10. Lelie PN, Cuypers TM, Reesink HW, et al. Patterns of serological markers in transfusion-transmitted hepatitis C virus infection using second generation HCV assays. J Med Virol 1992; 37:203–209.
11. Yuki N, Hayashi N, Hagiwara H, et al. Improved serodiagnosis of chronic hepatitis C in Japan by a second generation enzyme-linked immunosorbent assay. J Med Virol 1992; 37:237–240.
12. Ranjan D, Burke G, Esquenazi V, et al. Factors affecting the 10-year outcome of human renal allografts: the effect of viral infections. Transplantation 1991; 51:113–117.

Discussion

DR. JOHN L. HUSSEY (New Orleans, Louisiana): Michael, you are to be congratulated for this very scholarly and well-presented paper. However, knowing you as I do, I would have been very surprised if it had been otherwise. As HCV infection is more common than previously thought, more specific screening tests have been developed, the Abbott HCV second-generation being the most recent that I'm aware of. The disturbing reality that you point out is the significant risk of HCV seropositivity in transplant patients. In fact, as you mentioned, this is probably an underestimation. The 50% or greater risk in some studies of false negativity reported with the original ELISA test, the one which you referred to, the C100-3, was reduced to less than 20% by the second generation test and really has been further reduced to less than 5% with the so-called RIBA test, the recombinant immunoblot assay. A greater incidence will probably be shown as more refined tests are developed. It is chilling to note the 17% risk of chronic liver disease that you report. You might ask, how can this be reduced? We can eliminate blood and blood products transfused. The widespread use of EPO, the human recombinant erythropoietin will certainly reduce and possibly eliminate transfusion in dialysis patients. Certainly specific antigen testing techniques should be developed to develop those who are at the greatest risk for the ravages of the HCV infection that you pointed out. And of course anti-viral agents specifically directed against HCV are much needed and long awaited. What about other sources of HCV that you perhaps did not discuss completely, the seropositive organ being a good example? In the February 1991 meeting at the Southeastern Organ Procurement Foundation, members unanimously stated that they would not use organs from HCV-positive donors. The United Network for Organ Sharing held a similar opinion stating that the majority of American transplant centers would not accept HCV-positive organs. However, because we really incompletely understood HCV at that time and because of the shortage of donor organs, we took a bolder position stating that we would use HCV-positive organs under the following circumstances: 1) When the recipient was also HCV-positive by conventional testing, 2) for patients with 90% or greater panel reactive antibodies and having a negative cytotoxic crossmatch with the donor, and 3) for those individuals who had been on a waiting list for greater than 5 years and had not received a first kidney transplant. I think in view of your work and the work of others coming out that we may want to rethink our position in the light of this, although in point of fact we have never used this scheme in any of our transplants.

DR. RICHARD J. HOWARD (Gainesville, Florida): Dr. Rohr, I enjoyed your paper and its furthering of our understanding of hepatitis and liver dysfunction following renal transplantation. We also recently looked at 100 patients who had undergone kidney transplants with both serological testing for antibody to hepatitis and by the polymerase chain reaction, and our findings were substantially similar to yours, that is 18% of the patients had evidence of hepatitis C before transplantation. We also found that 25% had dysfunction of their liver or elevated ALT levels after transplantation. If they were hepatitis C positive, 52% had elevated liver ALT levels. What I would like to ask you is, how good the second-generation test is for antibody to hepatitis C. The first-generation test, as you pointed out, the C100-3 assay, had a very poor sensitivity and specificity when compared to PCR testing. In fact, in our own studies and those of Arida from Japan approximately 50% of individuals who were negative by first-generation test for antibody to hepatitis C were positive by the polymerase chain reaction. If they were positive by antibody testing, they also generally were positive by PCR testing. Do you have any idea how much better the second-generation test is than the first test? You showed that 16 out of 29 individuals reacted by the first-generation testing, but 13 individuals did not. But do you have any independent study of how many individuals who were positive by the second-generation test, in fact, had hepatitis C as determined by any other means? And similarly do you have any measurements of how many individuals who were negative by your testing for antibody to hepatitis C, in fact, were positive when measured by some other test? We've thought that until now the gold standard for hepatitis C testing was the polymerase chain reaction. Is the second-generation test as good?

DR. FREDERICK BENTLEY (Louisville, Kentucky): I also would like to congratulate the authors for another piece of the puzzle and adding to the chapter that is currently being written about hepatitis C. It is a very curious virus that I find in that it has many similarities to hepatitis B but yet it has many dissimilarities to it. Certainly in renal transplantation in the past, chronic liver disease has been one of the more common causes of death in renal transplant patients who have survived 5 years or longer. In patients who have chronic liver disease at the time that they received a renal transplant, mortalities as high as 50% occurred in the 2 years after transplantation. Therefore, the implications of hepatitis C positivity in chronic renal failure patients and their suitability for transplant has yet to be defined. This paper adds to the developing body of information on hepatitis C in patients with chronic renal failure. I have a couple of questions for Dr. Rohr. First of all, do they have sera available from any of the donors of these patients to be able to check this for the presence or absence of the hepatitis C antibody in a retrospective fashion? There have been reports looking at sera from donors in a retrospective fashion and then looking at how the recipients did when they received these hepatitis positive C organs. Their conclusion was that it was a very safe thing to do. That study was also before the second-generation of testing. The patients with chronic liver disease, were they biopsied to determine exactly what type of chronic liver process was going on, such as a histology pattern consis-

tent with chronic active hepatitis, and if they were, would the authors consider treating these patients with interferon to see if they could suppress the active process? Finally, do the authors have an opinion about whether or not patients who are hepatitis C positive should be transplanted or not, or any other special precautions taken in approaching them.

DR. MICHAEL S. ROHR (Closing Discussion): I would like to thank all three discussants for their comments. In response to Dr. Hussey's question, I don't have any comparison between the Abbott second-generation and the recombinant immunoblot technology. I do agree that the use of recombinant erythropoietin probably will dramatically reduce the number of transfusions that dialysis patients are required to be exposed to, and I would expect that in a decade or so HCV-positive dialysis patients will be probably rare in number. It is true that you could reduce exposure to HCV by eliminating the HCV-positive organ donor. This is also apropos of Dr. Bentley's comments that this is a very controversial topic in transplantation and organ procurement at this time and relates, in part, to the fact that most of the data was generated with first-generation testing technology and that was so unreliable that many times you could put a so-called positive organ into a negative recipient with impunity. But I think as the testing becomes more sophisticated and more specific that view about the risk at least to a kidney recipient will change. There are papers that conclude that it is safe to use HCV-positive donors at least when they are positive in the first-generation assay. Dr. Howard's question about the relationship between the antibody detected in the second-generation assay and detection of viral RNA by polymerase chain reaction is very appropriate. There is not a straight line correlation between the two technologies. The second-generation antibody assay does identify a much higher percentage of PCR-positive specimens than the first generation assay. This has been looked at by Lalie, a Dutchman, who runs the transfusion service in Holland. He has determined that 78% of blood donors who are implicated in the infection of a patient with hepatitis C are positive in the second-generation assay. And there is a recent Japanese paper by Yuki who has a 95% correlation between PCR and second-generation testing in antibody-positive patients who have liver disease. Should we transplant HCV-positive recipients? A specific answer to Dr. Bentley's question, at this time I continue to do so. I inform them about the data. One problem with transplanting these patients is that we don't know exactly how they are going to fare on dialysis as compared to transplantation. Most of the patients that I see desperately want to get off of dialysis and are prepared to embrace a fair amount of risk in order to get transplanted. I think, if they're informed about that risk and can understand it is probably not inappropriate to transplant them. I agree with Dr. Bentley that we are in the middle of things about our understanding of hepatitis C disease and that our understanding of this problem and its consequences is likely to increase dramatically in the next couple of years as more is learned about the virus.