Urban Trench Fever and Cat Scratch Disease

Str—I read with interest the article on urban trench fever by Safdar [1]. The article did not comment on cat contact, nor did it appear that PCR for Bartonella henselae (or Bartonella quintana) was performed on either blood or lymph node specimens. Since there is a great deal of cross-reactivity between these organisms, it would be prudent to perform PCR before diagnosing a case of trench fever on the basis of serological test results, particularly since cat scratch disease is far more common and could account for the patient’s symptoms.

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References

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Uncertain Generalizability of Switch Studies

Str—Drechsler and Powderly [1] review well the available studies on switching effective antiretroviral therapy. However, they do not note a flaw inherent in switch studies. Because entrance criteria for these studies produce study populations skewed in unclear ways, switch studies have uncertain generalizability to the entire population of persons who are HIV positive. This problem is not mitigated by randomizing subjects to continue the former therapy or to switch to the alternative therapy, nor is it mitigated by reproducibility.

When the regimen switched from is producing favorable results, the new regimen is disadvantaged in that it is unlikely to produce better results than did the former one. For instance, in the BID Efficacy and Safety Trial (BEST)[2], subjects with undetectable levels of HIV who were tolerating an indinavir regimen with doses administered every 8 h (hereafter, indinavir t.i.d.) were randomized to continue receiving indinavir t.i.d. or to receive a ritonavir-boosted indinavir regimen administered twice per day (hereafter, IDV/r b.i.d.). A greater proportion of subjects receiving the new regimen developed nephrolithiasis than did subjects who continued to receive the previous regimen. But the universe of HIV-positive persons might contain a greater number of persons who develop this complication while receiving the indinavir t.i.d. regimen but not while receiving the IDV/r b.i.d. regimen than the number of persons who develop this complication while receiving the IDV/r b.i.d. regimen but not while receiving the indinavir t.i.d. regimen. The former group could not participate in the BEST trial. The BEST trial result indicates that the IDV/r b.i.d. regimen caused more cases of nephrolithiasis among persons who tolerate the IDV t.i.d. regimen. It does not establish that the IDV/r b.i.d. regimen causes more cases of nephrolithiasis than does the IDV t.i.d. in the universe of HIV-positive persons.

Similarly, when the regimen switched from is producing unfavorable results, a switch study may misleadingly favor the new regimen. Switch studies of persons with lipodystrophy who are receiving stavudine, for instance, have tended to show that subjects switched to abacavir therapy have less progression, or even remission, of the lipodystrophy. But the universe of HIV-positive persons might contain more persons who develop lipodystrophy when receiving abacavir but not when receiving stavudine than persons who develop lipodystrophy when receiving stavudine but not when receiving abacavir. The former group could not enter these trials. These studies indicate that abacavir therapy causes less lipodystrophy in persons who develop lipodystrophy when receiving stavudine. They do not establish that abacavir therapy causes less lipodystrophy in the universe of HIV-positive persons.

Only prospective, randomized studies in more-general populations provide generalizable results.

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Voriconazole Inhibition of Tacrolimus Metabolism

Str—Voriconazole (Pfizer) is a new triazole antifungal agent used in the management of invasive infections caused by molds such as Aspergillus species, Fusarium species and Scedosporium apiospermum. This agent is known to inhibit the cytochrome P450 (CYP) isoenzymes 3A4, 2C9, and 2C19, and is consequently associated with a number of drug interactions [1]. Preliminary observations have demonstrated that voriconazole significantly increases the trough concentrations of tacrolimus [2]. The manufacturer recommends reducing the daily tacrolimus dose by one-third when it is concurrently administered with voriconazole [3]. We describe a patient who required a 90% reduction in the manufacturer’s recommended maintenance dose of tacrolimus.

A 44-year-old, 62-kg woman with a history of hepatitis C, alcoholic liver disease, and liver transplantation (6 years earlier)