

The silent infection: should we be testing for perinatal hepatitis C and, if so, how?

We recommend screening all infants whose mothers are HCV antibody-positive

Perinatal transmission of hepatitis C virus (HCV) is the main source of newly diagnosed paediatric HCV infections in Australia.¹ About 5% of infants born to women who are positive for both HCV antibody and HCV RNA during pregnancy will acquire HCV infection.² The risk of transmission is increased by HIV coinfection during pregnancy. It is estimated that 1%–2% of women of childbearing age in Australia are infected with HCV.³ Assuming that 75% of these have chronic hepatitis and viraemia in the third trimester of pregnancy, we would expect about 75–100 new cases of vertically acquired childhood HCV infection in Australia per year. However, rates reported from national deidentified laboratory data⁴ and from the Australian Paediatric Surveillance Unit¹ are much lower, suggesting that paediatric HCV infection may be underrecognised in Australia. We thus recommend a more standardised approach to identification and follow-up of infants exposed perinatally to HCV.

Why identify infants with HCV infection? Although most HCV-infected children have good health for at least the first two decades of life, HCV-induced chronic liver disease and liver failure have both been reported in childhood.^{5,6} As it is not possible to predict which children will develop severe liver disease, long-term monitoring of HCV-infected children is needed.⁶

In addition, children identified as HCV-positive should be offered vaccination against both hepatitis A (after 2 years of age) and hepatitis B. Superinfection of HCV-infected individuals with hepatitis A virus increases the risk of fulminant hepatitis and death, while coinfection with HCV and hepatitis B virus is associated with a higher risk of cirrhosis and hepatocellular carcinoma.⁷

HCV-infected children with severe hepatic involvement should be offered antiviral therapy. A number of treatments (interferon-alfa, ribavirin and pegylated interferon) successfully eradicate HCV in 40%–80% of HCV-infected adults, depending on the HCV genotype. Although data about their efficacy in childhood are limited, these treatments have been used safely and effectively in children. Identifying Australian children with HCV infection could also allow them access to novel therapies and ongoing international multicentre randomised controlled trials.⁵

Why is HCV infection underdiagnosed in childhood? Children with HCV infection may not be identified for several reasons:

- They are unlikely to attract medical attention, as most have no symptoms or signs of liver disease, while a small proportion have mild hepatomegaly.^{1,5} Consequently, their identification relies on careful follow-up of offspring from at-risk pregnancies.
- Antenatal HCV screening practices vary widely around the country,⁸ and therefore many HCV-exposed infants are missed. The Royal Australian and New Zealand College of Obstetricians and Gynaecologists recommends universal antenatal screening for HCV.⁸ However, other national bodies recommend selective testing for HCV infection in pregnant woman with identifiable risk factors (eg, intravenous drug use, tattooing, body piercing, needle sharing, or receipt of blood products or invasive procedures overseas or before 1990 in Australia).^{8,9}

- Appropriate methods of testing HCV-exposed infants and children are not widely understood, and national guidelines for testing and follow-up of offspring of HCV-infected mothers^{8,9} are not detailed or widely known to child health care providers. In children aged under 18 months, persistence of maternal antibody complicates the interpretation of HCV antibody tests, while in infants aged under about 2 months qualitative HCV RNA polymerase chain reaction (PCR) testing is insensitive.¹⁰

How should we screen for vertically transmitted HCV infection? For diagnosing perinatal HCV infection, the most cost-effective strategy may be to screen offspring of HCV RNA-positive women. However, as HCV RNA levels can fluctuate in pregnancy, and as antenatal HCV screening practices vary, we recommend:

- Screening all infants born to women who are HCV antibody-positive, using HCV antibody and liver function tests, at 18 months of age or older. If results are negative, then the infant can be safely assumed not to have HCV infection. If antibody results are positive or liver function is abnormal, then the child should be referred to a paediatric gastroenterologist.
- Testing infants who are considered unlikely to attend for 18-month follow-up, using HCV RNA and liver function tests at 3 months of age, when they are more likely to be receiving local medical care. Those with positive HCV RNA results or abnormal liver function should be referred to a paediatric gastroenterologist. If both tests give negative results, we recommend repeating HCV antibody testing at age 18 months, as both viraemia and transaminitis can be intermittent in HCV infection. HCV RNA testing for the diagnosis of vertically transmitted HCV infection (in isolation) is not an approved item on the current Medicare Benefits Schedule¹¹ and costs about \$90 (ie, six times the cost of HCV antibody testing).

Testing for HCV should be performed only after pre-test family counselling and with the consent of the infant's parent(s) or guardians.

There is an urgent need to disseminate clinical practice guidelines in Australia for the screening, diagnosis and management of children born to women with HCV infection during pregnancy. Ongoing collection of national data on HCV infection in children is needed to document the scale of this emerging disease in the paediatric population, and the groups of children at risk of infection. Identification and referral of HCV-infected children will allow early initiation of therapy and monitoring of outcomes.

Winita Hardikar

Head, Department of Hepatology, Royal Children's Hospital Melbourne, VIC

Elizabeth J Elliott

Paediatrician, Discipline of Paediatrics and Child Health, University of Sydney and The Children's Hospital at Westmead, Sydney, NSW

Cheryl A Jones

Paediatric Infectious Diseases Consultant
Discipline of Paediatrics and Child Health, University of Sydney and
The Children's Hospital at Westmead, Sydney, NSW
cherylj@chw.edu.au

EDITORIALS

Acknowledgements: We thank the other members of the Australian Paediatric Surveillance Unit (APSU) Hepatitis C Study team, in particular Ms Sue Polis, Associate Professor Greg Dore and Professor John Kaldor (National Centre for HIV and Hepatitis C Epidemiology and Clinical Research [NCHECR]) for their valuable comments, and the contributors to the APSU. The APSU Hepatitis C study is funded by the NCHECR and the Department of Health and Ageing.

- 1 Kaldor J, Jones CA, Elliott E, et al. Hepatitis C virus infection. In: Elliott E, Cronin P, Rose D, Zurybski Y, editors. Australian Paediatric Surveillance Unit Report 2002–2003. Sydney: Australian Paediatric Surveillance Unit, 2003: 37–38.
- 2 Conte D, Fraquelli M, Prati D, et al. Prevalence and clinical course of chronic hepatitis C virus (HCV) infection and rate of HCV vertical transmission in a cohort of 15,250 pregnant women. *Hepatology* 2000; 31: 751–755.
- 3 Sfameni SF, Francis B, Wein P. Seroprevalence and assessment of risk factors for hepatitis C virus infection in pregnancy. *Aust N Z J Obstet Gynaecol* 2000; 40: 263–267.
- 4 Australian National Council on AIDS Hepatitis C and Related Diseases Hepatitis C Subcommittee 2002, Hepatitis C Virus Projections Working Group. Estimates and projections of the hepatitis C virus epidemic in Australia. Sydney:ANCAHRD, 2002: 1.
- 5 Hardikar W. Natural history and treatment of hepatitis C in children. *J Gastroenterol Hepatol* 2004; 19: S379–S381.
- 6 Birnbaum AH, Shneider BL, Moy L. Hepatitis C in children. *N Engl J Med* 2000; 342: 290–291.
- 7 Keeffe EB. Acute hepatitis A and B in patients with chronic liver disease: prevention through vaccination. *Am J Med* 2005; 118 Suppl 10A: S21–S27.
- 8 Spencer JD, Tibbits D, Tippet C, et al. Review of antenatal testing policies and practice for HIV and hepatitis C infection. *Aust N Z J Public Health* 2003; 27: 614–619.
- 9 Australian National Council on AIDS Hepatitis C and Related Diseases. National Hepatitis C testing policy. Sydney: ANCAHRD, 2003. Available at: <http://www.ancahrd.org/pubs/pdfs/hepctestng.pdf> (accessed Oct 2005).
- 10 Buttery J. Hepatitis C virus. In: Palasanthiran P, Starr M, Jones CA, editors. Management of perinatal infections. Sydney: Book House, 2002: 13–15.
- 11 Australian Government Department of Health and Ageing. Medicare Benefits Schedule. Canberra: The Department, 2005: 592. □