product by contacting Bayer Customer Service (203-812-2000). It is hoped that praziquantel will soon be available for normal distribution.

This is not the only trouble I've recently had treating parasitic infections, even in this affluent corner of the United States. Simple consults are turning into 10-hour nightmares, attempting to obtain appropriate therapies for my capitated HMO-based Asian Indian population. It is now believed that ~40% of the software engineers in Silicon Valley are Asian Indians (~70% of whom have positive PPDs—you do the math), all of whom make sufficient salaries to afford annual visits back home and frequent visits from elderly parents. I recently saw an engineering manager who frequently travels between Silicon Valley and Bangladesh, who developed acute left upper extremity swelling, axillary lymphadenitis, and significant peripheral blood eosinophilia (~42%). Thinking he might have contracted lymphatic filariasis, I ordered the appropriate laboratory studies and prescribed a single 12-mg dose of ivermectin (Stromectol).

Again, none of the local pharmacies were able to provide the drug. Stanford Medical Center's pharmacy promised me over the phone that they would hold onto 12 mg for this patient, but when he arrived to pick up his prescription, they turned him away—he did not have a Stanford prescription. Apparently it wasn't enough that I was on staff and the patient was willing to pay cash, the patient had to have been seen at their facility. The Santa Clara Valley Medical Center's (SCVMC) pharmacists were willing to help and secured a supply of the drug for us, but the patient also had to be registered at the county's facility before the drug could be dispensed. This entailed scheduling him an appointment in SCVMC's Infectious Disease Clinic, which wasn't a big deal, except that the county does not accept his HMO insurance and his insurance refused to authorize the visit. Why should the HMO pay to have the patient seen by me in the SCVMC ID Clinic when I had just seen him in the HMO clinic? It was all too confusing for capitated HMO care. Finally, the patient in desperation agreed to pay for his visit to the county clinic, we waived as much of the fee as we could, got him registered in the system, and got him the drug. All for three little tablets of ivermectin. ❖

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VICE PRESIDENT/GROUP PUBLISHER:
Donald R. Johnston.

EDITORIAL GROUP HEAD: Glen Harris.

MARKETING PRODUCT MANAGER:
Schandale Kornegay.

ASSOCIATE MANAGING EDITOR: Robin Mason.

ASSISTANT MANAGING EDITOR: Neill Larmore.

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Vertical Transmission of HCV

ABSTRACT & COMMENTARY

Synopsis: *HCV infection of maternal peripheral blood mononuclear cells is predictive of transmission of infection to offspring.*

Source: Azzari C, et al. Vertical transmission of HCV is related to maternal peripheral blood mononuclear cell infection. *Blood* 2000;96:2045-2048.

Azzari and colleagues in florence, italy, examined the relationship of the presence of hepatitis C virus (HCV) RNA in maternal peripheral blood mononuclear cells (PBMNCs), obtained at delivery, to transmission of HCV infection to their offspring. A total of 66 HIV-negative HCV-infected mothers were studied, of whom 13 had transmitted infection to their offspring.

Positive-strand HCV RNA was detected in PBMNCs of all 13 (100%) transmitting mothers and in only 13 of 53 (24.5%) of nontransmitters ($P < 0.000001$). Negative-strand HCV RNA was found in five (38.5%) of transmitters and none of the nontransmitters ($P = 0.0001$). In contrast, there was no significant correlation between transmission and HCV genotype or serum viral load; the latter did not correlate with the presence of HCV RNA in PBMNCs.

COMMENT BY STAN DERESINSKI, MD, FACP

The overall risk of vertical HCV transmission is approximately 5%, and the presence of co-infection with HIV, a history of maternal post-transfusion hepatitis and, possibly, a history of maternal injection drug use, are each reported to increase the risk of transmission. In contrast, vaginal delivery and breastfeeding are not associated with increased risk. This study also confirms other work indicating that HCV viral load and genotype are not predictors of transmission. In contrast, HCV infection of PBMNCs is strongly correlated with vertical transmission of this viral infection.

Persisting PBMNC infection has been suggested to be the source of relapse in patients after liver transplantation for complications of chronic HCV infection. Exposure of the fetus to maternal blood cells appears to be a constant occurrence; such cells are found in cord blood samples at a frequency of 10^{-4} to 10^{-5} nucleated cells.[1]

HCV contains a single positive strand of RNA (HCV-RNA$^+$). It receives this "positive" designation as a result of its ability to act like messenger RNA and, thus, directly code for protein. HCV-RNA$^+$ may also serve as a template for negative-strand RNA (HCV-RNA$^-$). The latter is believed to be a marker of active viral replication, whereas HCV-RNA$^+$ may be detected in cells in which the virus is not undergoing replication.

This investigation found that the presence of HCV-RNA of either type in maternal PBMNC is highly associated with transmission to the newborn. The presence of HCV-RNA$^+$ had a sensitivity of 100%, but a low specificity for prediction of transmission. In contrast, the presence of HCV-RNA$^-$ had a low sensitivity (it detected only 5 of 13 transmitters) but had positive and negative predictive values of 100%.

This study provides new insight into transmission of this common viral infection. Furthermore, if the assay used here can be commercialized, and if it can be demonstrated that there is a similar correlation with risk of transmission when maternal blood is studied early in pregnancy or even when pregnancy is being considered, it may prove very useful in counseling of potential mothers who are HCV infected. ❖

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Catheter Replacement Before Antimicrobial Therapy for Symptomatic UTI

ABSTRACT & COMMENTARY

Synopsis: *Changing the indwelling urinary catheter can improve clinical and bacteriological outcomes of UTI by about 50%.*

Source: Raz R, et al. Chronic indwelling catheter replacement before antimicrobial therapy for symptomatic urinary tract infection. *J Urol* 2000;164:1254-1258.

Chronic indwelling urinary catheters are frequently associated with urinary tract infections (UTIs). The inner surface of the catheter becomes coated with a dense bacterial biofilm. Organisms may become embedded in this biofilm and survive due to

Table

Catheter Replacement in UTI: Clinical and Bacteriological Outcomes

	During Rx Day 3		Post Rx Day 7		Post Rx Day 28	
	REPLACE	NO REPLACE	REPLACE	NO REPLACE	REPLACE	NO REPLACE
No growth on urine culture (%)	89%	30% $P < 0.001$	67%	33% $P = 0.01$	48%	19% $P = 0.02$
Clinical cure or improvement (%)	93%	41% $P < 0.001$	93%	78%	89%	54%
Clinical relapse rate (%)			7%	29%	11%	41% $P = 0.015$

catheter replacement (REPLACE)

no catheter replacement (NO REPLACE)

decreased diffusion of antimicrobials into it. This explains why bacterial counts are higher in urine specimens aspirated from a chronic in situ catheter compared with a specimen obtained after catheter replacement. While routine catheter replacement in non-infected individuals does not lead to better outcomes, would catheter replacement prior to instituting antibiotic therapy for UTI result in improved outcomes in patients with chronic indwelling catheters in long-term care facilities? Raz and colleagues conducted a prospective, randomized, open clinical trial at two long-term care facilities to answer the question.

Fifty-four nursing home residents, 21 male and 33 female, mean age 72.6 years with a clinical diagnosis of UTI were enrolled in the study. Those with gross hematuria or obstruction were excluded from the study. Patients were randomized to either catheter replacement or no replacement. Ciprofloxacin or ofloxacin was used and treatment was continued for 14 days. Clinical and bacteriological outcomes were assessed after three days of therapy, and then seven and 28 days after therapy completion.

The two groups, catheter replacement and no replacement, had similar characteristics. There were similar numbers of diabetics in both groups, and the presenting features, including fever, leucocytosis, bacteremia, and the organisms cultured were also similar. Catheter replacement was associated with a shorter duration of fever, 2.9 ± 1.9 days compared with 4.6 ± 1.9 days ($P = 0.05$) for those without catheter replacement. Catheter replacement was also associated with improved clinical and bacteriological outcomes during and post-therapy (*see Table*). The relapse rate 28 days post-therapy was only 11% in those with catheter replacement compared with 41% in those without replacement ($P = 0.015$). There were only two deaths and both were inpatients without catheter replacement.

COMMENT BY KAMALJIT SETHI, MD, FACP

Up to 10% of elderly long-term care individuals have chronic indwelling urinary catheters. Polymicrobial bacteriuria and serious invasive UTIs are serious complications and contribute to both morbidity and mortality. While it is accepted that asymptomatic bacteriuria should not be treated, clearly symptomatic UTI with and without bacteremia merits therapy. This study suggests a simple intervention: changing the indwelling urinary catheter can improve clinical and bacteriological outcomes both during and after therapy by about 50%. This means better, faster, and less expensive care for a common clinical problem. It makes sense to consider that removal of the catheter and hence, adherent biofilm in symptomatic UTI, would lead to improved outcomes. (*Dr. Sethi is Clinical Professor of Medicine, Georgetown University School of Medicine; Attending Physician, Providence Hospital, Washington, DC.*) ❖

Special Feature

Corticosteroid Treatment for Septic Shock: New Insights

By Francisco Baigorri, MD, PhD

Activation of the hypothalamic-pituitary-adrenal (HPA) axis is an essential component of the general adaptation to stress and contributes to the main-

tenance of homeostasis. Cortisol, in particular, has a vital supportive role in the maintenance of vascular tone, endothelial integrity, vascular permeability, and the distribution of total body water within the vascular compartment. It also potentiates the vasoconstrictor actions of cathecolamines.[1,2] Moreover, cortisol exerts important metabolic and immune functions in response to infection. It is now widely accepted that the glucocorticoid action counteracts the systemic inflammatory response, thus protecting the host against its own inflammatory defense reactions.[3] (*See Table 1.*)

Table 1

Some Effects of Corticosteroids That May be Involved in a Beneficial Action in Patients with Septic Shock

- Inhibition of the migration of leucocytes to inflammatory sites
- Inhibition of the adhesion of neutrophils to endothelial cells and their subsequent production of humoral factors
- Inhibition of macrophage and endothelial function
- Increment in blood pressure through blockade of nitric oxide synthesis
- Increment in myocardial contractility
- Stimulation of the function of alpha$_1$-adrenoreceptors and beta-adrenoreceptors, and by increasing the number of these receptors
- Attenuation of down-regulation of adrenergic receptors induced by the use of cathecolamines for long periods
- Increment of gluconeogenesis
- Shift of the oxygen dissociation curve

In the last three decades, the anti-inflammatory properties of corticosteroids have encouraged researchers to investigate the potential benefit of pharmacologic doses of these substances in severe infections. However, despite a substantial amount of data supporting the use of glucocorticoids in experimental models of septic shock, the results of randomized, controlled trials in humans have been controversial. Two meta-analyses concluded that glucocorticoids are not beneficial in sepsis and septic shock, and in one of them, that the use of glucocorticoids may be harmful.[4,5]

In recent years, several authors have hypothesized a syndrome of relative adrenocortical deficiency in septic shock in the presence of normal or even elevated serum cortisol concentrations. Moreover, a few uncontrolled studies indicate that stress doses of hydrocortisone improve hemodynamics in patients with hyperdynamic septic shock unresponsive to conventional therapy.[6,7] As a result, there is renewed interest in corticosteroids as therapy for septic shock.[8,9] This essay will focus on recent investigations in this field.

Sepsis and Adrenal Function

New insights into glucocorticoid physiology and regulation during septic shock reveal that the functional integrity of both the HPA axis and glucocorticoid receptors in target cells is altered in several ways, and that this may result in an insufficient endogenous glucocorticoid action.[3] Consequently, in the setting of sepsis, adrenal function can be difficult to evaluate. Cortisol levels, normally elevated by the stress of sepsis, are occasionally reduced, signifying possible adrenal dysfunction. On the other hand, even elevated cortisol levels do not assure that adrenal reserve is adequate. Paradoxical though it may seem, several studies showed that the higher the plasma cortisol concentrations, the worse the patient's outcome. Thus, in severe sepsis, the evaluation of the appropriateness of the activation of the HPA axis requires dynamic testing.

The most commonly used test is the short corticotropin test, absolute adrenocortical deficiency being defined by a low basal cortisol concentration that is not increased with the rapid 250 µg corticotropin stimulation test (usually, basal and stimulated cortisol concentrations are < 20 µg/dL). The fact of the matter is that basal plasma cortisol levels are commonly greater than 20 µg/dL in severe sepsis, and the use of the absolute increase in plasma cortisol levels after the injection of corticotropin may be more useful to evaluate adrenal function.[1]

Annane and colleagues recently investigated the spectrum of serum cortisol levels and the cortisol response to corticotropin stimulation in patients with septic shock.[10] In multivariate analysis, Annane et al found that a basal cortisol level greater than 34 µg/dL, and a cortisol response to corticotropin of no more than 9 µg/dL were independent predictors of death. Moreover, they defined three different patterns of activation of the HPA axis in septic shock according to the combination of the value of basal cortisol levels (≤ or > 34 µg/dL) and the highest value of the cortisol response to corticotropin (≤ or > 9 µg/dL). These patterns were associated with three different outcomes:

- Patients with basal cortisol level below 34 µg/dL and a cortisol response to corticotropin above 9 µg/dL. These patients with a seemingly adequate HPA axis activation had the lowest risk of death (28-day mortality rate of 26%).
- Patients with basal cortisol level above 34 µg/dL but a cortisol response to corticotropin below 9 µg/dL. These patients with occult adrenal insufficiency had the highest risk of death (82%).

- Patients with basal cortisol level below 34 µg/dL and a cortisol response to corticotropin below 9 µg/dL, or a basal cortisol level above 34 µg/dL and a cortisol response to corticotropin above 9 µg/dL. These patients had an intermediate risk of death (67%).

Only 30% of patients studied by Annane et al had an adequate HPA axis activation (pattern 1).[10] According to the results of this study, adrenocortical deficiency is undoubtedly a predictor of a worse prognosis. However, it could be either the cause or simply a consequence of the severity of illness with which it is associated.

New Randomized, Clinical Trials of Corticosteroids in Septic Shock

Recently, two small, double-blind studies have been published showing that moderate stress doses of hydrocortisone (200-300 mg daily) improve hemodynamics and reduce the time of vasopressor support.[11,12] These trials were different from the previous, negative studies in that hydrocortisone was administered in lower doses, relatively late in the course of sepsis, prolonged for 5-6 days and progressively reduced, and all patients were treated with cathecholamines.

The study of Bollaert and colleagues displayed an encouraging trend toward reduced 28-day mortality (32% in the treatment group vs 63% in the placebo group; $P = 0.091$).[11] Unfortunately, the study was discontinued at the halfway point because of the positive effect on shock reversal. Moreover, this study deserves special consideration because all eligible patients underwent a short corticotropin stimulation test 24 hours before inclusion. Patients with absolute adrenal deficiency (as defined by a plasma cortisol concentration < 18 µg/dL after the corticotropin stimulation test) were excluded from the study. Forty-one patients were randomized (22 to receive active treatment, 19 to receive placebo).

Baseline plasma cortisol concentrations did not differ in the treatment group and in the placebo group. However, there were four patients with a maximal absolute increase of plasma cortisol concentration of less than 6 µg/dL after corticotropin administration in the treatment group vs. eight in the placebo group ($P = 0.093$). One might reasonably suppose that this difference could have influenced the results of the study, but there were no significant differences in outcome in the group of patients with an adequate response to corticotropin administration as compared with the group with an inadequate response (*see Table 2*). These findings support the view that either the beneficial effects of hydrocortisone replacement may be unrelated to adrenocortical deficiency or the biochemical diagnostic tools are inappropriate for ICU patients.[8] Further randomized trials using the three-level classification of Annane et al could be helpful.[10]

Therapeutic Implications

In the meantime, what conclusions can be drawn from all this? Should we consider treating all septic patients who remain dependent for several days on cathecholamines with stress doses of hydrocortisone?[8,9]

Table 2

Number (%) of Patients who Achieved Shock Reversal or Survived According to the Results of the Corticotropin Test[11]

	Treatment (n = 22)	Placebo (n = 19)	P value
Responders	n = 18	n = 11	
7-day shock reversal	12 (67)	2 (18)	0.03
28-day survival	12 (67)	4 (36)	0.22
Nonresponders	n = 4	n = 8	
7-day shock reversal	3 (75)	2 (25)	0.03
28-day survival	3 (75)	3 (37)	0.54

Responders are patients with a maximal absolute increase of plasma cortisol concentration ≥ 6 µg/dL after corticotropin administration. Nonresponders are patients with a maximal absolute increase of plasma cortisol concentration < 6 µg/dL after corticotropin administration.

Certainly, studies showing a beneficial effect of corticosteroids have comprised small groups of patients. Moreover, it remains to be seen whether corticosteroids can improve survival. Added to that, we must not forget the side effects of hydrocortisone. It is worth stating at this point that patients with a recent history of gastroduodenal ulcer or gastrointestinal bleeding were excluded from the study of Bollaert et al.[11] Anyway, all in all, the new randomized clinical trials testing corticosteroids in septic shock did not report differences in the rates of gastrointestinal bleeding and secondary infections between treated patients and placebo patients.[11,12]

Undoubtedly, more studies are needed to elucidate the role of corticosteroids in the treatment of septic shock. However, if one weighs the pros and cons, treatment with stress doses of hydrocortisone may be considered in patients with septic shock unresponsive to

fluid resuscitation and dependent of vasopressor therapy for more than 96 hours as some authors maintain, provided that: careful elimination of curable causes of hypotension is performed; absolute adrenocortical deficiency is checked with corticotropin stimulation testing; and, corticosteroids are used for at least five days and progressively reduced.[11] (*Dr. Baigorri works for Intensive Care Services, Corporacio Sanitaria Parc Tauli, Sabadell, Spain.*) ❖

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CME Questions

24. Administration of stress doses of glucocorticoids to critically ill patients with septic shock in whom absolute adrenocortical deficiency has already been ruled out:

a. should be considered as soon as possible in the course of sepsis.
b. should not be considered as long as the patients require vasopressor therapy.
c. should be strongly considered in those patients dependent on vasopressor therapy for more than 96 hours.
d. should be routinely considered but in large, "suprapharmacological" doses.
e. should always be used to improve survival.

25. In patients in long-term care facilities with indwelling urinary catheters, catheter replacement should be considered:

a. when bacteriuria is documented.
b. when symptomatic UTI occurs, prior to therapy.
c. on a regularly scheduled basis every 4-8 weeks.

26. A 39-year-old woman who has chronic hepatitis C virus (HCV) infection is pregnant. Her HIV test is negative. What is the approximate risk of vertical transmission of HCV infection?

a. Less than 1%
b. 3-7%
c. 10-15%
d. Greater than 20%

27. Which of the following maternal characteristics is associated with an increased risk of vertical transmission of HCV infection?

a. Vaginal delivery
b. Breastfeeding
c. Serum HCV viral load
d. HCV genotype
e. The presence of HCV RNA in peripheral blood mononuclear cells at the time of delivery.

28. It has been shown that stress doses of glucocorticoids given to patients with septic shock:

a. increase the risk of bleeding.
b. reduce morbidity and mortality.
c. reduce the time of vasopressor support.
d. increase the risk of secondary infections.
e. have no effect unless an absolute adrenocortical deficiency was detected.

In Future Issues:

Bronchiectasis: Take a Deep Breath of Tobramycin?

UPDATES

By Carol A. Kemper, MD, FACP

Itraconazole in HIV

Source: Koks CH, et al. *AIDS* 2000;14: 89-90.

Ritonavir (rtv) is a potent inhibitor of the p450 hepatic enzyme system (CYP450), and is often used in combination with saquinavir (SQV) or other protease inhibitors to block the metabolism of these agents, thereby increasing their blood levels and allowing the use of lower dosages. However, RTV, even at the lower dosages used for these purposes (100-400 mg twice daily, depending on the agent used in combination) can be poorly tolerated. Why not a different and better tolerated blocking agent?

During routine drug monitoring of antiretroviral therapy in HIV-infected patients, Koks and colleagues noted that two patients had SQV levels 5-fold higher than expected in the absence of RTV. Both patients, it turned out, were receiving itraconazole, another inhibitor of CYP450. Serial blood samples to assess SQV levels were then obtained in three patients receiving long-term SQV 1200 mg t.i.d. (without RTV) before and after the administration of itraconazole for two weeks. Itraconazole was administered as a loading dosage of 200 mg twice daily for three days, and then 200 mg once daily.

Following the administration of itraconazole for two weeks, there was a median 5-fold increase (range, 2.5-6.9) in the area under the curve for SQV. Trough levels increased a median of 3.1-fold (range, 1.6-16.8). These SQV concentrations, in combination with itraconazole, were comparable to those observed when SQV is combined with RTV (using a dosage of 400 mg twice daily for both agents). Itraconazole may be a reasonable alternative in those patients receiving SQV therapy who are intolerant of RTV. Although it is not clear that the entire 1200 mg t.i.d. SQV dose is necessary when used in combination with itraconzole, Koks et al cautioned that because the pharmacokinetic interaction of itraconazole appears to be smaller and more varied than that of RTV, the dose of SQV should not be reduced to 400 mg twice daily as it is when combined with RTV. ■

Perinatal Hepatitis C Transmission

Source: Gibb DM, et al. *Lancet* 2000; 356:904-907.

Gibb and associates in the united Kingdom and Ireland assessed the risk of perinatal transmission of hepatitis C virus (HCV) in 441 mother-infant pairs. Twenty-two moms were co-infected with HIV (the HIV status was not known for 91 moms). Of 144 children who became HCV antibody-negative, 135 (93.8%) had negative confirmatory HCV RNA PCR test results. Of the remaining 297 children, 248 of whom were tested by PCR, HCV RNA PCR results were positive in 14 (5.6%), negative in 221 (89.1%), and discordant in 13 (5.2%). The overall risk of vertical transmission was estimated to be 6.7%. In children born to HIV-infected mothers, the risk of HCV transmission was significantly higher (odds ratio, 3.8).

Gibb et al acknowledged that the risk of transmission could only be based on estimates of the rate of loss of antibody to HCV and the known sensitivity/specificity of HCV RNA PCR. In apparently uninfected children, rates of detectable HCV antibody were ~50% at eight months and 5% at 13 months. Serological testing should, therefore, be delayed until at least 12-15 months of age. On the other hand, PCR testing was only 22% sensitive during the first month of life, but increased to 97% thereafter. While a negative PCR test after one month of life rules out infection, a positive PCR test after one month increases the risk of HCV infection to 73% and requires longer-term follow-up. ■

Urokinase of Benefit in Percutaneously Drained Abscesses

Source: Haaga JR, et al. *AJR Am J Roentgenol* 2000;174:1681-1685.

Forty-two patients with abscesses requiring percutaneous drainage were randomly assigned to receive intracavitary urokinase or sterile saline within 24 hours of placement of the drainage catheter. Urokinase or sterile saline was administered every eight hours for a total of four days; the dose was dependent on the size of the abscess cavity. Only those patients with abscess material that was culture positive or those who were receiving antibacterial therapy for treatment of an abscess were included. Patients with pancreatic abscess or pseudocyst were excluded from study.

Abscess location and size were similar between the two groups, as was the proportion of abscesses that were loculated. The proportion of patients with a partial or complete response to therapy was similar between the two groups (86% response rate). However, the length of hospital stay was significantly shorter for patients receiving urokinase compared with those receiving saline (29 vs 13 days; P = 0.0025), and the resulting treatment costs were significantly less. There was also a trend toward fewer days of fever, leukocytosis, and required catheter drainage in patients receiving urokinase. The number of days of catheter drainage for patients receiving urokinase was seven vs. 15 for those receiving saline (P = 0.14). No complications of urokinase therapy occurred.

Intracavitary administration of urokinase, whether for an empyema, intraabdominal abscess, or infected hematoma, may help to decrease the viscosity of the abscess material, resulting in more rapid and effective drainage. ■