



## *The High Risk Recipient*

### **Mellow Yellow in a Non-Liver Fellow: Hepatitis C in the Extrahepatic Recipient**

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Many patients with chronic HCV are often considered not to be candidates for organ transplantation for a variety of poorly defined reasons. It is often assumed that the benefits of organ transplantation will be obviated by accelerated viral induced liver disease that is induced by immunosuppression. When considering organ transplantation for individuals with suspected HCV, it is important to ascertain that the person is currently infected with the virus. Most screening diagnostic tests are dependent upon the detection of antibodies generated against viral structural and nonstructural proteins. The likelihood that a person has/had HCV infection is increased by the number of HCV antigens that are identified by antibodies in the patient's sera. However, it is currently estimated that 15-30% of individuals will clear HCV after exposure, so the detection of antibody should not immediately lead to the conclusion that the individual has chronic HCV infection. Detection of viral RNA in the sera is the most definitive test to discern the presence of active HCV infection.

A major HCV-specific consideration in discerning the risk of transplantation in such a person is predicated upon the degree of liver damage that is present. Although someday reliable predictors for the presence of liver fibrosis or cirrhosis may be available, biopsy is necessary today. Liver function tests can be normal with significant liver disease. In the event of cirrhosis, careful assessment for the possible need of combined liver/extrahepatic organ is warranted. In these settings, the immunosuppress and HCV risks appear to be dominated by the liver risks.

The natural history of HCV in the ESRD patient is difficult to accurately predict, but the literature supports the concept that HCV+ individuals fare worse on dialysis than HCV- counterparts (32% vs 58% after 8 years). Although survival after kidney transplantation appears less good than for the HCV+ recipient compared with HCV- recipients (65% vs. 80% after 10 years), it is better than those reported from dialysis series. This literature suffers from the lack of patient disease stratification and should be viewed with some skepticism. However, an increased incidence of liver complications appears to occur in late (more than five years) follow-up after kidney transplantation.

A differential effect of specific immunosuppressive agents on upon HCV-induced liver disease is difficult to ascribe. In vitro testing has suggested beneficial effects of cyclophilin inhibition upon viral replication, but these effects have yet to have clinical demonstration. Clinical series have suggested that protracted treatment with lymphocyte depleting antibody is associated with progressive liver dysfunction, but inconclusively. Seemingly, eradication of the virus prior to transplantation would provide the best strategy to avoid potential deleterious effects. Interferon- $\alpha$ /ribavirin is the "best" current therapy for HCV, but is difficult to administer to patients with impaired renal function (hemolytic anemia).

However, successful, sustainable eradication of the virus pre-transplant has been achieved in HCV+ candidates. Genotype 2 and 3 are most likely to respond to such therapy.

The use of organs from HCV+ donors has been a source of discussion. If an organ from an infected donor gets transplanted, the recipient will be exposed to the donor's virus. This event, which may be devastating for the immunologically naïve person, appears to be of little consequence for the recipient with chronic HCV. In the few studies that have assessed viral infection, it appears that around 50% of cases that the donor virus supplants the recipient's virus. Rarely a hepatitis flare occurs after transplantation. Although there is no convincing information that the risk of hepatocellular carcinoma and progression of HCV-induced liver disease is accelerated by immunosuppression and transplantation, the observation that these people die succumb from liver related complications 5-10 years after transplantation provides a rationale for surveillance strategies.

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