Reviewer's report

Title: High frequency of Human Cytomegalovirus DNA in the Liver of Infants with Extrahepatic Neonatal Cholestasis.

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Reviewer: Björn Fischler

Reviewer's report:

General
This manuscript deals with the possible connection between CMV infection and biliary atresia, as well as other cholestatic diseases in the infant. As the authors point out, further progress in the definition of these etiological factors is essential to improve the therapeutical possibilities. Their findings support a few previous reports suggesting that CMV infection is frequently found in these patients.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
1. The description of the patients is less thorough than that of the virological methods. For example, how was the diagnosis biliary atresia settled? By liver biopsy? Cholescintigraphy? Intraoperative cholangiogram? Postoperative examination of bile duct remnants?
What was the age of the control children?
Table 1 is confusing since it is hard to understand the division into 2 groups (with and without asterisk?!). Are the ALT, GT and DB mean values?
2. Much work seems to have been put into histological examination. However, some of the parameters are hard to understand. For example, the exact nature of the cholestasis intracellular? Canalicular?- is not stated. Cholestasis may occur without cholangitis and vice versa.
Not only ductal proliferation, but also paucity of intrahepatic bile ducts need to be looked for.
Table 2 is of interest but these findings need to compared to those of CMV negative BA patients.
What was the distinction between mild and moderate chronic active inflammation?
3. Clear discrepancies between CMV serology and CMV detection in liver tissue were noted. However, this does not necessarily mean that the serology had a low sensitivity/accuracy. The authors need to discuss other possibilities. For example, the aspect of timing of infection and the duration of IgM antibodies need to be accounted for. Concomittant CMV testing in the mothers of these children would probably have been informative too.
The traditional gold standard method for diagnosing congenital CMV is the detection of CMV in the urine before 4 weeks of age. This method seems more sensitive than CMV-IgM in serum (see for example reference 13). The authors need to discuss why they have not used CMV isolation in urine, nor PCR detection in blood.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
1. In the abstract BA is used a short form for biliary atresia, without stating its connotation.
2. Details on the ELISA and PCR methods concerning sensitivity would be clarifying.
3. For the PCR detection in liver tissue either fresh material or parafin-embedded fragments were used. Did the authors see any differences in the results between these two groups?
4. It is rightly pointed out that a positive CMV finding might delay further diagnostic procedures in
these patients. In fact, this has already been described by Tarr et al in reference 16. Was there a difference in the age of BA diagnosis between CMV positive and CMV negative patients?

5. Was the study approved by the ethics committee?

Discretionary Revisions (which the author can choose to ignore)

**What next?:** Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No

**Declaration of competing interests:**

I declare that I have no competing interests