Finally, readers might be interested in a second report on the salvage of renal function after the treatment of renal vein thrombosis, which appeared shortly after ours was published.[3]

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Antituberculosis Drugs and Breast-feeding

To the Editor.—In the March ARCHIVES, Snider and Powell[1] presented a well-organized review of the sparse and scattered data available in the literature concerning the appearance of antituberculosis drugs in human breast milk. The information available to these authors indicated that *p*-aminosalicylic acid and pyrazinamide were either not detectable or unknown at the time of publication; however, my laboratory has recently analyzed both of these components in human breast milk.

A 27-year-old woman (non–breast-feeding) was given 4 g of *p*-aminosalicylic acid and breast milk collected at 0, 1, 2, 3, 4, 9, and 12 hours following oral administration. A maximum concentration of 1.1 mg/L was obtained at three hours with an elimination half-life of 2.5 hours. The maximum plasma concentration of the mother at two hours was determined to be 70.1 mg/L. Gastrointestinal tract irritation later developed and the *p*-aminosalicylic acid was withdrawn from the therapeutic regimen.

In another case, a 29-year-old woman (non–breast-feeding) received 1 g of oral pyrazinamide and the milk was collected at the time intervals described. At three hours, the maximum concentration in milk was 1.5 mg/L with an estimated half-life of 9.0 hours. A plasma maximum of 42.0 mg/L was determined at two hours. At the ninth hour of collection, the metabolite pyrazinoic acid was detected at a level of 0.8 mg/L.

In both cases, *p*-aminosalicylic acid or pyrazinamide were the only agents given during the time of the experiment and each was quantitated by high performance liquid chromatography with positive identification via mass spectrometry.[2] Although limited data, the concentration of each of these components in breast milk was far below the therapeutic range and, therefore, could be considered safe for use should the mother prefer to nurse the infant. Should therapeutic drug monitoring not be available, toxic effects that could be observed in the mother and infant are hepatitis, gastrointestinal tract disturbance, hypokalemia, thrombocytopenia, and hemolytic anemia for *p*-aminosalicylic acid and hepatitis, jaundice, and arthralgia for pyrazinamide.[3,4]

Coadministration of *p*-aminosalicylic acid with isoniazid will increase the serum half-life and concentration of INH (nonacetylated), which may well elevate the levels of INH in breast milk. Also, in kwashiorkor serum, PAS is essentially totally unbound to serum proteins as opposed to being approximately 15% bound in normal serum, which leads to significantly elevated concentrations of *p*-aminosalicylic acid. Therefore, one should take into consideration the state of health of the patient and possible drug interactions, both of which have demonstrated alterations in the pharmacokinetic profiles of these antituberculosis agents, which, in turn may either decrease or increase the concentrations that could appear in breast milk.[5]

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Atrial Fibrillation

To the Editor.—Lowenstein et al[1] recently described 40 cases of new-onset atrial fibrillation admitted to Denver General Hospital from the emergency room. They concluded that alcohol caused or contributed to 35% of the cases. Although there does seem to be some theoretical support for their proposition, there are methodological problems in their observational report that make the results uninterpretable. No attempt was made to establish causality by comparing cases of atrial fibrillation with an appropriate control group. Also, there was no adjustment for potentially confounding variables.

Causality was established by declaration. The authors considered alcohol to be the cause of atrial fibrillation if the patient was intoxicated and no other cause could be identified, and considered alcohol to be a contributing cause if the patient was intoxicated and other known causes of atrial fibrillation were identified. Alcohol intoxication was present in 14 of 40 cases; therefore, the authors concluded that alcohol caused or contributed to 35% of the cases of atrial fibrillation.

The presence of alcohol intoxication in 35% of the cases reported does not by itself suggest an association between atrial fibrillation and alcohol intoxication. The prevalence of alcoholism in patients admitted to general hospitals has been variously reported to be between 15% and 29%.[2-4] Furthermore, informal surveys in university teaching hospitals and Veterans Administration Hospitals have shown a prevalence of 50% or more.[5] In this study, the prevalence of alcohol intoxication among patients with atrial fibrillation should have been compared with the prevalence of alcohol intoxication among an appropriate control group, perhaps age- and sex-matched admissions from the emergency room for diseases other than atrial fibrillation.

In support of the proposition that alcohol caused atrial fibrillation in the nine intoxicated patients with no other known cause, it may be noted that these patients had a relatively benign course when compared with those patients with known coronary or lung disease. Unfortunately, the authors do not indicate whether the course of atrial fibrillation in intoxicated patients differed from that of the six patients with idiopathic atrial fibrillation who were not intoxicated.

The authors also conclude that alcohol was more likely to cause or contribute to atrial fibrillation in patients under the age of 65 years, since a greater percentage of these patients were intoxicated with alcohol. Although the breakdown of causes of atrial fibrillation may differ between age groups, the difference in the percentage who were intoxicated is likely to be unrelated. That is, those under the age of 65 years may be more likely to be admitted to the emergency room intoxicated regardless of whether or not they have atrial fibrillation. Adjustment for age and other potentially confounding variables may substantially alter the results.

The relationship between alcohol in-