Follow-up of the adult patient after transplantation

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Introduction

The purpose of liver transplantation is to allow the patient to return to a normal quality and quantity of life. In practice, however, the quality of life is never completely normal and there are insufficient data to know whether the patient's life expectation is normal. The quality of life cannot realistically be considered as normal as the patient usually remains on long-term immunosuppressive therapy, with all the attendant side-effects, is at risk of complications of the procedure itself and also of the underlying condition that resulted in the original cause of liver failure.

In this review, I will discuss some of the issues arising from medical management of the transplanted patient after the first few months when the patient's condition becomes stabilized and many, but by no means all, of the technical complications of the procedure will have been resolved.

The patient mortality is greatest within the first few months after transplantation when the patient is usually in hospital and relates to either surgical complications, sepsis or multi-organ failure. After the first year, complications are fewer but potentially more severe. Apart from recurrent malignancy, the commonest causes of death after one year in our own series of 1500 patients were de novo malignancy, infection, recurrent benign disease, cardiac disease and renal failure (table 1). Other causes of death included multi-organ failure, which was probably associated with sepsis ; one patient, not grafted for paracetamol overdose, committed suicide 55 months after transplantation.

Table 1. — **Causes of deaths in patients after liver transplantation surviving one year Causes are shown as number (n) and median (range) time of death after transplantation**

	n	Time
Recurrent malignancy	14	28 (12-69) months
De novo malignancy	11	46 (23-88) months
Infection	11	44 (14-129) months
Cardiac failure	7	80 (29-119) months
Renal failure	7	81 (51-114) months
Recurrent benign disease	6	23 (20-82) months
Lymphoma	5	47 (29-68) months
Chronic rejection	3	35 (18-110) months
Others	11	

Follow-up

The pattern of follow-up will depend on many factors, relating to the time after transplant, health of the patient, distance the patient has to travel to the Transplant Unit and locally available expertise. There are several reasons for the routine transplant follow-up of transplant patient and these are shown in table 2. The frequency of visits will depend on the time after transplantation, function of the graft, experience of local practitioners and confidence of the patient.

Table 2. — **Routine Follow-up of transplant recipients**

Monitoring of immunosuppression and its complications
renal dysfunction
hypertension
others
Early detection, diagnosis and treatment of graft dysfunction
Advice on intercurrent problems
Advice on rehabilitation
Detection and possible treatment of recurrent disease

There are few controlled studies on how to best to monitor the patient. At the clinic visit, the patient should be questioned about any new symptoms. The patient's weight and blood pressure should be measured. Obesity after transplant is common and, in our experience, is related primarily to excessive calorie intake rather than any other factor even though most patients deny over-eating and attribute weight gain blame on other factors. If the history and examination is normal, routine blood tests should be taken : full blood count, renal and liver tests and cyclosporin or tacrolimus levels should be requested. Patients are at risk of other complications of their original disease so that, for example, patients grafted for primary biliary cirrhosis should be assessed regularly for thyroid disease or Coeliac disease. Any abnormality of liver function should be investigated : if the cause is not clear, then the patient should be admitted for further investigation. In general, neither acute nor chronic rejection can be diagnosed reliably without liver histology. A patient who develops late, acute rejection should be treated aggressively with high dose steroids (such as prednisolone 200 mg daily for 3 days) and consideration given to altering the immunosuppressive drug regimen. Be-

cause of the high risk of developing chronic rejection, we now change these patients to therapy based on tacrolimus and mycophenolate (1).

In addition to the routine out-patient visits, some Transplant Units undertake routine, protocol liver biopsies. While it is recognised that liver biopsy is associated with a small but finite morbidity, our practice is to do routine biopsies after the first year and then at 2 to 3 yearly intervals, dependant on the indication. The reasons for this practice are

(i) defining normal graft histology : the histology of the graft is rarely normal, since there is often an inflammatory infiltrate, the significance of which is uncertain. In our practice, where patients are maintained on mono or dual therapy without corticosteroids there are concerns about under immunosuppression so if there is a moderately heavy cellular infiltrate, steroids are re-introduced.

(ii) Liver tests do not correlate with liver histology : in a recent analysis (2) comparing liver histology with liver tests in over 650 routine biopsies, we found that of the 48 with normal liver histology, liver tests were abnormal in one third ; conversely, of the 607 with abnormal histology, liver tests were normal in over half (331).

(iii) Recognition of graft damage not detectable by other, non-invasive means : some factors affecting the graft, such as azathioprine toxicity, can be detected only on histology and require alteration of therapy.

(iv) Recognition of recurrent disease is important for several reasons : the patient and clinician needs to be aware of disease recurrence ; interpretation of liver tests will be influenced by the development of disease, there may be therapeutic implications for treatment of the recurrent disease.

Monitoring immunosuppression

The increasing number of immunosuppressive agents available to the clinician has made the monitoring of patients more complex. While there is a broad consensus that patients should be maintained on the minimum effective immunosuppressive regime, there is little agreement as to what that regime should be and indeed how to ensure that the patient is indeed on the minimum. There is increasing evidence that liver allograft recipients are over-immunosuppressed but little agreement on what constitutes minimal immunosuppression (3). Certainly, in most patients corticosteroids can be safely withdrawn and several centers are undertaking a programme of complete withdrawal of immunosuppression. While it is clear that some patients do not need long-term immunosuppression (although the mechanism is unclear), the problem faced by the clinician of identification of those tolerant patients ; withdrawal of immunosuppression may lead to rejection and graft loss.

There are many problems in maintaining minimal immunosuppression. For instance, although most centres will aim to maintain patients on cyclosporin A with a trough whole blood level around 100ng/ml, there are few data to suggest that this is indeed the optimal level and, indeed, whether using whole blood trough levels is the best guide to effective immunosuppression. Some centers are advocating the use of peak levels of cyclosporin to monitor immunosuppression and are undertaking controlled trials to compare the two approaches. It is suggested that the peak levels correlate better with toxicity ; however, logistic reasons may make this approach less practicable.

While it is often assumed that the nephrotoxicity of cyclosporin and tacrolimus is related to over-dosage of the agents, there are few data to suggest that the dose and levels that maintain immunosuppression are different to those levels which result in renal damage.

Compliance

Patients need to comply with the prescribed medication and the clinician must ensure that the patient understands the need for compliance. Although it may be possible to withdraw immunosuppression totally from some patients, this has to be done in a defined way with close medical supervision ; non-compliance may lead to graft rejection and, occasionally, to graft loss (4). Thus, Schweizer and colleagues (4), following a cohort of almost 600 renal, heart and liver grafts, found non-compliance in up to 15% patients : non-compliance may occur at any stage after transplantation, is usually unpredictable and often without any identifiable reason but was seen more commonly in younger recipients and those in a lower socioeconomic group. Mor and colleagues (5) undertook a retrospective analysis of 375 liver transplant recipients and defined a total of 31 episodes of late acute rejection in 26 patients : of the 18 with sub-therapeutic levels of cyclosporin, 7 were due to non-compliance. There is continuing concern that patients grafted for alcoholic liver disease may be at greater risk of non-compliance and subsequent graft loss but there is little evidence at present that this represents a major clinical problem.

Complications of immunosuppression

The complications of immunosuppression may relate to the drugs themselves or the general effects of immunosuppression.

Renal failure

Renal impairment is a recognised complication of immunosuppression, whether based on tacrolimus or cyclosporin and was first recognised in cardiac allograft recipients. The renal impairment may occur as a consequence of pre-existing renal disease which may be associated with the liver disease (such as IgA nephropathy) or other co-morbid conditions such as diabetes mellitus. Furthermore, renal impairment post-transplant is more likely if hepato-renal failure is present pre-transplant.

Recently, we analysed our own experience of 883 consecutive adult patients undergoing liver transplantation (6). Severe chronic renal failure, defined as serum creatinine greater than 250 µmol/l for more than 6 months, developed in 25 patients, representing 4% patients surviving more than 1 year. Of these patients, end-stage renal failure developed in 12 and the overall mortality related to end-stage renal failure was 44%. High serum creatinine within the first three months identified those patients at risk of developing end-stage renal failure. Retrospective analysis of the patient cohort to identify risk factors, suggested that there were two groups : those with renal dysfunction developing within the first year tended to be older, needed perioperative renal support, and had a higher incidence of re-grafting ; those whose renal failure developed after the first year tended to have higher cyclosporin levels in the first three months and higher daily and cumulative cyclosporin doses. However, it was disappointing that even in those who developed end-stage renal failure, levels of cyclosporin were rarely greater than 200ng/ml (trough whole blood, measured by RIA). Reduction of cyclosporin or switching to other immunosuppressive protocols rarely resulted in significant improvement in renal function. There is no reason to assume that the nephrotoxicity of tacrolimus will be any different from that seen with cyclosporin.

Our current practice is, when serum creatinine exceeds 200 µmol/l, ensure cyclosporin levels are around 100 ng/ml and the patient is not taking other potentially nephrotoxic drugs such as non-steroidal anti-inflammatory drugs. If liver function is normal and if there is no history of late rejection, then the levels of cyclosporin maintained at 50-75 ng/ml and the patient given azathioprine. If there is evidence of azathioprine toxicity or liver dysfunction, the patient is switched to corticosteroids (usually prednisolone 7.5 mg/day) and mycophenolate 1 g twice daily. Whether this strategy will result in less nephrotoxicity remains to be shown.

Diabetes mellitus : diabetes mellitus is relatively common in patients with end-stage liver disease and may be due either to a relative deficiency of insulin or a failure of end-organ responsiveness. After liver transplantation, the incidence of newly diagnosed diabetes is 10-15% ; the probability of developing diabetes is greater in patients on high dose corticosteroids and in those receiving tacrolimus compared with cyclosporin. Short-term studies have failed to demonstrate that the onset of diabetes after liver transplantation has an adverse effect on survival but there may be an increase in nephropathy. In some patients, the diabetes may resolve in time without alteration in medication. Diabetes in the liver allograft recipient should be treated as in the non-grafted patient.

Hypertension : Hypertension is seen more commonly in patients maintained on cyclosporin compared with those on tacrolimus. The choice of treatment is uncertain : while some centres advocate diuretics, we tend to avoid their use because of the possibitiy of increasing serum urea. Calcium channel antagonists and ACE inhibitors are the drugs of choice although serum potassium must be monitored in those on ACE inhibitors who are also taking cyclosporin. Nifedepine does not interact with cyclosporin.

Malignancy

The development of de novo malignancies following liver transplantation is well described (7). Approximately 2% of liver allograft recipients will develop a post-transplant lymphoproliferative disorder (PTLD). Penn's world-wide registry of de novo cancers in organ allograft recipients describes 329 malignancies developing in 324 liver allograft recipients. The main malignancies described were mainly lymphoma, accounting for 189 cases ; other commonly occurring cancers were cancer of the skin and lips (48), carcinoma of the rectum and colon (48), lung (18) and Kaposi's sarcoma (10). Compared with renal allograft recipients, liver allograft recipients are more likely to have lymphoma and less likely to have skin cancers ; the reasons for this difference is unclear although it is of interest that the pattern of malignancies resembles that seen in cardiac allograft recipients.

Although the registry has generated invaluable information on many aspects on post transplant malignancy, interpreting the conclusions must be done with caution : the registry is dependent on the voluntary reporting of cases so it is likely to under-report cancers ; there may be inconsistencies in how the data are collected and variations in the management of patients. Frezza (8) reported in 1997 the Pittsburgh experience of non-lymphoid malignancies in 3394 adult liver transplant recipients grafted before 1993 : Of the 1657 recipients available for study, a total of 64 tumours in 50 patients were identified. The tumours were mainly skin cancers (basal cell carcinoma (25%), squamous cell carcinoma (20%), Bowen's tumour (6%), warts (3%) and melanoma (6%). Other tumours accounting for over 3% each were Kaposi's sarcoma, cancer of the colon, breast, lung, stomach, ovary, cervix and larynx. Compared with renal allograft recipients, there were fewer cancers ; and tumours were more common in those receiving cyclosporin based immunosuppression than those on tacrolimus based therapy.

There are several risk factors for the development of PTLD but the degree of immunosuppression is probably the greatest risk factor. Whilst they can occur anytime after transplantation, they are usually seen in the first post-operative year. There are two broad patterns of PTLD : those with a polyclonal B cell lymphocytic proliferation are associated with an illness resembling infectious mononucleosis. There is usually a good clinical response to reduction or cessation of immunosuppression and the use of acyclovir, although withdrawal of immunosuppression may result in graft loss. In contrast, those PTLD with a monoclonal B

cell proliferation respond poorly to these measures but may respond to intensive chemotherapy.

Post-transplant lymphoma appears to have a different clinical presentation to lymphoma in the non-immunosuppressed patient : about half the cases are localised, with the allograft being the main site affected ; other sites affected include the head and neck region, lymph nodes and bowel.

De novo infection

Pyrexia may be due to many factors, including infection and rejection. Those with Roux loops are at risk of cholangitis. Unexplained pyrexia may be the first sign of hepatic artery thrombosis and a Doppler ultrasound of the hepatic artery considered.

Bacterial infection : the immunosuppressed patient is at risk of infection and these may involve pathogens unfamiliar to the clinician and present in atypical ways. There are many case-reports and series describing bacterial, protozoal, parasitic, helminthic and fungal infections in the immunosuppressed patient presenting in unusual ways. The golden rule for the physician is to be aware of the possibility of unusual infections and investigate any abnormality with care.

Viral infection : in addition to recurrent viral disease (discussed elsewhere), de novo viral infection may occur. With respect to Hepatitis B viral infection, those patients at greatest risk are those who receive a liver from a donor who is HBc antibody positive, although may occur where the donor is negative for all markers of previous HBV infection (9,10). If a patient receives a graft from a donor who is anti-HBc positive, there is a 50% chance of developing a viral infection although the disease in the allograft may not be as severe as those with recurrent HBV infection but numbers of patients on which these observations are based are small. Infection with cytomegalovirus usually presents within the first three months but may occur at any stage. Diagnosis is difficult ; detection of RNA by PCR or the demonstration of IgM antibodies is not always diagnostic of tissue invasive disease ; the diagnosis is best confirmed by showing tissue invasion of the liver, duodenum or rectum or other affected site.

Daily Living

The attending clinician will need to be aware of the problems the patient may have in rehabilitation.

Quality of life

As indicated earlier, while the quality of life after transplantation is usually very much better than that immediately prior to surgery, life is rarely normal. There have been several studies evaluating quality of life but comparison has been difficult since there is usually considerable variation in the timing of the questionnaire and variations in the instruments used. Goff and colleagues recently reviewed quality of life outcome studies and concluded that although most reports had used validated instruments, there was significant heterogeneity making it difficult to reach generalisable conclusions (11).

Using the NIDDK Liver Transplantation database, Belle (12) compared five quality of life domains (measures of disease, psychological distress and well-being, personal function, social/role function, and generalised health perception) before and after liver transplantation in 346 adults who had survived more than one year. Perceptions of health improved considerably as did all facets of social/role functioning (except marriage). Although psychological status improved considerably after transplantation over half remained distressed and 60% were feeling depressed. Similarly, there were major improvements in personal functioning but one third were unable to work and three-quarters were limited in vigorous physical activity.

Our own analysis was based on the returns of 121 patients grafted either at this institution or the Royal Free Hospital (13). This represented 82% of those invited to participate. Compared with the general population, matched for age and sex, there was no major differences in the various dimensions analysed, although the scores showed a wider distribution. The most marked differences between the transplanted patients and the general population were in the dimensions of physical role and physical functioning (23% and 13% lower respectively). When the pre-transplant factors were analysed to determine whether any factor could be identified which predicted a poor outcome, we found that those who had received one graft only had a better outcome and that those who were Child-Pugh grade C also had a better outcome.

Depression may present at any time after transplantation but, in our experienced, is most marked at the end of the first year ; this appears most marked when the patient has to return to normal activities and ceases to be an invalid. Anti-depressants may be indicated for a short period.

Menstruation and Pregnancy

Female patients with liver disease may complain of a variety of abnormalities of menstruation including irregular or heavy bleeding, oligomenorrhoea or amenorrhoea. Following transplantation, these irregularities return to normal and the woman is usually able to conceive (14). Contraception is often requested but there are no clear data on the safest approach. Barrier methods and sterilisation are undoubtedly the safest forms of contraception but are often unpopular with the patients. Intra-uterine contraceptive devices (IUCD) are often avoided as they represent an additional source of infection. Although there are potential risks of the oral contraceptive tablets, such as hepatic damage and an increased tendency to vascular thrombosis, our experience and that of others shows that this is well tolerated and we have not, as yet, observed any adverse effect.

There are still relatively few reports of the outcome of pregnancy in liver allograft recipients and so conclusions must remain cautious. Most patients are advised to wait at least six months after surgery before considering pregnancy. Immunosuppressive drugs should be maintained during pregnancy although there is no evidence that pregnancy has an adverse effect on rejection. There does however appear to be a higher incidence of pre-term delivery, pre-eclampsia, renal impairment and infection. Babies appear to have a higher incidence of prematurity and low birthweight (15). Renal dysfunction pre-pregancy may be the main determinant of the outcome of the pregnancy (16). Many of the immunosuppressive drugs are teratogenic : in the UK, tacrolimus and mycophenolate are not indicated in pregnancy and so should be avoided. However, Jain described 27 patients in 21 female liver allograft recipients treated with tacrolimus before and during the pregnancy (17). There was no maternal mortality : two infants died shortly after birth at 23 and 24 weeks gestation. The other 25 babies did well although transient perinatal hyperkalaemia and mild reversible renal impairment was noted. However, animal studies show that mycophenolate is teratogenic and patients should be advised to ensure contracepation whilst taking this drug.

There does not appear to be any adverse effect on the children of liver transplant male recipients.

Bone Disease

After transplantation, the rate of bone loss may rise up to 20% in the first six months but thereafter the rate of bone loss falls and may actually reverse. Post-operative bone loss is greatest in those with the lowest bone density prior to transplantation. There are two contributing factors to osteopenia after liver transplantation : one factor is the post-operative factors such as bed-rest and the use of corticosteroids, the other factor is pre-existing osteoporosis seen in many patients with liver disease and chronic cholestasis of any cause.

Corticosteroids induce osteopenia by increasing bone resorption, decreasing bone formation and inhibiting the absorption of calcium, leading to hypocalcaemia, secondary hyperparathyroidism and further bone resorption. This affects primarily trabecular bone. Since cytokines affect osteoclastic and osteoblastic activity, it is possible that other immunosuppressive drugs will affect bone formation.

In practice, bone fractures are relatively rare after transplantation ; however, patients should be given the smallest doses of corticosteroids necessary, mobilised early and, for those with significant bone loss, offered calcium supplements and, where appropriate, hormone replacement therapy.

Osteonecrosis is uncommon after liver transplantation but is probably related to corticosteroids. The femoral head is the site most commonly affected and usually occurs in the first six months.

Lipids and Heart Disease

Cardiovascular disease is becoming an increasing problem in the liver allograft recipient. There are many factors that contribute to this problem : more elderly patients are successfully grafted and other associated diseases that predispose to vascular damage, such as diabetes, are no longer contra-indications.

Most studies have shown that serum lipids are increased after liver transplantation (18-22) : our own study of 20 patients randomised to receive either cyclosporin or tacrolimus (18) showed no significant difference in lipids in either group. Patients were not receiving corticosteroids after 3 months. Other studies (19-22) have suggested that both serum triglycerides and cholesterol are greater in those on cyclosporin compared with tacrolimus, however, there is no difference in serum HDL (high density lipoprotein cholesterol). Rapamycin in particular is associated with hyperlipidaemia. Patients with hyperlipidaemia should be given dietary advice and if this fails to improve the hyperlipidaemia, then therapy given. Although the statins may cause liver dysfunction, they seem well tolerated in the liver allograft recipient.

Additional Drugs

Following transplantation, patients may well need additional medication for treatment of co-morbid conditions. In practice, patients tolerate such additional medication well although the clinician has to be aware of possible drug interactions :

Drug interactions : There are many drugs which have the potential for interaction with cyclosporin and tacrolimus (table 3) : while those drugs which do interact with the immunosuppressive agents may be used safely, the clinician must monitor the drug levels during and following co-administration of the drugs.

Nephrotoxic drugs : there are many drugs (table 3) which may increase the nephrotoxicity of cyclosporin and tacrolimus. In particular, non-steroidal anti-inflammatory drugs should be used with caution. The clinician has to balance the benefit with the toxicity of the drugs and advise and monitor the patient accordingly.

Immunization : live and attenuated vaccines should be avoided in immunosuppressed patients but there is no reason to restrict the use of inactivated or particulate vaccines, although the immune response may be impaired. Of concern is the use of oral polio vaccine : since the virus is excreted in the faeces, patients and their families should be given only the inactivated preparation.

Recurrence of disease

Disease recurrence is well-recognized after liver transplantation and those diseases where recurrence has been documented are listed in table 4. The clinician needs to be aware of the possibility of recurrence and advise the patient accordingly.

Table 3. — **Drugs which interact with cyclosporin/tacrolimus**

Drugs which increase cyclosporin/tacrolimus levels	
Antimicrobials :	Erythromycin, norfloxacin, imipenim,
Antifungals :	Ketoconazole, fluconazole, itraconazole
Calcium channel antagonists	Diltiazem, verapamil, nicardepine
Sex steroids	Corticosteroids, oral contraceptives, androgens, oestrogens
Others	Amiodarone, colchicine, metoclopramide Cimetidine
Drugs which reduce cyclosporin/tacrolimus	
Anti-convulsants	Phenytoin, phenobarbitone, carbamazepine
Antimicrobials	Rifampicin, sulphonamides
Drugs which increase nephrotoxicity	
Non-steroidal anti-inflammatory drugs	
Aminoglycosides	
Others eg cisplatin, amphotericin	
Drugs with increased neurotoxicity	
Acyclovir, ciprofloxacillin, imipenim, ganciclovir, norfloxacin	
Drugs which exacerbate hyperkalaemia	
Angiotensin converting enzyme inhibitors	
Potassium sparing diuretics	

Table 4. — **Diseases which may recur after transplantation**

(in some cases, recurrence is suggested but not fully confirmed)	
Immune mediated :	Primary Biliary Cirrhosis
	Primary Sclerosing cholangitis
	Autoimmune Hepatitis
Infectious :	Hepatitis A virus
	Hepatitis B virus
	Hepatitis C virus
	Hepatitis D virus
	Alveolar echinococcus
Metabolic	Alcoholic liver disease
	Genetic haemochromatosis (?)
	Erythropoetic protoporphyria
	Niemann-Pick (?)
	Gaucher's disease
	Sarcoidosis
	Sea blue histiocyte syndrome

Recurrent viral hepatitis is discussed elsewhere.

Recurrent auto-immune diseases : recurrence of autoimmune hepatitis may occur several years after transplantation and differentiation from acute rejection may be difficult. The features in favour of recurrent disease include cutaneous stigmata of chronic liver disease such as spider naevi, elevated serum immunoglobulins, autoantibodies and interface hepatitis. There is usually a good response to corticosteroid therapy.

Primary biliary cirrhosis may recur in the liver and features of recurrent disease may develop in up to 20% at 5 years. The diagnosis is made on the basis of clinical, biochemical and histological features. There is no effective therapy but many centres are giving these patients treatment with ursodeoxycholic acid, 10-15 mg/kg/day, on the grounds that the drug may be effective in patients with PBC in the native liver. Whether primary sclerosing cholangitis recurs in the grafted liver remains uncertain : most reports suggest that those grafted for PSC have a greater incidence of intra-hepatic biliary strictures but differentiation between recurrent primary sclerosing cholangitis and secondary cholangitis remains uncertain at the present time.

Recurrent/persistent metabolic disease : where the metabolic defect arises in the liver, transplantation (as with haemophilia or Wilson's disease), transplantation will be curative. However, where the metabolic defect arises outside the liver either in part or completely, the disease may recur. It remains uncertain whether liver replacement will correct the fundamental defect in genetic haemochromatosis so these patients should have their iron stores assessed at regular intervals. Erythropoetic protoporphyria will not be cured by liver replacement, so treatment will need to be continued.

Extra-hepatic disease

Inflammatory Bowel Disease : Inflammatory bowel disease (IBD) usually has a fairly indolent course in patients with liver disease so it would be anticipated that liver allograft recipients taking immunosuppressive drugs, effective in IBD, would have few problems with IBD. However, several studies have failed to show this. A recent survey by Papatheodoridis and colleagues (23) concluded that IBD often runs an aggressive course in patients after liver transplantation irrespective of the immunosuppressive regime used. The dose of corticosteroids needed to maintain immunosuppression may be inadequate to retain remission in IBD. Furthermore, IBD, especially ulcerative colitis, may develop de novo after liver transplantation. Furthermore, there is an increased risk of colonic malignancy after liver transplantation in patients with IBD, which appears to be greatest in the first two post-operative years. Whether this represents the natural course of disease of whether this observation is an artefact of the relatively short follow-up is unclear. Although a strategy of 6 monthly surveillance colonoscopies for the first two years has been suggested, there are no clear guide-lines on which to base practice. In our own centre, we do routine colonoscopies every two years and have detected three colonic cancers.

Other Factors

Alcohol : there remains much uncertainty whether patients should be 'allowed' to drink alcohol after transplantation ; most centres do allow those some alcohol consumption in those who were transplanted for conditions other than alcoholic liver disease, provided the alcohol drunk is not excessive and will not cause liver or other organ damage and will not affect the metabolism of cyclosporin or tacrolimus. While it could be argued that controlled drinking is possible in those grafted for alcoholic liver diseases, in practice this is rarely achieved so most centres advise (but rarely monitor) abstinence.

Conclusions

For the majority of patients, the medical management of the liver allograft recipient is straight forward : the clinician should encourage the patient to return to a normal life and place as few restrictions as possible on the patient. However, it is important that the clinician keeps a careful watch on the patient to detect and remedy early signs of problems.

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