Correspondence

Ischemic Hepatitis and Collateral Damage to the Liver in Severe Viral Respiratory Tract Infections

To the Editor-in-Chief:

Polakos and colleagues¹ investigated immunological causes of hepatic involvement by influenza virus respiratory tract infection manifesting itself in alanine and aspartate aminotransferase elevation and found evidence for a role of antigen-specific T cells in their pathogenesis. Transaminase levels are not routinely determined in ward or ambulatory patients with influenza virus infection because transaminase level elevation is not associated with clinically significant hyperbilirubinemia and jaundice. Transaminase levels are, however, frequently determined in patients in the intensive care unit. Adams and Hubscher² mention in their commentary on the work of Polakos and colleagues¹ our observational study,³ in which we reported on the finding of elevated transaminase levels in 46% of children ventilated in the pediatric intensive care unit with severe respiratory syncytial virus bronchiolitis. In our study we found evidence for a cause of collateral hepatic damage in respiratory syncytial virus infection, which is not related to immunological processes. Eighty-six percent of patients with, but only 27% of patients without, congenital heart disease had elevated transaminase levels ($P < 0.001$). In patients with congenital heart disease, we also found elevated cardiac troponin T levels, probably indicating myocardial failure. Influenza virus pneumonia has been associated with heart failure in elderly patients,⁴ and congenital heart disease has been associated with elevated transaminase levels due to hepatic venous congestion in children.⁵ Right ventricular failure in severe respiratory disease causes ischemic hepatitis due to hepatic venous congestion. Elevated transaminase levels in patients with severe respiratory viral infections on the intensive care unit, therefore, may not just indicate collateral damage due to an immunological process but may more commonly be an indicator of myocardial decompensation.

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References

1. Polakos NK, Cornejo JC, Murray DA, Wright KO, Treanor JJ, Crispe IN, Topham DJ, Pierce RH: Kupffer cell-dependent hepatitis occurs during influenza infection. *Am J Pathol* 2006, 168:1169–1178

2. Adams DH, Hubscher SG: Systemic viral infections and collateral damage in the liver. *Am J Pathol* 2006, 168:1057–1059
3. Eisenhut M, Thorburn K, Ahmed T: Transaminase levels in ventilated children with respiratory syncytial virus bronchiolitis. *Intensive Care Med* 2004, 30:931–934
4. Yap FH, Ho PL, Lam KF, Chan PK, Cheng YH, Peiris JS: Excess hospital admissions for pneumonia, chronic obstructive pulmonary disease, and heart failure during influenza seasons in Hong Kong. *J Med Virol* 2004, 73:617–623
5. Mace S, Borkat G, Liebman J: Hepatic dysfunction and cardiovascular abnormalities. *Am J Dis Child* 1985, 139:60–65

Authors' Reply:

In his letter to the editor, Dr. Eisenhut rightly points out that ischemic liver damage may contribute to the elevated serum transaminase levels seen in severe respiratory viral infections in the critically ill. In critically ill patients, liver damage is usually multifactorial, and the contribution of one specific factor may be difficult to ascertain. However, the collateral liver damage reported by Polakos and colleagues¹ was observed in healthy vaccine-study volunteers given a mild influenza infection. Although liver biopsies were not obtained, it is inconceivable that such samples would show ischemic changes in healthy volunteers. Furthermore, the histopathological assessment of livers from influenza-infected mice showed a focal active hepatitis without any evidence of ischemic hepatic necrosis. Although Dr. Eisenhut's point is well taken in the context of life-threatening illness requiring critical care, we do not think it is relevant in the context of most cases of influenza-associated hepatitis. Furthermore, collateral damage should be considered as a possible contributory mechanism of liver damage in all patients with severe viral infections.

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References

1. Polakos NK, Cornejo JC, Murray DA, Wright KO, Treanor JJ, Crispe IN, Topham DJ, Pierce RH: Kupffer cell-dependent hepatitis occurs during influenza infection. *Am J Pathol* 2006, 168:1169–1178