that the current prevalence of PTH would be well below this rate. Indeed, based on the USA experience, the current risk for PTH is approximately 3 per 10 000 units transfused[6] and since we have similar prevalence rates among our donors, it is likely that the risk in South Africa is similar. It is also important to bear in mind that recent studies with long-term follow-up indicate that post-transfusion HCV infection has a negligible effect on morbidity and mortality.[12]

The current practice therefore is to screen all donors for HCV antibodies. Should the test be repeatedly reactive, the unit will be discarded and the donor informed by letter of the results and advised to consult a physician for further testing and clinical follow-up. Should further clinical and laboratory follow-up suggest a false positive result we would accept the donor back, but only if the screening test and currently available confirmatory tests are non-reactive 6 months after the initial screen. However, as indicated in the article by Voigt and Smuts in this issue (pp 535-548), confirmatory testing is a problem and ideally all donors with positive tests should be confirmed as truly infected by sensitive viral detection methods such as polymerase chain reaction (PCR) techniques. This is relatively time-consuming and expensive, but recent sensitive recombinant immunoblot assays (RIBAs) appear to correlate reasonably well with PCR technology, particularly if the antibodies show reactivity with either C33C and C22 antigens.[13] Reactivity with C100 and/or 5-1-1 antigens correlates poorly with PCR positivity and is regarded as indeterminate.[11]

Clearly, the present anti-HCV tests are still overly sensitive and not sufficiently specific in terms of diagnosing individual patients. Nevertheless, in the context of screening blood donors, erring on the side of sensitivity is preferable. Unfortunately this leads to the unnecessary exclusion of some donors and uncertainty as to whether some are truly infected. This must, however, be balanced against the maintainance of a safe blood supply and the likelihood that more specific, yet sensitive, tests for HCV infection will be developed during the next few years.

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Liver transplantation for viral hepatitis — which patients will benefit?

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Liver transplantation constitutes a significant part of the hepatologist's armamentarium and has become the treatment of choice for most patients with chronic end-stage liver disease. The results continue to improve and many centres are now able to achieve 1-year survival figures in excess of 90% in selected patients. The surgical techiques involved in liver transplantation and the immunosuppressive protocols used postoperatively have been standardised.[1] In contrast, the indications for and contraindications to liver transplantation continue to be modified. Large numbers of patients have undergone liver transplantation in recent years and analyses of large series of patients have made it possible to determine more accurately the outcome of liver transplantation in specific hepatic disease processes. As a result, subsets of patients who are more likely to survive long term have been identified. This is particularly true of patients with viral hepatitis.

Hepatitis B

Liver transplantation in HBsAg-positive patients remains controversial.[1] For many years a carrier state of HBsAg was regarded as a contraindication to transplantation.[1] After transplantation patients with hepatitis B are at high risk of becoming reinfected with the virus which caused the original disease, and once reinfection occurs it almost invariably leads to chronicity and recurrence of the chronic active hepatitis.[1] Thus patients who are HBsAg positive have a significantly worse prognosis after transplantation than patients who are HBsAg negative.[1]

The ethical dilemma is compounded by the magnitude of the epidemiological problem. In HBV endemic areas, such as southern Africa, HBsAg-positive patients constitute a large, if not the largest, proportion of disorders causing end-stage liver disease. Exclusion of patients who are HBsAg-positive from transplant waiting lists would deprive many young patients, who are in the most productive years of life and otherwise ideal transplant candidates, from the only option available to them. Thus identification of subsets of patients with hepatitis B who have a better outcome or the introduction of measures to improve the outcome after liver transplantation would have important implications locally.

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Several recent studies with valuable new information provide encouragement for HBsAg-positive patients.[2-5] The European Hepatitis (EUROHEP) Project evaluated the results of liver transplantation in HBsAg-positive patients in European centres and have identified subgroups of patients who have lower HBV recurrence rates and better survival after liver transplantation.[3,4]

Recurrence rates

The EUROHEP Project included 372 consecutive HBsAg-positive patients transplanted at 17 European centres between 1977 and 1990.[3,4] At the end of the follow-up period 47,3%6edicted a lower risk of HBV recurrence after liver transplantation included long-term administration of anti-HBs immunoglobulin, HDV superinfection and acute liver disease. In the patients with HBV-related cirrhosis, the factors which independently predicted a lower risk of HBV recurrence after liver transplantation included long-term administration of anti-HBs immunoglobulin, the absence of HBV DNA in the serum before transplantation, and the absence of HBeAg in the serum before liver transplantation.

A disturbing aspect of recurrent HBV after transplantation has been the natural history of this infection.[6-8] In non-transplant patients with chronic HBV, the progression to cirrhosis generally takes 10 - 20 years whereas in patients with recurrence of HBV after liver transplantation, the progression to cirrhosis is quicker, often less than 2 years.[6,8,9] In patients with recurrent HBV infection, a specific histological lesion, termed 'fibrosing cholestatic hepatitis' (FCH), has been described.[7,10] This histological lesion is manifested in a relative paucity of inflammation, ballooning degeneration of hepatocytes, periportal fibrosis and a variable degree of cholestasis. There is also dramatic expression of HBV antigens such as HBsAg and HBeAg within hepatocytes. The role of overexpressed viral antigens in the cell destruction remains unclear.[11] In general, patients who develop FCH in the graft survive less than 6 months.

Survival

The overall actuarial survival rate after liver transplantation in patients who were HBsAg-positive pre-transplant was 75% and 63% at 1 year and 3 years respectively.[3] The nature of the original liver disease had a significant effect on survival after liver transplantation. The actuarial survival rate at 3 years after liver transplantation was approximately 90% in patients with HDV-related cirrhosis, approximately 70% in patients with fulminant HBV and fulminant HDV, and below 50% in patients with HBV-related cirrhosis. The patients who received long-term immunoprophylaxis after liver transplantation had significantly better survival (actuarial survival rate at 3 years of over 75%) than patients who received short-term or no immunoprophylaxis (actuarial survival rate at 3 years below 50%). The patients who had recurrences of the HBV infection (3-year actuarial survival rate of 54%) had significantly worse survival rates than the patients who remained HBsAg-negative after liver transplantation (3-year actuarial survival rate of 83%). Among the patients with recurrence of HBV after liver transplantation, the 3-year actuarial survival rates were 44% for those patients transplanted for HBV-related cirrhosis and 83% for those transplanted for HDV-related cirrhosis. In a univariate analysis, the factors predictive of better survival included the presence of HDV superinfection (fulminant HDV or HDV-related cirrhosis), long-term administration of anti-HBs immunoglobulin, the absence of HBV DNA before liver transplantation and the absence of HBeAg before liver transplantation. The multivariate analysis identified the long-term administration of anti-HBs immunoglobulin and HDV superinfection as independent predictors of better survival among all patients studied, and the long-term administration of anti-HBs immunoglobulin as independent predictors of better survival in patients with HBV-related cirrhosis. Eleven per cent of the patients in the EUROHEP Project died as a direct result of recurrence of HBV. Fifteen per cent of the patients with HBV-related cirrhosis died of recurrence of HBV, as compared with 3% of the patients with HDV-related cirrhosis, 14% of these with fulminant HDV and none of those with fulminant HBV.

Immunoprophylaxis

Several therapeutic agents have been used in HBsAg-positive patients undergoing liver transplantation in attempts to decrease the incidence of recurrent HBV-associated liver disease after transplantation. HBsAg-positive patients in Hannover were treated with a polyvalent hepatitis B immunoglobulin (HBIg) during the anhepatic phase and for the first 8 days postoperatively.[2,12] Thereafter the anti-HBs titre was maintained at over 100 IU/l for either 6 or 12 months. The outcome was compared with a historical group of untreated patients and patients given HBIg in the anhepatic phase only. The HBV DNA-positive patients received a bigger dose of HBIg. HBV recurrence rates in patients given long-term HBIg were very low and amounted to 18% and 25%, respectively, after 6 - 12 months of prophylaxis. The frequency of recurrent HBV increased after discontinuation of HBIg administration. Recurrent infection was almost universal in the patients who were HBV DNA and/or HBeAg positive, and was successfully prevented by long-term HBIg administration in most HBV DNA-negative recipients. None of the patients without HBV recurrence died, as compared with a mortality rate of 42% in the patients with recurrence of HBV infection. Furthermore the histological picture in the biopsies of the patients with recurrence varied from acute hepatitis to cirrhosis and spanned the whole spectrum of liver lesions associated with HBV infection. The efficacy of long-term treatment with anti-HBs immunoglobulin had been demonstrated previously.[13,14]

In the EUROHEP Project there was no difference in the risk of HBV recurrence between the patients given no immunoglobulin and those given short-term therapy (< 2 months), but there was a significant reduction of risk in the patients given long-term therapy (> 6 months).[3,4] Among the patients who received long-term therapy, the 3-year actuarial risk of HBV recurrence was 56% for patients with HBV-related cirrhosis and 17% for those with HDV-related cirrhosis.

Although the use of long-term immunoglobulin appears to be successful, the major drawback is the prohibitive cost. Other measures aimed at lowering the viral burden before transplantation include the use of interferon-alpha and antiviral agents such as lamivudine.[15]

The beneficial effect of long-term therapy with anti-HBs immunoglobulin supports the hypothesis that reinfection of the graft with HBV is related to the presence and replication of the virus in extrahepatic sites.[16]

Hepatitis C

Hepatitis C virus (HCV) infection is a leading cause of end-stage liver disease requiring liver transplantation and is responsible for much of the non A, non B (NANB) hepatitis that follows blood transfusions. Information on hepatitis C in liver transplant recipients has increased dramatically in recent years because of the development of new diagnostic tests for hepatitis C. Originally HCV was a diagnosis of exclusion. The first-generation enzyme-linked immunosorbent assays (ELISAs) for detecting anti-HCV antibody were not reliable indicators of HCV infection. In contrast, RIBA II is a more specific assay which detects antibodies against four different HCV proteins and two nonviral proteins. The second-generation ELISAs detect antibodies to the C-22 HCV protein and are more sensitive and specific. With the development of new molecular techniques such as polymerase chain reaction (PCR), HCV can now be detected with a high degree of confidence even in the early stages of the disease and even in those immunosuppressed patients without adequate antibody response to infection.

The problems of liver transplantation in patients with HCV infection have not been as clearly delineated as in patients with HBV infection.[17-20] Much of the early information about HCV infection and liver transplantation was based on first-generation ELISAs which detected antibody to the HCV C-100-3 protein and which lacked sensitivity and specificity. In patients with HBV infection undergoing liver transplantation, reinfection is almost universal. Since the modes of transmission of HCV and HBV infections are similar, one would predict that reinfection with HCV would also occur. However, the incidence, timing and natural history of HCV infection in liver transplant recipients has been studied to a limited extent.

A study from Pittsburgh documented the HCV status of donors and recipients, using a first-generation ELISA in combination with a RIBA II assay.[17] Of the patients who had negative HCV serology pre-transplant, 9,2% became anti-HCV positive following liver transplant. According to this report the prevalence of HCV infection in transplant recipients was only 13,6%. Histological evidence of hepatitis after liver transplantation was found in 13,8% of the recipients. The time interval from transplantation to the first histological evidence of hepatitis was 9,6 months (1 - 27 months). Only 1,6% of the recipients developed histological chronic active hepatitis following liver transplantation and none of these patients developed cirrhosis. The survival rate in the different donor-recipient HCV-serological status combinations was excellent and ranged from 89% to 100%.

In a study from San Francisco, polymerase chain reaction was used to detect HCV RNA in the sera of liver transplant recipients.[18] It was clear that the magnitude of HCV infection as an aetiological agent of post-transplant hepatitis had been underestimated. Of the patients with pre-transplant HCV infection, 95% were HCV RNA-positive post-transplant. Of the patients who were HCV-negative pre-transplant, 35% acquired HCV infection in the post-transplant period. Patients with pre-transplant HCV infection were more likely to develop post-transplant hepatitis than those without prior infection. The mean time to the first histological diagnosis of hepatitis in patients with and without pretransplant infection was 7,3 months and 8,0 months respectively. Histological evidence of hepatitis in the allograft was present in 29% of the patients. The mean time to the first histological diagnosis of hepatitis was 7,5 ± 1,4 months (range 2 - 32 months). Of the patients with histological hepatitis post-transplantation, the majority developed chronic hepatitis. Of the patients with histological evidence of hepatitis in the allograft, 96% were found to have post-transplant HCV infection.

A subsequent report on the San Francisco group defined the pathological features of HCV infection in liver transplant recipients.[21] At some time after the liver transplant, 51% of the patients with HCV infection detected by PCR post-transplant had histological evidence of hepatitis other than CMV or HBV infection. In this study, in contrast to that described in the above study, patients who were HCV-negative pre-transplant were more likely to develop hepatitis than those who were HCV-positive pre-transplant (71% v. 41%). Four of the patients progressed to a moderate or severe form of chronic active hepatitis (CAH) with fibrosis, end-stage cirrhosis or both. Two of these patients were retransplanted, 1 died before retransplantation and 1 had stable cirrhosis. The other patients exhibited mild CAH, chronic persistent hepatitis or chronic lobular hepatitis. In 21 patients (49%) who were HCV RNA-positive, no evidence of hepatitis could be detected on more than one liver biopsy after liver transplantation.

From a histological standpoint, HCV infection usually begins with spotty necrosis and variable degrees of mononuclear inflammation and cell swelling, followed either by an active phase that subsides into a chronic hepatitis or by a consistent histological picture of chronic hepatitis that remains at a stable level of activity throughout the course.[21]

The origin of the virus that leads to reinfection in patients who are HCV positive pre-transplant is unknown.[18] Although it is possible that extrahepatic sources of HCV replication may be responsible, as in the case of HBV reinfection, it is more likely that the new liver is instantly exposed to the virus in the recipients' blood, since the vast majority of patients are viraemic at the time of surgery.

The peritransplant acquisition of hepatitis C in HCV-negative patients is most likely from infected blood products. In the San Francisco study, none of the patients received an organ from an anti-HCV positive donor.[18] Despite the screening of blood for anti-HCV antibodies, the risk of acquisition of HCV infection persists.

Thus in summary, HCV infection recurs post-transplant in almost all infected patients and the acquisition of HCV infection with the transplant is also common. Evidence of HCV infection pre-transplant is an independent risk factor for the development of post-transplant hepatitis. Finally, infection with HCV accounts for the majority of cases of post-transplant hepatitis not due to CMV, and although many of the patients with post-transplant HCV infection have little evidence of histological hepatitis, significant hepatic damage can sometimes occur.

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The doctor with hepatitis B — some legal issues

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The purpose of this brief article is to discuss certain legal issues in respect of a doctor who contracts hepatitis B in the course of his practice or in the performance of his duties as an employee. Firstly, there is the question of whether the doctor is entitled to compensation for having fallen prey to an ever-present occupational risk of health-care workers. Secondly, there is the question of whether an infected doctor, who is now a risk to his patients in that he may infect them in the course of his professional activities, would expose himself to a claim for damages should a patient be infected by him. Thirdly, there is the question of whether a doctor who is infected with the disease may continue to practise.

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Although this article deals specifically with hepatitis B, the issues examined here are not necessarily confined to that condition. The same issues arise in respect of any serious communicable disease, particularly AIDS. The questions addressed have given rise to a good deal of debate in recent years. A major point of distinction, however, is that the contracting of hepatitis B is preventable by means of immunisation, while there is no vaccine against HIV as yet. Another difference is that AIDS is an incurable condition whereas hepatitis B may resolve spontaneously, although a favourable prognosis is less certain than in cases of virus A infection, especially in the elderly and post-transfusion cases, where the mortality rate may reach 10 - 15%.

Is the infected doctor entitled to claim compensation?

It is almost inconceivable that a doctor who is infected by a patient whom he knows (or ought to know) is suffering from a particular disease would be entitled to claim damages from the patient under common ('uncodified') law on the basis of a delict (civil wrong). The essentials of delictual liability will be elaborated below. Suffice to say that the prudent doctor, who treats a patient who to his (the doctor's) knowledge is or may be suffering from a communicable disease, is expected to take reasonable steps to prevent himself from being infected. Failure to do so may result in the defence of contributory negligence being raised; this may partially defeat a claim for damages. To the extent that there is a known risk of infection, the doctor may be said to have voluntarily assumed that risk — a defence which, if upheld, would defeat a claim for damages. The job of a doctor, like that of a fireman, policeman or soldier, entails certain inherent risks.

In any event, the act of a patient who is ill and consults a doctor with a view to receiving treatment, can by no stretch of the imagination be said to be wrongful. Nor can fault in the legal sense of the word attach to the patient's conduct. In theory, it would seem, the question of liability on the part of the patient can only arise if there was an act of fraud on his part, e.g. fraudulent concealment of his symptoms. But the question would of course arise as to whether the prudent doctor would allow himself to be fooled in that way!

In the situation where a doctor or other health-care worker contracts the virus in the work situation in consequence of the negligence of an employer, the employee-doctor will be entitled under common law to sue the employer for damages, unless the employer-employee relationship falls within the ambit of the Compensation for Occupational Injuries and Diseases Act 130 of 1993 (COIDA) (the successor to the Workmen's Compensation Act 1941).

Private-sector employees and state employees generally fall under the COIDA, although there are major categories of employee who do not. Certain categories of employer are individually liable. The requirement (in terms of the older legislation) that employees earn salaries or wages lower than a prescribed limit in order to be entitled to claim compensation under the COIDA no longer applies. Claims