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Discussion

DR. ACHILLES A. DEMETRIOU (Los Angeles, California): I congratulate Dr. Morris and his colleagues from Vanderbilt for conducting this important, timely, and clinically relevant study. They demonstrated the effectiveness of introducing surrogate testing for hepatitis C using ALT and CORE-level measurements in reducing the incidence of post-transfusion hepatitis C at their institution. I have several questions for the authors. First, is the 0.2% incidence of post-transfusion hepatitis C per unit of blood product representative of your medical center or the community at large? And how does it compare with national figures in other geographic areas, especially large urban centers? Second, do you plan to continue follow-up of these patients and continue screening of all future patients in this category? Third, will you institute treatment, for example, with interferon in patients who go on to develop hepatitis C? And, finally, is there any advantage in screening the specific population of trauma patients over, say, a population with a genetic blood clotting like the hemophilia-type patients who are receiving blood products in large amounts for long periods of time?

DR. LEON PACHTER (New York, New York): I also want to compliment Dr. Morris and the Vanderbilt group on this excellent analysis of post-transfusion hepatitis C in a patient population that had a mean of 72.3 units of exposure. For those of us involved in trauma or transplantation, it's not unusual to transfuse 50 units of blood. I was happy to see at least from this study that not a single patient showed HIV positivity 1 year down the line, and that was somewhat comforting to me, John. I'm sure it was comforting to a lot of other people as well. This study, as Dr. Morris has shown, broke up two different groups, one before the ALT screening and CORE, and one afterwards, and was able to decrease the incidence of hepatitis C by 84%. In fact, the actual incidence in Dr. Morris's study is 0.23 per unit of transfusion. And I think that this is an excellent advance in trying to stamp out this disease, although as you can see, it has not been completely eradicated despite the prescreening. I have several questions for Dr. Morris, in the manuscript, you postulated that not all patients with an elevation in alanine aminotransferase were positive for hepatitis C and should therefore be screened with second generation tests such as the RIBA (the recombinant immunoblot assay) and the HCV (2.0). The result could then be a decrease in the number of blood units discarded and a subsequent increase in the donor pool. The key question is, what percentage of your patients had elevated ALT and were in fact negative for hepatitis C? Because if the numbers are small, then the cost/benefit ratio certainly would not be worth it. The second question, if you noticed in the slide, over 50% of the patients were positive for CMV? What implication does this have for the population in general, specifically, what implication does this have for the transplant patient? If you're going to transplant a liver and use 50 units of blood and 50% are positive for CMV, what implication does it have? I also notice on the program for tomorrow Dr. Haller is going to talk about nonoperative management of splenic injuries, which brings me back to the question here—since the incidence of overwhelming post-splenectomy infection in the adult after removal of the spleen is at best between 0.25 and 0.5 and that the incidence of hepatitis C is going to be 0.23 per unit transfused, then the window that we have of transfusion allotment is probably only 1 to 2 units. This has been an argument by people who are against nonoperative management. HIV, I guess, has been eliminated for the most part, but hepatitis C has not. Lastly, although the blood is screened, 0.23% is a significant number. Do you feel that some of the newer second, perhaps third generation tests, such as the anti-HCV2 would specifically—looking at nonstructural 3 portion of the HCV genome help reduce this further? I enjoyed this paper, and I think it will be a landmark reference for the future.

DR. JOHN A. MORRIS, JR. (Closing Discussion): I thank both Dr. Demetriou and Dr. Pachter for their comments. First of all, Dr. Demetriou asked the question as to whether these numbers were applicable just to our institution or nationwide. Indeed, they're applicable to our region. They really are blood bank-specific numbers. In the manuscript we have provided a risk profile for various assumptions under prevalence of the donor population. So that the risk profiles—the mathematics of the risk profile that we've done—can actually be taken for various populations. If you know what the prevalence of hepatitis C in your community is, you can then go back to the graphs in the manuscript and calculate what your threshold might be for

bringing patients back to screen. Do we plan to continue screening these patients? Yes. But to answer that question and one of Dr. Pachter's questions, we believe that the new generation of tests—the HCV2 test, which was just introduced—will probably reduce the incidence of hepatitis C by an order of magnitude. So, yes, we need to screen, to continue to follow patients, but we are going to need to not just follow our trauma patients, but our bone marrow transplants and the genetic defects that Dr. Demetriou alluded to, we're going to need to follow them. And we're probably going to need to follow them all in a multi-institutional basis to be able to get the numbers of patients necessary to do this analysis again in the next generation of screening tests. Dr. Pachter alluded to the ALT test and the sensitivity and specificity of the ALT test and whether indeed we could do away with that test and increase the number of people in the donor pool. And indeed if we dealing with the same sorts or donor shortages in the blood supply as we deal with in the liver transplantation population, we would do that. The fact of the matter is, however, we have enough blood donors to be able to meet our needs. And, at least theoretically, the ALT/CORE markers will become elevated earlier than the HCV3 marker. So that we may be able to pick up a small subgroup of patients in the donor population who have just recently been exposed to hepatitis C and where we might not get an elevation of our hepatitis C marker. The question that Dr. Pachter made about post-splenectomy sepsis is an essential question to ask. Clearly, we have to consider the risks of alternative therapy very closely when we postulate such things as nonoperative therapy. And if the risk of the nonoperative therapy—or the benefit of the non-operative therapy—is superseded by the risk of transfusion, clearly we cannot advocate nonoperative therapy. It is my guess that over the past 10 years it's been a trade off between post-splenectomy sepsis and transfusion risk. Remember, however, that only 20% of patients who develop hepatitis C go on to develop cirrhosis. So, indeed, we may have made some progress in that way. But I think that the new screening tests will clearly tip the balance in favor of the nonoperative therapy as we all have been espousing over the last several years. Finally, the implications for CMV virus in the transplant population. I'm not sure I'm qualified to speak about that, except I would give you one caveat: that CMV is relatively common in the overall patient population. And while we wouldn't expect to see patients in this massively transfused group who had either AIDS or hepatitis B pre-transfusion, we would certainly expect to see a number of these patients pre-transfusion who are positive for CMV. So our numbers with CMV may very well be spuriously high.