

1. Morley CJ, Davis PG, Doyle LW, Brion LP, Hascoet J-M, Carlin JB. Nasal CPAP or intubation at birth for very preterm infants. *N Engl J Med* 2008;358:700-8. [Erratum, *N Engl J Med* 2008;358:1529.]
2. Stevens TP, Harrington EW, Blennow M, Soll RF. Early surfactant administration with brief ventilation vs. selective surfactant and continued mechanical ventilation for preterm infants with or at risk for respiratory distress syndrome. *Cochrane Database Syst Rev* 2007;4:CD003063.

**TO THE EDITOR:** Morley et al. found that early CPAP did not significantly reduce the rate of bronchopulmonary dysplasia, but as compared with infants in the intubation group, fewer infants in the CPAP group received oxygen at 28 days, and they had fewer days of ventilation.<sup>1</sup> However, there was no reference to whether chorioamnionitis was an antenatal risk factor for bronchopulmonary dysplasia in these patients.<sup>2</sup> We would be interested to know whether there was a relationship between an antenatal diagnosis of chorioamnionitis and the outcomes.

Vincenzo Zanardo, M.D.  
Daniele Trevisanuto, M.D.  
Silvia Chiarelli, M.D.  
Padua University School of Medicine  
35128 Padua, Italy  
zanardo@pediatria.unipd.it

1. Jobe AH, Ikegami M. Antenatal infection/inflammation and postnatal lung maturation and injury. *Respir Res* 2001;2:27-32.
2. Watterberg KL, Demers LM, Scott SM, Murphy S. Chorioamnionitis and early lung inflammation in infants in whom bronchopulmonary dysplasia develops. *Pediatrics* 1996;97:210-5.

**TO THE EDITOR:** When receiving air at above atmospheric pressure through nasal prongs, a baby has to breathe out against both increased pressure and increased resistance. While nasal prongs are being used, handling of the baby or his or her crying may cause an abrupt change in alveolar pressure. The association of pneumothorax with CPAP may be related to these factors rather than to “airway” pressures measured outside the baby. A mask might carry less risk than prongs.

Tom Hughes-Davies, F.R.C.P.  
Breamore Marsh  
Fordingbridge SP6 2EJ, United Kingdom  
thhd@thhd.fsnet.co.uk

**THE AUTHORS REPLY:** In response to Nanan et al., infants in the Continuous Positive Airway Pressure or Intubation at Birth (COIN) trial who were randomly assigned to CPAP treatment after birth were not intubated specifically for surfactant treatment. They received surfactant only if they were intubated and ventilated, and surfactant was administered according to local protocols. We collected data only on whether surfactant was given — not on the timing of surfactant therapy after birth — so we cannot answer this question.

With regard to the comments by Zanardo and colleagues, data on chorioamnionitis were not collected for three reasons. First, the trial was started before we knew that chorioamnionitis might be important. Second, since diagnosing chorioamnionitis is subjective or depends on placental histologic findings, we decided it would be impractical to collect this information for all infants. Third, the COIN study was a randomized trial, and there was no reason to believe that the rate of chorioamnionitis would differ between the groups.

In response to Hughes-Davies, there is no clinical evidence that infants treated with nasal CPAP exhale through the CPAP prongs. As Hughes-Davies suggests, this would mean that they would breathe out against increased pressure and resistance. Our experience is that infants treated with nasal CPAP breathe out through their mouths or around the prongs. With face-mask CPAP and intubation, infants who undergo mechanical ventilation would be forced to breathe out against the pressure. It is therefore unclear why infants treated with a nasal mask would have lower rates of pneumothorax than those treated with nasal prongs.

Colin J. Morley, M.D.  
Peter G. Davis, M.D.  
Lex W. Doyle, M.D.  
Royal Women's Hospital  
Carlton, VIC 3053, Australia  
colin.morley@rwh.org.au

## Chronic Hepatitis E and Organ Transplants

**TO THE EDITOR:** Kamar and colleagues (Feb. 21 issue)<sup>1</sup> report eight cases of chronic hepatitis E virus (HEV) infection in immunosuppressed organ-

transplant recipients, a constellation that was hitherto not observed. One wonders whether the persistence of HEV infection is a more general con-

sequence of immunosuppression, which has implications for all so-called nonpersistent pathogens. Previously, we observed prolonged and possibly chronic shedding of human metapneumovirus in two patients with cancer who were immunosuppressed because they were receiving chemotherapy.<sup>2</sup> Furthermore, it was recently reported that immunosuppression induced by lactate dehydrogenase-elevating virus led to increases in the severity and duration of the acute phase of friend virus infection in mice, most likely because of diminished CD8<sup>+</sup> responses.<sup>3</sup> Such observations may provide support for earlier assumptions that if the CD4<sup>+</sup> defense is insufficient because of immunosuppression, the CD8<sup>+</sup> response is unlikely to eliminate infection.<sup>4</sup> The study by Kamar et al. revealed significantly reduced CD4<sup>+</sup> counts in patients with chronic HEV infection. Under these specific circumstances, so-called nonpersistent viruses may cause chronic colonization and recurrent infection. Hence, reducing drug-induced immunosuppression during acute HEV infection might be a strategy to prevent the progression to chronic hepatitis.

Oliver Schildgen, Ph.D.  
Andreas Müller, M.D.  
Arne Simon, M.D.

University of Bonn  
53105 Bonn, Germany  
schildgen@virology-bonn.de

1. Kamar N, Selves J, Mansuy J-M, et al. Hepatitis E virus and chronic hepatitis in organ-transplant recipients. *N Engl J Med* 2008;358:811-7.
2. Wilkesmann A, Schildgen O, Eis-Hübinger AM, et al. Human metapneumovirus infections cause similar symptoms and clinical severity as respiratory syncytial virus infections. *Eur J Pediatr* 2006;165:467-75.
3. Robertson SJ, Ammann CG, Messer RJ, et al. Suppression of acute anti-friend virus CD8<sup>+</sup> T-cell responses by coinfection with lactate dehydrogenase-elevating virus. *J Virol* 2008;82:408-18.
4. Wherry EJ, Ha SJ, Kaech SM, et al. Molecular signature of CD8<sup>+</sup> T cell exhaustion during chronic viral infection. *Immunity* 2007;27:670-84. [Erratum, *Immunity* 2007;27:824.]

**THE AUTHORS REPLY:** With regard to the comments by Schildgen et al., prolonged acute hepatitis A virus and HEV infections have been reported previously in both immunocompromised and nonimmunocompromised patients.<sup>1,2</sup> Our report indicated that HEV infection may evolve to chronic hepatitis in organ-transplant recipients. In addition, a unique case of HEV-related cirrhosis has recently been reported.<sup>3</sup> Schildgen et al. suggest that the evolution of HEV infection to chronic hepatitis is related to marked immunosuppression. They base their assumption on two studies of viral infections that appear to be unrelated to those that have been observed in organ-transplant recipients. We agree that the evolution of HEV infection to chronic hepatitis in the setting of marked immunosuppression may be a mechanism, since we have found a lower CD4<sup>+</sup> cell count in patients in whom chronic hepatitis evolved than in patients who were clear of the virus. Hence, in HEV-infected transplant recipients, we suggest reducing immunosuppressive therapies that target T cells (i.e., mainly calcineurin inhibitors) in order to allow clearance of the virus.

Nassim Kamar, M.D., Ph.D.  
Jacques Izopet, Pharm.D., Ph.D.  
Lionel Rostaing, M.D., Ph.D.

Toulouse University Hospital  
31059 Toulouse, France  
kamar.n@chu-toulouse.fr

1. Costa-Mattioli M, Allavena C, Poirier AS, Billaudel S, Raffi F, Ferré V. Prolonged hepatitis A infection in an HIV-1 seropositive patient. *J Med Virol* 2002;68:7-11.
2. Tamura A, Shimizu YK, Tanaka T, et al. Persistent infection of hepatitis E virus transmitted by blood transfusion in a patient with T-cell lymphoma. *Hepato Res* 2007;37:113-20.
3. Gérolami R, Moal V, Colson P. Chronic hepatitis E with cirrhosis in a kidney-transplant recipient. *N Engl J Med* 2008;358:859-60.

## Phototherapy for Neonatal Jaundice

**TO THE EDITOR:** In their Clinical Therapeutics article on phototherapy for neonatal jaundice, Maisels and McDonagh (Feb. 28 issue)<sup>1</sup> describe various mechanisms for maximizing the efficacy of phototherapy. They state, “The dose and efficacy of phototherapy are also affected by the infant’s dis-

tance from the light (the nearer the light source, the greater the irradiance).” However, this statement must be applied with great care. Indeed, guidelines from the American Academy of Pediatrics Subcommittee on Hyperbilirubinemia specifically urge caution when halogen lamps, which