

ulations at risk of HCV infection such as haemodialysis patients await this type of screening.

We declare that we have no conflict of interest.

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### Authors' reply

Juan A Quiroga and Vicente Carreño raise the issue of to what extent hepatitis C virus (HCV) is truly cleared from the body, even for individuals in whom virus is no longer detectable by conventional analyses of plasma or serum.<sup>1</sup> This issue applies not only to patients whose recombinant immunoblot assay (RIBA) results are indeterminate, but more commonly to those in whom RIBA results are positive, indicating an acute resolving infection. Additionally, the question has been applied to those who have had persistent infection, which has been apparently successfully treated by interferon-based regimens.<sup>2</sup> The detection of viral RNA, including the negative strand (indicative of replicating virus), has been possible with very sensitive assays of both peripheral blood mononuclear cells and liver tissue in some such patients.

The replicative capacity of these viral forms is currently not understood. However, virally derived antigen might be produced in such settings, which could contribute to the maintenance of immunological memory, and thus the T-cell responses we saw. The issue of the role of antigen in the maintenance

of long-term immunological memory after viral infection has been extensively investigated in mouse models, such as lymphocytic choriomeningitis virus. Memory CD8+ T cells seem to persist in situations where antigen is no longer detectable, although if low-level antigen is present it can lead to restimulation of T cells and increases in functional capacity, including protection against rechallenge.<sup>3,4</sup>

In HCV, recent studies suggest that virus-specific T cells found in blood after infection exist in a quiescent memory state.<sup>5</sup> However, we have seen quite some variation in both CD4+ and CD8+ T-cell responses, and some of this variability could result from the presence of viral antigens in some individuals, in whom it is associated with low-level viral persistence, but not in others. Additionally, the observation that such immune responses can change in immunodominance over time in selected individuals also suggests that antigen presentation could continue in some form long after apparent resolution of infection.

Since we saw maintenance of cellular immune responses in individuals with RIBA-indeterminate antibody status, a proportion of such patients could also possess very low-level viral RNA in particular sites, as could RIBA-positive individuals after spontaneous resolution of acute infection. However, the key point of the study was that T-cell responses were detectable in the RIBA indeterminate group, suggestive of exposure to HCV antigens at some point. Further detailed studies are clearly required to define the origins of this state and its natural history, as well as the potential role of persistence of viral RNA.

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### Appropriate technology in tuberculosis diagnostics

We would like to make three points in response to Alwyn Mwinga's Comment (Jan 8, p 97)<sup>1</sup> on our comparison of diagnostic techniques for tuberculosis in HIV patients with inadequate sputum production.<sup>2</sup>

First, the statement that the use of the string test "will be hampered by the need for sputum induction" seems to be a misunderstanding: sputum induction added nothing to the results of the string test and was used only as a comparative test for this research. In fact, our findings clearly show that the string test alone offers better diagnostic sensitivity than sputum induction. By obviating the need for sputum induction, it could remove an important risk factor for nosocomial transmission of tuberculosis, particularly in resource-poor settings with a high tuberculosis burden, no isolation facilities, and wards crowded with highly susceptible HIV-infected patients. We would therefore suggest that the string test should supersede sputum induction if these data are borne out in other settings.

Second, we believe that the string test might indeed have a potential role in the difficult diagnosis of paediatric pulmonary tuberculosis, and we have shown that the string test procedure is well tolerated by children with sus-

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pected tuberculosis as young as 4 years, and highly acceptable to their parents and attendant nursing staff.<sup>3</sup> Such findings could open the way for a comparative efficacy study with other diagnostic procedures including sputum induction.

Third, we strongly concur with Mwinga's observations that the slowness of conventional solid media culture hampers tuberculosis diagnosis and that availability of specialist equipment marketed for more rapid liquid-culture-based techniques is limited. Fortunately, however, the liquid-culture method used in our research (the microscopic observation drug susceptibility [MODS] assay), which involves the simple microscopic observation of characteristic *Mycobacterium tuberculosis* colonies in broth, requires nothing more complex than an incubator and an inverted light microscope and standard laboratory consumables which are available widely.<sup>4,5</sup> Detection of tuberculosis with simultaneous readout of rifampicin and isoniazid sensitivities takes a median of 7 days. At less than US\$2 per sample, we believe that MODS warrants more widespread use, especially in developing countries where most tuberculosis occurs.

We declare that we have no conflict of interest.

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## Strangulation by intravenous tubes

The risk of accidental childhood asphyxia in various recreational and domestic settings has been repeatedly stressed, and represents an important target for preventive action. In infants, most unintentional deaths associated with asphyxia are sleep related—eg, suffocation by an overlying adult, smothering by bedding or a pillow, or wedging between a mattress and bed frame.<sup>1</sup> Strangulation is less common in infants than in toddlers, and is very seldom reported in the hospital setting.

In 2004 we investigated a fatal strangulation by intravenous (iv) tubing during hospital treatment. A 10-month-old girl with a history of acute lymphoblastic leukaemia was admitted to a local hospital for cytostatic therapy and received iv antibiotics and liquids via a central venous catheter for treatment of suspected sepsis. The patient's temperature decreased over the next few days to about 36°C. 3 days after admission, the girl was restless in the evening but eventually fell asleep after being given an analgesic. The nurse on duty checked the infant early the next morning, at which time she was sleeping; an hour later, the nursing staff found her lying prone in her crib. She had no pulse, and was cyanotic and apnoeic. The iv tubing inserted into her right clavicular vein was tightly wrapped twice around her neck. The tubing was cut immediately, but despite prompt efforts at resuscitation the girl was declared dead shortly after.

The case was referred to the Department of Forensic Medicine, University of Helsinki, where an autopsy confirmed the cause of death as asphyxia by strangulation. The National Authority for Medicolegal Affairs inves-

tigated and concluded that there was no negligence by staff. All relevant authorities were, however, informed as to the risks of strangulation associated with iv tubing.

Unintentional strangulation by iv tubing and lines in hospital is rarely reported. In addition to this case, only one other fatal has been described, in Canada in 2002.<sup>2</sup> Two deaths were reported in the 1980s in the USA, but details about the patients' ages and circumstances surrounding the incidents are unavailable.<sup>2</sup> Two non-fatal cases of strangulation, one by iv tubing and one by the wires of a monitor, have also been described.<sup>2,3</sup> However, we believe that fatal and non-fatal cases of strangulation might be more common than a search of the published work implies; eventually, wider disclosure of such incidents might lead to more effective prevention.

After the 2002 death, Health Canada<sup>4</sup> issued an official notice to all Canadian hospitals, aiming to warn staff, parents, and care-givers about the risk of strangulation posed by iv devices and monitor leads, and recommending preventive measures—eg, individual risk assessment, an appropriate degree of supervision, and use of accessories to stabilise flexible lines.

In addition to use of a rigid tube through which the iv line is run, Finnish authorities also recommend a video surveillance system.

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