Management of the Acute Transplant

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In only a little over a single working lifetime from the late 1950s, kidney transplantation has moved from a startlingly novel, exciting, and dangerous new therapy for the then-terminal diagnosis of end-stage renal failure to become a routine and common operation throughout the developed world and in many developing countries. The charismatic surgical pioneers of the early decades have given way, as the health and economic benefits of successful transplantation have become apparent, to a dense superstratum of protocols, guidelines, and legal requirements constraining activity within the highly ethically complex landscape of deceased donor organ retrieval and allocation and live donor directed (and undirected altruistic) kidney donation.

Outside a few marginal geographical sites, where the wild old ways of unregulated activity persist, all kidney transplants will therefore take place within the fairly tight constraints of national or regional legislation below which sit the local institutional protocols within which units strive to drive up the now startlingly high success rates of this procedure.

No text can conform to all the different protocols in current use in the UK, let alone further abroad, so this chapter is focussed on identifying the underlying principle involved along with universal practical considerations so that practitioners can understand and implement the local regimen of the institution where they find themselves looking after the recent recipients of kidney transplants in an effective manner.

Because surgical and medical practice in renal transplantation are now highly developed and successful, the overwhelming majority of renal allografts proceed without complications with 1-year survival with functioning grafts >90 % in UK deceased donor programmes and >95 % for live donor transplants [1]. There remain a small number of rare but important adverse events however (principally haemorrhage or vascular thrombosis related to the transplant vessels and aggressive early antibody-mediated rejection) which can threaten the survival of the graft or patient so that even in apparently straightforward and uncomplicated cases, a high degree of vigilance is required to anticipate, prevent, identify, and reverse severe complications.

Preoperative Management

Calling in Potential Recipients

Issues around when and who to call in to hospital as the potential recipient of a deceased donor kidney transplant revolve around the desirability of minimising cold ischaemic time (CIT – when the organ has been retrieved, flushed with cold perfusion fluid, and stored, usually on ice, for transport to the implanting centre). Prolonged CIT is associated with increased ischaemia-reperfusion injury to the graft, and increased risk of delayed graft function, and (especially in extended criteria donors) with poor long-term outcomes in terms of graft survival [2]. CIT will be significantly increased if a recipient is unexpectedly found to have a positive cross-match against a particular kidney and (the relevant organ allocation scheme allowing) an alternative recipient has to be called up and undergo pre-transplant checks and an appropriate period of preanaesthetic starvation. Because of this, it has

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been common practice to call in two or even more potential recipients, with the unlucky back-up patients being sent away, disappointed (and hungry) when the highest-ranked patient with a negative cross-match is assigned the organ. This rather dismal practice is becoming increasingly unnecessary as advances in tissue typing allow increased accuracy in determining exactly which HLA specificities a patient has alloantibodies against, so that these specificities can be declared as 'unacceptable' (unacceptable donor antigens or UDAs within the UK system) so that the patient will not be offered organs carrying those HLA antigens, and an unexpected positive cross-match is becoming increasingly rare. In the context of a highly sensitised patient with low-level donor-specific antibodies which are thought to be of low clinical significance (a situation the consequences of which are currently the subject of much debate), it may be unclear from the available data whether the cross-match (especially the more sensitive flow cross-match) will be positive or not, and the identification and calling in of a back-up recipient may be appropriate (after discussion with the deceased donor allocation centre to find out whether, in the event of a positive cross-match, the organ would have to be forwarded to another centre for the next-highest scoring individual on the allocation run).

Deceased donor kidney offers will usually be associated with a specific named recipient, and there will often be many hours between the potential recipient being identified and the organ being available at the implanting centre. In this situation it may be unclear when to contact the potential recipient. However, given the potential uncertainties in relation to getting the patient ready for theatre, it is usually appropriate to inform the potential recipient as soon as the offer has been made to allow them to get to the transplant centre in a timely fashion. Discussion with the transplant surgical team and their anaesthetic colleagues will usually provide a clear idea of the likely time of availability of operating theatre space, and plans for getting the potential recipient to hospital, dialysing them if necessary, and undertaking preoperative investigations need to be made so as to avoid unnecessary delays in getting to theatre.

Preflight Checks

The potential recipient must be reviewed with particular reference to clinical issues which may have an impact on their early post-transplant clinical course. Most of these issues will or should have been carefully thought through by the physician activating the patient on the transplant list long before the day of transplantation. However, it is important to perform a final brief review of a number of issues including:

(i) Primary renal diagnosis.

1. Focal and Segmental Glomerulosclerosis (FSGS)

The most important primary glomerular disease with known risk of significant recurrence post-transplant is FSGS which may recur aggressively and very early in paediatric recipients, presenting with proteinuria and progressive graft dysfunction [3]. Care should be exercised in accepting a primary underlying renal diagnosis of 'hypertension', especially in patients of African, Afro-Caribbean, or African American ethnic origin as this may conceal an underlying diagnosis of FSGS. A positive family history of renal disease or known significant proteinuria as part of the original presentation is important pointer.

2. Atypical haemolytic uraemic syndrome (aHUS)

aHUS caused by genetic abnormalities in complement control proteins can recur early post-transplant, requiring plasma exchange or (currently experimentally) blockade of complement activation pathways to rescue the graft.

3. Membranoproliferative glomerulonephritis (MPGN)

Recurrence of the complement-related MPGN spectrum is common post-transplant, especially the type II dense deposit type associated with acquired activating auto-antibodies against the complement system (C3 nephritic factors). Late recurrence is commoner than significant early recurrent disease.

4. Other glomerular diseases

Almost all glomerular diseases may recur post-transplant. This is most commonly seen at ultrastructural level in IgA nephropathy, and membranous nephropathy, but very rarely produce significant clinical impact in the early post-transplant period. Systemic diseases (diabetes, amyloid, Anderson-Fabry, sarcoidosis) may also affect the late course of transplant function.

5. Primary hyperoxalurias

These inherited defects of glyoxalate metabolism can recur with rapid oxalate deposition early post-transplant, often triggered by reduced graft function from other causes leading to reduced oxalate clearance. Post-transplant management of high oxalate levels is important to prevent significant renal damage, and a plan for intermittent haemodialysis may be appropriate to reduce the total body and plasma oxalate burden.

6. Lower urinary tract abnormalities

Congenital or surgical abnormalities of the bladder and urethra present a significant technical challenge to transplant surgeons, and such patients should have had careful planning during the transplant workup phase to ensure that any necessary investigation (in terms of assessing bladder, urethral, or alternative channels of urine outflow such as ileal conduits for their anatomical and functional status) has been undertaken prior to activation on the transplant list. These complex and often difficult to interpret assessments cannot be easily

undertaken in the time-limited context of deceased donor organ transplantation but at least need to be flagged and planned for before urethral catheter removal.

(ii) Coronary artery disease
All patients with renal impairment are at significantly increased risk of coronary artery disease, and although the renal transplant surgical procedure is not usually a very prolonged or difficult operation from an anaesthetic point of view, peri- or post-transplant coronary ischaemia or myocardial infarction remain an important and difficult to manage complication in transplant recipients. Units will usually have a local protocol for attempting to identify clinically silent coronary artery disease in high-risk populations (such as diabetics) prior to listing for transplant, and the details of the results of these investigations (whether they consist of coronary angiography or non-invasive tests such as radionuclide scanning or stress echocardiography) need to be clearly recorded prior to transplantation with results readily accessible out of hours.

Patients with known severe left ventricular dysfunction are at particular risk in the immediate post-transplant period as they may not be able to sustain the traditional aggressive fluid loading used to encourage prompt graft function, and poor graft perfusion due to pump failure can leave them at increased risk of delayed graft function.

(iii) Peripheral vascular disease
Atheromatous disease, which is very common in renal patients (especially that involving circumferential calcification of the iliac vessels), causes problems with the forming of a successful arterial anastomosis to the transplant artery and needs to be identified preoperatively to allow the transplant surgeon to anticipate the optimum surgical site for the arterial anastomosis.

Haemodialysis access procedures involving the proximal leg vessels (such as thigh Gore-Tex grafts) are usually distal to the normal sites of arterial vascular anastomosis, but need to be known about prior to surgery.

(iv) Venous anatomy
Although much rarer than arterial atheromatous disease, venous occlusive disease of the proximal leg veins secondary to DVT or the use of femoral dialysis catheters may determine the site of transplant implantation. NB Avoid the use of femoral lines on the side of the transplant.

(v) Previous transplant history
A careful history in relation to previous transplantation is necessary, as any previous graft will (by definition) have failed or be failing. The cause of previous graft failure will often have an impact on the initial immunosuppressive regimen used, and the presence of previous vascular anastomoses will need to be considered by the transplant surgeons.

The Cross-Match (See Chapter 67)

It is the responsibility of the transplant team to double-check donor-recipient blood group compatibility; this is usually the responsibility of the consultant surgeon, but there needs to be a clear and robust system in place to triple check.

Standard Cross-Matching

Following the demonstration, quite early in the historical development of renal transplantation, that the presence of preformed, complement fixing, donor-specific antibodies (almost always directed against HLA antigens) detected by in vitro killing of donor cells by recipient serum (the cytotoxic or cell-dependant cytotoxicity: CDC cross-match) [4] was frequently (but not quite always) associated with immediate graft failure due to hyperacute antibody-mediated rejection, it has been a standard practice to undertake some form of assessment of the presence of preformed donor-specific antibodies (dsAb) prior to proceeding with the kidney transplant operation. The modalities for doing this have grown progressively in their complexity and sensitivity, with the division of the target cells into T and B cell cross-matches (assumed to present class I and class I and II molecular targets for dsAb binding, respectively), the use of techniques to remove the effects of IgM dsAb (generally although not universally believed to be of little clinical significance), the development of flow-cytometric cross-matches (which will detect the binding of dsAb which cannot mediate in vitro cytotoxicity), and most recently the use of recombinant HLA molecules bound to tagged flow-cytometry beads [5]. The significance of low-level dsAb is currently debated, although the history of clinical developments in this area clearly suggests that outcomes are better in non-sensitised recipients and that antibodies detectable by the highly sensitive recombinant/solid-phase assays, while they may not be directly harmful to grafts in the short term, are important markers of medium-term risk [6].

Non-HLA Antibodies

Donor-specific antibodies directed against non-HLA antigens do exist and are not detected by assays based on recombinant HLA targets (nor necessarily by cell-based assays if the target is expressed on graft endothelium, but not on the lymphocytes used in standard cellular and flow-cytometric cross-matching). Early antibody-mediated rejection due to such antibodies is rare [7], but as outcomes in renal transplantation improve, the relative significance of this pathway

is increasing, as is interest in the detection of non-HLA antibodies, although none of the potentially useful systems has yet made its way into standard practice.

Virtual Cross-Matching (See Chapter 67)

The high sensitivity of solid-phase/recombinant target platforms has allowed the confident recognition of the complete absence of HLA-specific antibodies in unsensitised individuals, allowing the transplant procedure to go ahead without a formal cross-match (so-called virtual cross-matching), potentially reducing cold ischaemic time for deceased donor transplant recipients [8].

Immunosuppression (See Chapter 70)

The choice of immunosuppressive drugs used for the initial post-transplant period will be determined by local protocols, often with different regimens aiming to address different levels of immunological risk. Improvements in immunosuppressive strategies and the associated reduction in allograft rejection and minimisation of side effects have been central to the improved survival seen in renal transplantation. Because of the range of drugs available and possibly the different stakeholders in each transplant unit, there is considerable variation of immunosuppression protocols between units, despite the UK National Institute for Health and Clinical Excellence (NICE) guidelines [9]. The commonly used drugs are described here briefly.

Calcineurin Inhibitors (CNIs)

Within the modern era of renal transplantation, CNIs have become the mainstay of immunosuppression, and their use can be credited with decreased rates of rejection and better short- and long-term survival in the last decade. The pharmacokinetics of CNIs can be monitored with 12 h trough values. Elevation or depression of immunosuppressive drug concentrations can be toxic and predispose to graft dysfunction, infection, and neurotoxicity; subtherapeutic values can predispose to rejection. Therefore it is important to remember that a number of other drugs can interfere with the (cytochrome P450) metabolism of CNIs.

The last 20 years of clinical research in transplant immunosuppression have been dominated by a still-unresolved debate about the extent to which the undoubted short-term benefits of CNI use (in terms of acute rejection and graft survival) are undermined by the long-term consequences of chronic CNI toxicity. High-dose cyclosporin-based regimens are undoubtedly associated with essentially universal medium- and long-term graft dysfunction associated with histological changes attributable to CNI toxicity [10], but it is not clear whether the moderately more effective and less nephrotoxic agent tacrolimus suffers from the same long-term disadvantages, and attempts to develop CNI-free regimens (at least those based on sirolimus plus MMF) have been broadly unsuccessful in terms of high rejection rates and poor graft survival [11].

Ciclosporin or Cyclosporin (CsA or CyA)

Ciclosporin binds to cyclophilin and this complex inhibits calcineurin phosphatase and T cell activation. The modern formulation Neoral is a microemulsion and provides more reliable absorption from the gastrointestinal tract. Long-term side effects specific to ciclosporin are hirsutism, hypertension, dyslipidaemia, and gum hypertrophy (especially in conjunction with calcium antagonists).

Tacrolimus (FK506)

The mechanism of tacrolimus action is similar to that of CyA. It is more effective in preventing acute rejection than CyA [12, 13], and the improved graft survival associated with the low-dose tacrolimus regimen in the highly influential SYMPHONY study [14] has led to its adoption as the de facto CNI agent of choice.

Tacrolimus binds to FK-binding proteins creating a complex that inhibits interleukin 2 (IL-2) transcription and T cell activation. Although tacrolimus is widely accepted as having a preferable cardiovascular profile to CyA in terms of blood pressure and lipids, it is associated with new onset diabetes after transplantation (NODAT) due to peripheral insulin resistance. This problem can be diminished by the avoidance of long-term steroid exposure; 12 h trough values are more predictable which may be why the potential for long-term toxicity is lessened. A non-generic, modified release version of tacrolimus (Advagraf) and an expanding range of generic slow-release versions offer once-daily dosing regimens.

Antiproliferative Agents

Azathioprine

Azathioprine is derived from 6-mercaptopurine which interferes with DNA synthesis. Together with corticosteroids, it provided the mainstay immunosuppressive agent until the introduction of CyA in the 1980s and subsequently became part of standard triple therapy immunosuppression with both steroids and CyA thereafter. Despite NICE recommendations for azathioprine use in low-risk transplantation (NICE 2004), it has been abandoned by many units in favour of mycophenolate mofetil.

Mycophenolic Acid (MPA/MMF/Myfortic)

Mycophenolic acid (MPA) is a non-competitive and selective antagonist to inosine monophosphate dehydrogenase, which is an enzyme important in the de novo synthesis of purines. The concentrations of MPA, although not com-

monly measured, can be monitored with 12 h tough levels (easy) or with longer area under the curve sampling and calculation to avoid side effects (leucopenia, infection, and gastrointestinal) while maintaining effective immunosuppression. The routine use of MPA is not recommended by NICE in the absence of a perceived immunological risk (NICE 2004). Despite this, and the absence of formal demonstration of benefit over azathioprine in terms of graft survival, most units seem persuaded that the fact that MMF is associated with reduced acute rejection [15, 16] justifies its use. The inclusion of MMF in the optimum arm of the SYMPHONY study [14] has cemented its widespread in regimens including an antiproliferative agent.

mTOR inhibitors (Rapamycin: Sirolimus and Everolimus)

Rapamycin also binds to FK-binding protein and inhibits cytokine-induced signal transduction pathways by impairment of progression through the G1 phase of the cell cycle. Consequently it inhibits the proliferation of T cells. Because it does not produce the long-term nephrotoxicity associated with CNIs, rapamycin has been used as a replacement for CNIs in both the acute and chronic settings. It has also been used in association with CNIs in place of antiproliferative drugs. Although the predominant benefit is the reduction of calcineurin toxicity, it has been shown to be superior to CyA and steroids (both with and without azathioprine) in the prevention of acute rejection [17, 18], but this may be associated with an increased risk of infection (especially infections associated with delayed wound healing) [19].

Blocking mTOR has been shown to reduce tumorigenesis in vitro, and anecdotal reports do exist in vivo such as in Kaposi's sarcoma. Side effects include hyperlipidaemia; proteinuria with associated focal glomerular sclerosis; marrow suppression (mostly erythropoietin-requiring anaemia), especially when used in combination with MPA; lymphocoele formation; poor wound healing; testicular atrophy in men; and cystic ovaries. In some patients with a low glomerular filtration rate (GFR), rapamycin has been associated with proteinaceous bronchiolitis. In addition, poor wound healing has made this drug difficult to use in the immediate postoperative period.

Corticosteroids (Prednisolone, Methylprednisolone)

Corticosteroids act as agonists of glucocorticoid receptors at low doses, but at higher doses their effects become non-specific and receptor independent. It is a great pity that corticosteroids, which have been the mainstay of immunosuppression throughout the evolution of transplantation, are associated with deleterious side effects such as susceptibility to infection, weight gain, NODAT, hypertension, hyperlipidaemia, and osteopenia. The increased cardiovascular risk and death associated with steroid side effects have led many transplant centres to reduce or avoid steroid exposure in the immediate postoperative period or alternatively to withdraw steroids at a later date after successful transplantation.

Attempts to run long-term steroid-free maintenance regimens from CyA-based immunosuppressive platforms were associated with inferior graft survival [20], but the availability of tacrolimus and MMF has allowed the development of steroid-free long-term regimens with excellent outcomes [21] despite the slightly increased rejection risk associated with early steroid withdrawal, even under 'modern' immunosuppression [22].

Induction Agents: Monoclonal and Polyclonal Antibodies

Antibody therapy is becoming increasingly popular in transplantation for both the induction phase and treatment of rejection and can be categorised as depleting or nondepleting. These are covered in the Chap. 70 on transplant immunosuppression, but depleting antibodies are not risk-free, and while units will have well-developed protocols, it is important to consider the pros and cons of these agents for the individual due to be transplanted (ideally as part of transplant workup).

Data Collection

Once the renal transplant recipient is discharged to outpatient follow-up in the transplant clinic, it is important that baseline information is easily available. If not already recorded in the local renal data system, a clear record needs to be available of the donor details (age, cause of death, comorbidity, hypertension, diabetes, vascular disease), baseline and pre-mortem renal function, and donation details (DCD vs DBD). The recipient's primary renal diagnosis; renal replacement therapy history; CMV, EBV, and VZV serological status; and state of sensitisation to HLA antigens should also be reviewed and recorded. The available data should be reviewed preoperatively and any samples required for missing information sent. Postoperatively, a clear record of the cold and warm ischaemic time and the vascular and urological anatomy of the transplant should be clearly and accessibly recorded; see Table 69.1.

In Recovery

In the immediate postoperative period, the recipient should undergo a careful volume status assessment including a chest X-ray and review of anaesthetic charts for fluids in and out during surgery.

Table 69.1 Data collection

Recipient details
Primary renal diagnosis
Renal replacement therapy timeline (include positive confirmation if pre-emptive transplant)
CMV, EBV, HIV, VZV status
Hypertension history (including drugs)
Vascular history (coronary/cerebral, peripheral)
Dry weight pre-transplant
Donor details
Live vs deceased donor
Donor age
Donor comorbidity (hypertension, diabetes, renal impairment)
Deceased after cardiac death (DCD) vs deceased after brain death (DBD)
Cold ischaemic time
Surgical warm ischaemic time (and pre-agonal WIT for deceased donors with prior out-of-hospital arrest)
Agonal WIT for DCDs
Number of arteries and veins
Surgical comment on on-table perfusion
Surgical comment on any vessels sacrificed
Surgical comment on bladder
Presence of (and plan for) ureteric stent
Infections bacterial or viral
Transplant details
HLA matching (A:B:DR)
Presence of any repeat mismatches
Any known antibody incompatibility (ABO, HLA) and what/whether desensitisation undertaken
Induction immunosuppressive therapy (if used)
Maintenance immunosuppression used (and planned)
Prompt vs delayed graft function
Problems or issues with wound
Rejection episodes
Discharge details
Creatinine at discharge
Weight at discharge
Drug levels (including trend) at discharge
Prophylaxis for opportunistic infection given
Dialysis access (venous lines/PD catheter) action and plan

Distal perfusion of the leg on the side of the transplant should be checked and the presence or absence of foot pulses recorded.

If consistent with local institutional practice, an ultrasound of the graft in recovery is extremely useful as establishing a baseline and allowing prompt return to theatres for reexploration in the (extremely rare) event of impaired perfusion following wound closure, caused by direct compression of the graft or vessels in recipients who have had a large kidney implanted into a narrow pelvis or where torsion of the vessels has occurred. This may be particularly helpful if the recipient has a native urine output as augmentation of this with osmotic diuretic, loop diuretics, or dopamine intra-operatively, as has commonly been a dogma from the dawn of surgical approaches to transplantation, may cloud assumed allograft output and thereby the implication of adequate perfusion.

An urgent potassium is essential to determine dialysis requirement, especially if no urine is forthcoming.

When there is primary graft function, initial urine output is often high (it is not uncommon for loop diuretics and or mannitol to be administered in theatre despite the complete lack of evidence suggesting any benefit) after the release of vascular clamps. Attention should be paid to blood loss from surgical drains, and the patient should be haemodynamically stable prior to return to the transplant ward.

The First 24 h

Recipients with primary graft function are usually straightforward to manage during the initial post-transplant period with the focus being on maintaining satisfactory fluid balance, administration of immunosuppression, and vigilance for early surgical complications. Common practice is to provide intravenous fluid (usually crystalloid) to match the urine output, but care must be taken to factor in the volume of other fluids being administered intravenously (blood, other colloids, and intravenous drugs) or by mouth, since overenthusiastic fluid administration leading to overload is a common problem. As soon as the patient is able to mobilise, daily weights are a helpful check on the tendency to overfill the recently transplanted (and can be compared to the pre-transplant weight or dialysis target dry weight).

Autoregulation of renal blood flow is impaired after even short periods of cold ischaemia, so the graft needs to be protected from hypoperfusion by ensuring an adequate blood pressure (aiming for mean arterial pressure of at least 65 mmHg). If this cannot be achieved with the establishment of adequate intravascular fluid volume, then pressor agents may be used; some units still use dopamine (at or slightly above the traditional 'renal' dose of 2–5 μg/kg/h), although the formal evidence that this agent has any renal protective effect other than the promotion of diuresis in this context is limited [23, 24].

Recipients who remain oliguric post-transplant or whose urine output declines steadily after an initial period (typically of 2–6 h) of reasonable urine output require careful management. An ultrasound of the graft and chest X-ray should be arranged, and after a careful clinical assessment of fluid balance and assessment for evidence of bleeding, a fluid challenge (usually 250–500 ml colloid) should be given. *If* the recipient is adequately filled and not bleeding, a furosemide infusion may help manage hyperkalaemia and avoid acute dialysis but does not shorten the AKI, and it

is important to ensure intravascular volume is adequately maintained.

The First Week

Obsessive attention should be paid to urine output, haemoglobin, serum creatinine, and clinical examination directed towards the wound and fluid balance in the first week after transplantation, with monitoring of all of these likely to occur several times a day and night. Ideally the creatinine should fall by 50 % on a daily basis and failing that fall by >10 % which may be considered therefore to be more than the variability of the laboratory analyser. Should creatinine not fall, or worse rise, then addressing the volume status is paramount. It is an unfortunate paradox that CNIs have a narrow therapeutic window and are nephrotoxic at high doses so drug levels should be performed daily (12 h trough). A transplant USS will ensure that perfusion is adequate and exclude obstruction. If all of these are addressed systematically and the creatinine remains suboptimal, then renal allograft biopsy remains the gold standard for diagnosis and is performed as either an open or percutaneous procedure according to time from transplantation and local protocols. A post-perfusion biopsy in theatre is often very helpful in determining the severity of AKI and degree of chronic damage.

Baseline samples should be taken during the early post-transplant for analysis of proteinuria and the presence of anti-HLA antibodies, as these may be invaluable in establishing a time frame if subsequent problems with recurrent proteinuric disease or antibody-mediated rejection occur.

In the case of delayed graft function (DGF), it can be several weeks before independent kidney function is achieved, and regular dialysis may be required during this period. This can be a frustrating time for patients and physician alike, but be cautious in assuming that the pathology will not change as rejection can superimpose meaning that regular allograft biopsies (approximately weekly) should be performed to guide therapy. Meanwhile vigilance must be maintained with regard to urine output, fluid balance/weight, ensuring allograft perfusion with regular imaging, and drug therapeutic monitoring.

Early Graft Dysfunction

Early complications are predominantly based around poor or reducing urine volumes (Table 69.2), the failure of the creatinine to fall at a desirable rate, wound infections, catheter problems, and fluid balance difficulties. The catheter is usually removed in the first few days after transplantation, although this is often prolonged if intra-operatively there are surgical concerns about the bladder anastomosis and/or bladder wall thickness.

Local infection control protocols need to be carefully thought out and diligently implemented with the use of prophylactic antibiotics and guidance on first line treatments in the face of urinary tract or wound infections.

Table 69.2 Early oliguria post-renal transplant

Clinical symptoms suggestive of bleeding or graft thrombosis such as pain over graft/abdomen	
Risk factors – difficult anastomosis, multiple vessels, procoagulant state, patient with small pelvis	
Clinical signs suggestive of hypovolaemia, bleeding, or graft thrombosis such as hypotension, tachycardia, graft tenderness, and frank haematuria	
Exclude blocked catheter and clot retention	
Urgent ECG, CXR, bloods	
Cross-match 4 units	
Venous gas K and Hb	
With hypotension	*Without hypotension*
Resuscitate IV colloids	Fluid challenge if clinical evidence of hypovolaemia
If evidence of bleeding with falling Hb, transfuse	Treat hyperkalaemia if present
If deranged clotting or thrombocytopenia, consider FFP and platelets	Bladder washout +/– change of catheter if in clot retention by surgical team
Urgent USS/CT for perfusion and evidence of haematoma and exclude obstruction (e.g. compression from haematoma)	Urgent USS for graft perfusion and patency of vessels and exclude obstruction
Evidence of bleeding	Evidence of graft thrombosis
Contact surgical team	Contact surgical team
Prepare for theatre if necessary to control haemorrhage and evacuate haematoma	Prepare for theatre immediately
	If graft thrombosis with reverse flow in diastole is seen on USS
If hypovolaemia and bleeding excluded, consider other causes for hypotension such as cardiac causes	If reduced cortical perfusion/no flow in diastole with patent large vessels, consider intraparenchymal pathology such as AMR
	Check for DSA and pro-thrombotic screen

Chest expansion is rarely complete intra-operatively so deep breathing and, if possible, chest physiotherapy will assist with the avoidance of atelectasis and pneumonias postoperatively. Opiates may promote a postoperative ileus (remember the operation is conventionally extra-peritoneal, so there is no surgical bowel manipulation) that can be uncomfortable for the patient and interfere with the metabolism of some medications. The recipient should be sat out as soon as sensible and mobility encouraged; this will improve chest expansion and promote a return to normal gut motility.

Delayed Graft Function

Failure of the transplanted kidney to function promptly as a consequence of ATN/acute tubular injury is common, occurring (albeit only occasionally) in live donor kidneys with minimal cold ischaemia and more frequently than not in grafts exposed to extended, combined, warm, and cold ischaemia in the more extreme types of donation after circulatory death. The graft will be perfused (but with the completely non-specific finding of a raised resistive index) on ultrasound scan. It is not uncommon for oliguria to develop progressively after a few hours of urine production postoperatively (presumably as a result of the onset of the reperfusion phase of ischaemia-reperfusion injury).

Care must be taken to avoid overfilling the oliguric recipient, instituting dialysis in a timely fashion if required and careful, repeated assessment of the graft to give an indication of other causes of graft dysfunction which may supervene before the onset of function. This will usually entail daily ultrasound scans and regular biopsies (standard practice being to undertake a biopsy on postoperative day 7 and then at weekly intervals until function is established).

A common reaction to DGF is to delay or reduce the exposure to CNIs, although evidence that this is effective is marginal [25, 26].

Thrombosis and Anticoagulation

Transplant arterial or venous thrombosis remains a rare but difficult to manage complication. Patients at risk include those with a known pro-thrombotic tendency (although the predictive value of standard tests for thrombophilia is low [27], the anatomical situation of a kidney compressed by being transplanted into a narrow pelvis or by surrounding haemorrhage, and prolonged cold ischaemic time. Prophylaxis with low-dose aspirin is known to be effective [28], although this carries an increased risk of bleeding should early biopsy be required, so heparin (usually subcutaneously as unfractionated or LMW) is more frequently used with due appreciation needing to be given to the effects of low-GFR on the clearance of LMW heparins. The initiation of anticoagulation is a matter for careful discussion with the surgeons involved in the procedure (who will definitely have an opinion) and should be based on the amount of intra-operative or postoperative haemorrhage and an assessment of the patient's risk of thrombosis based on their past history of haemorrhage or thrombosis, the anatomy of the graft, and the early postoperative platelet count.

Main or intra-graft arterial thrombosis may be accompanied by platelet consumption with peripheral thrombocytopenia and can be identified by absence of parenchymal perfusion on ultrasound scan.

Renal transplant vein thrombosis may be accompanied by macroscopic haematuria and sudden onset of a painful and swollen graft. The ultrasound will show reversal of flow in diastole. In both situations, the availability of a prior baseline ultrasound is extremely helpful to allow assessment of the extent to which factors such as body habitus, juxtaposition of vessels, and existing variation in regional perfusion and pulse pressure may influence the reliability of ultrasound-derived information. The assessment of graft perfusion by CT scan with contrast provides more objective information that can be derived from ultrasound, but risks precipitating or prolonging AKI. More importantly it may delay the crucial intervention of surgical exploration of the graft with critical ischaemia. Contrast enhanced ultrasound may offer a rapid, bedside test with greater sensitivity than doppler ultrasound.

Acute Cellular Rejection

The increasing use of biological induction therapy (with mono- or polyclonal agents) combined with the use of high-efficacy agents such as tacrolimus and mycophenolate has been associated with a sharp reduction in the incidence of early acute cellular rejection (Fig. 69.1) [14]. This does however still occur, even in recipients not obviously at high risk as a result of prior sensitisation, history of previous immunological graft loss, low CNI levels, or young recipient age. In grafts with immediate function, the onset of graft dysfunction due to cellular rejection can vary from the indolent (over several days) to the very rapid, with rising creatinine and falling urine volume. Despite several decades of endeavour, no non-invasive test has proved to have sufficient predictive value to replace the creatinine as screening modality, and transplant biopsy as the definitive investigation, for cellular rejection [29].

The timing of transplant biopsy in the early postoperative period is largely determined by the desirability of maintaining anticoagulation in the initial post-transplant period and the potential difficulty of managing post-biopsy haemorrhage in a potentially unstable early postoperative window. Seven days post-transplant is generally considered a safe time-point for percutaneous biopsy. Prior to this, and especially in the first 3–4 days, consideration should be given to open biopsy as the safest method of obtaining a definitive tissue diagnosis for graft dysfunction, with the added benefit of allowing direct examination of the graft and vessels which will encompass important parts of the differential diagnosis of early graft dysfunction (Table 69.3 and Figs. 69.1 and 69.2).

Table 69.3 Differential diagnosis of cellular infiltrates in transplant biopsies, see [30, 31]

T cell rejection (ACR)	Tubulitis (Fig. 69.1) with or without vascular (Fig. 69.2) and glomerular involvement. Typically interstitial infiltrate is lymphocytic but may also contain eosinophils, neutrophils, and macrophages. More likely in under patients who are immunosuppressed, commonest cause of interstitial infiltrate
Polyoma virus nephropathy	BKV (95 %) or JC (≤5 %), interstitial infiltrate typically rich in plasma cells, enlarged atypical tubular nuclei but may be indistinguishable from ACR thus *SV40 large T antigen stain critical in all presumed ACR.* BKV is more likely in over immunosuppressed
Post-transplant lymphoproliferative disorder	More common in the graft early on EBV D+/R-, monotonous diffuse infiltrate suggestive, immunohistochemistry (EBNA) staining critical
Cytomegalovirus nephropathy	A rare cause of interstitial nephritis, other end-organ damage usually apparent before renal involvement. Viral inclusion bodies may be seen in glomerular and tubular cells with enlarged 'owl's eye' effect. Extensive infiltrate uncommon
Bacterial Pyelonephritis	Neutrophil casts in tubules highly suggestive but may coexist with ACR. Positive urine culture helpful but can frequently occur in the absence of positive MSU, especially after short course of antibiotics. Cellular infiltrate pleomorphic including neutrophils and the second commonest cause and more likely in those with recent UTIs especially if recurrent, diabetes, abnormal bladder, and stent in situ
Mycobacterial infection	Ethnicity and country of origin may indicate high risk, often associated with granulomas (acid-fast bacilli rarely seen)
Recurrent disease	Important to consider in patients with an original disease associated with acute interstitial nephritis such as sarcoid, vasculitis, SLE but all unusual in the early stages of a transplant due to augmented immunosuppression
Allergic interstitial nephritis	Common transplant drugs such as septrin, proton pump inhibitors, azathioprine, and penicillins may all cause an interstitial nephritis confused with ACR

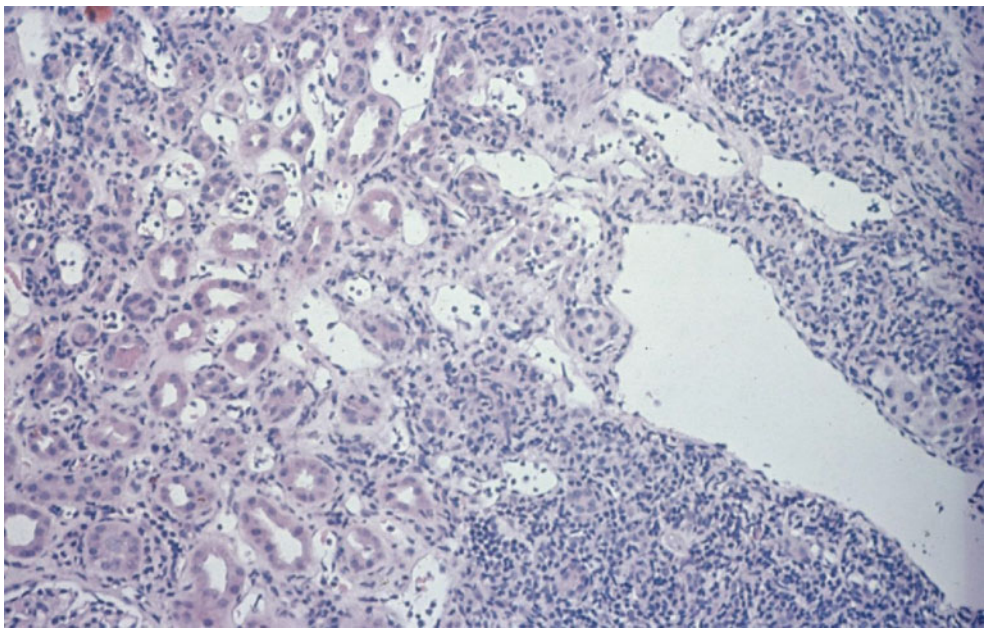

Fig. 69.1 Low-powered view of acute cellular rejection showing cellular infiltrate with lymphocytes invading tubules (tubulitis). Differential diagnosis is shown in Table 69.3

Acute Antibody-Mediated Rejection

Acute antibody-mediated rejection remains a rare complication except in the context of planned (or unwitting) transplantation against a pre-existing donor-specific antibody barrier, whether to HLA and non-HLA protein or ABO-blood group antigens, but the reducing incidence of cellular rejection makes this a proportionately increasingly important cause of early graft dysfunction [32]. The presentation may often be dramatic, with sudden onset anuria, often presaged by macroscopic haematuria. Classically, graft dysfunction will be preceded by the development of rapidly rising levels (as assessed by fluorescence intensity on solid-phase bead-based Luminex assay) of donor-specific antibodies.

With improvements in tissue typing, much of which has occurred alongside the development of solid-phase antibody assays, there has been improved detection of both pre-formed and de novo anti-HLA antibody which is associated with AMR. Controversy remains regarding the practical importance of these tests in the absence of a positive flow or cytotoxic cross-match, but undoubtedly their presence should raise suspicion of AMR. A renal allograft biopsy remains the gold standard for diagnosis (Fig. 69.2), either open (surgeon performed intra-operatively) or percutaneous

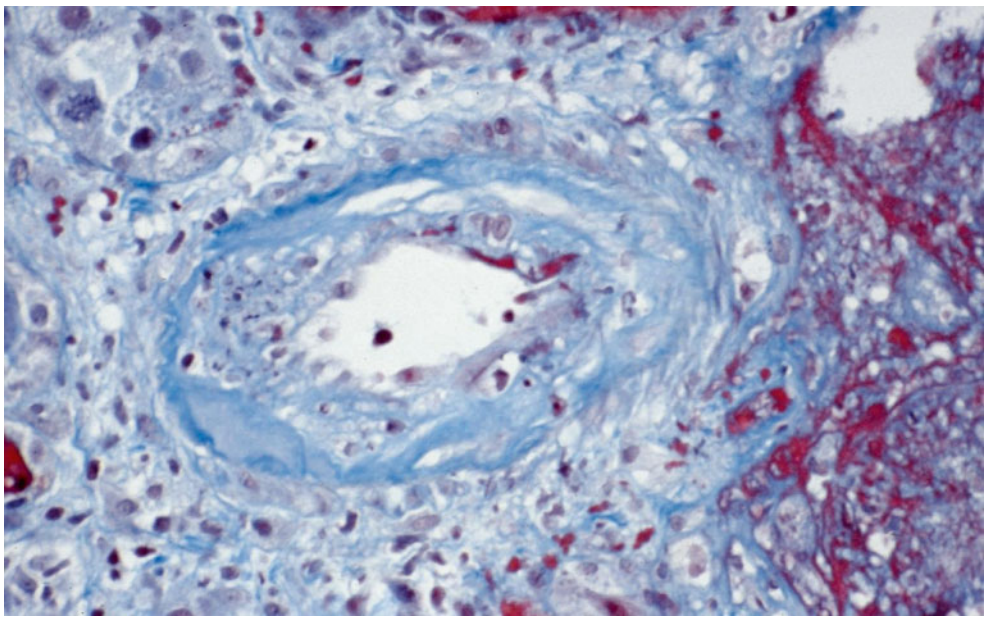

Fig. 69.2 Vascular rejection: arteriole showing lymphocytic infiltrate under the endothelium of the vessel

according to time from transplantation and local protocols, but if this is unsafe (proximity in time to surgery, overlying bowel, patient fitness, anticoagulation, risk of graft rupture), then presumptive therapy may be advised. Most protocols use a combination of intravenous corticosteroids and plasma exchange with or without the addition of intravenous immunoglobulin and mono- or polyclonal antibody therapy.

In the presence of early AMR refractory to standard therapy, the complement inhibitor eculizumab and proteasome inhibitor bortezomib are potential therapies still undergoing evaluation.

Urine Outflow Obstruction

If the patient is catheterised, then always ensure the catheter is not blocked, by external pressure (lying on catheter or clamped accidentally) prior to consideration of clot retention. The latter will require either a catheter change or flushing which should be performed by a transplant surgeon with care not to impact on the vesicoureteric anastomosis. Irrigation of the bladder can not only jeopardise the bladder anastomosis but make fluid balance incredibly difficult to record and can be complicated by hyponatraemia. Instrumentation of a renal patient's urethra, which often has not had urine passage, is not straightforward and can lead to false passages which should also be considered in terms of catheter placement. In elderly anuric men on dialysis, prostatic obstruction may only declare itself after renal transplantation and should be anticipated.

Hypotension

The crucial differential diagnosis for the hypotensive patient in the early post-transplant period lies between haemorrhage and sepsis. In the former case, the patient will usually be peripherally shutdown and cold, while in the latter they will be vasodilated and hot. Beyond basic clinical examination, including close attention to the contents of surgical drains, an ultrasound will demonstrate peri-transplant haematoma, but cannot easily detect retroperitoneal haemorrhage. CT scan will demonstrate this clearly (with the disadvantage of exposing the recently transplanted kidney to a contrast load) but should be undertaken if the recipient is clearly bleeding and does not stabilise promptly with administration of appropriate blood products (the alternative intervention being urgent surgical reexploration, which may be mandated by the clinical urgency of the apparent haemorrhage). When a CVP line is present, the response of the central venous pressure to fluid bolus administration can be used to gauge adequacy of filling, although the common complications in dialysis patients of thoracic vein stenosis or thrombosis and cardiac ventricular dysfunction/poor ventricular compliance may need to be borne in mind. It is often helpful to discuss the patient's prior behaviour on dialysis (in terms of the BP response to fluid loading) with the physician who looked after them on dialysis.

Patients with diabetes (or other primary renal diseases associated with autonomic dysfunction) will often have marked postural falls in BP in the early transplant period, and care must be taken on their initial postoperative mobilisation to avoid significant hypotensive episodes which may be sufficient to cause falls or compromise graft perfusion.

Cyto-depleting induction therapies, whether monoclonal (alemtuzumab, OKT3) or polyclonal (anti-thymocyte globulins), may be associated with a cytokine release syndrome presenting with hypotension, rigours, thrombocytopenia, and occasionally a brisk spike in temperature. If not already given as part of the induction regimen, IV steroids (100 mg hydrocortisone) and IV antihistamines will usually control the reaction which is relatively short lived (1–3 h).

Hypertension

The almost universal tendency to want to maintain a high urine output during the initial post-transplant period makes fluid overload with associated hypertension an extremely common phenomenon in the first few days post-transplant. Beyond attempting to avoid the all-too-common scenario of a patient with high blood pressure after intravenous administration of 10 L of excess fluid, patients will often require staged reintroduction (or commencement) of antihypertensive medication. ACE inhibitors and angiotensin receptor blockers are often viewed with anxiety in the early postoperative period because of the theoretical risk of interfering with intrinsic homeostatic responses to volume stress in a kidney in the process of recovering from ischaemia-reperfusion injury, but the definite long-term benefits of agents which interrupt the renin/angiotensin system in renal transplant recipients [33] do make them attractive agents even in the early postoperative period. The suggestion (popular in the late 1980s) that non-dihydropyridine calcium channel antagonists such as verapamil and diltiazem had a protective effect against CNI toxicity and has made these popular agents for use in early post-transplant hypertension. In any event, agents which are very long acting and renally excreted (such as atenolol) or liable to produce sharp drops in BP on first administration (such as standard-release nifedipine) should be avoided.

A proportion of recipients (especially the young and often in patients of Afro-Caribbean ethnic origin) will respond to volume depletion with a marked vasoconstrictor response accompanied by significant arterial hypertension. In this context, carefully controlled vasodilatation (with low-dose nitrates or other vasodilators) accompanied by cautious fluid replacement ('dilate-and-fill') will result in resolution of the hypertension, the vasoconstriction, and (hopefully) the associated hypoperfusion of the graft.

Careful attention to fluid balance with gradual reversion to a euvolaemic state (which may require careful use of loop diuretics) after any overenthusiastic initial fluid loading will usually bring the blood pressure under control, although the vasoconstrictor effects of calcineurin inhibitors mean that most transplant recipients require long-term antihypertensive medication.

Accelerated-Phase Hypertension/Thrombotic Microangiopathy (TMA)

Hypertension associated with failure of microvascular endothelial homeostatic protection mechanisms is a rare but always challenging and complex event early post-transplantation. The differential diagnosis includes the extreme manifestation of CNI toxicity (which is often invoked but rarely encountered), recurrence of underlying atypical HUS/complement regulatory disease, and antibody-mediated rejection. Although moderate degrees of thrombocytopenia are common after cyto-depleting induction therapies, any fall in platelet count should trigger a request for examination of a peripheral blood film, LDH, and whatever serves as the local haemolysis screen, since the presence of RBC fragments or evidence of haemolysis give early warning of microangiopathy. Consideration should also be given to the primary renal diagnosis since atypical HUS is difficult to diagnose and will frequently be labelled as 'hypertensive nephropathy'. Onset at a young age and a positive family history are important clues.

In the presence of established thrombotic microangiopathy, careful attention to CNI levels, an urgent search for donor-specific and anti-phospholipid antibodies, evidence of lupus or lupus-associated autoimmune disease, and the consideration of the possibility of recurrent atypical HUS or active hepatitis C should all be undertaken. If correction of fluid overload and control of hypertension using renin/angiotensin blockade do not result in resolution of the TMA, then plasma exchange with FFP infusion should be considered. The recently licensed (for paroxysmal nocturnal haemoglobinuria) and very expensive, terminal component complement inhibitor eculizumab has been reported to be highly effective in a range of acute post-transplant microangiopathies.

Heparin-induced thrombocytopenia (HIT) may mimic the clinical presentation of post-transplant TMA but is an even rarer entity. Most of transplant recipients (with the exception of those pre-emptively transplanted) will have had ample heparin exposure prior to transplantation, and the absence of catastrophic reaction to heparin when stable on dialysis means that the many alternative causes of thrombocytopenia in the early post-transplant period are overwhelmingly more likely than HIT to be the explanation of a low platelet count in this situation.

Sepsis

Significant CMV disease prior to 3 months post-transplant remains rare and is easily diagnosed and treated using modern PCR-based diagnostics and the highly orally active agent valgancyclovir. Local protocols may involve the administration of prophylactic antiviral therapy after determination of risk by donor and recipient CMV status or may avoid prophylaxis in favour or serial monitoring of post-transplant recipient CMV PCR levels. It is usual for prophylaxis to *Pneumocystis jirovecii* (previously known as *Pneumocystis carinii* or PCP) to be used universally with septrin or inhaled pentamide. TB prophylaxis should be considered and usually instituted in patients with previous history of TB and in patients deemed at high risk of developing TB post-transplant such as those of Indoasian ethnic origin. Together with these approaches, the progressive reduction in the amount of corticosteroid administered during the early post-transplant period over the last 3 decades (even in those regimens not focussed on steroid avoidance) has altered the landscape of early post-transplant sepsis, with herpes virus reactivation and fungal sepsis becoming much less common (and resulted in the abandonment of the previously standard practice of

requiring total dental clearance or prophylactic cholecystectomy prior to transplantation). Current immunosuppressive regimens are highly potent and effective, but leave patients a relatively low risk of significant early sepsis, except in the context of recipients at risk of chronic or recurrent urosepsis (such as those with polycystic kidney disease or abnormal lower urinary tract anatomy), respiratory tract sepsis (bronchiectasis, pulmonary scarring secondary to pulmonary-renal inflammatory disease, or, most dangerously, lung transplant recipients with their risk of fungal or multi-resistant bacterial colonisation) or those exposed to de novo infection from contaminated organs. Positive perfusion fluid culture results should be treated with great seriousness, as representing a very high-risk situation.

Common sources of sepsis during the primary admission will usually respond to broad-spectrum antibiotics.

Proteinuria

Moderate (presumably predominantly tubular) proteinuria is very common in the immediate post-transplant period as a consequence of the tubular injury during the cold ischaemic phase, but persistent, significant early proteinuria (protein/creatinine ratio >100 mg/mmol) indicates major glomerular pathology, with recurrent focal and segmental glomerulosclerosis (FSGS) the most important underlying cause. Membranous nephropathy and complement-abnormality-associated MPGN can recur post-transplant, but usually with a timescale presenting beyond the initial transplant admission. When associated with delayed graft function, this can be a difficult diagnosis to establish. Early biopsy may not detect focal glomerular scarring at an early stage, and electron microscopy may be required to identify the associated podocytopathy.

In the presence of established, or probable, recurrent FSGS, the main current therapeutic option is aggressive plasma exchange, with recent case reports suggesting that anti-CD 20 monoclonal antibody (rituximab) may have a therapeutic or even prophylactic role [34].

Discharge Planning

Patients facing discharge after successful kidney transplantation have to cope with a range of important challenges and tasks.

The first of these will be a new and often complex drug regimen which will often include agents with a narrow therapeutic index and important toxicities. The discharge drug combination must be reviewed carefully with the patient to ensure they understand what the different drugs are for and how they should be taken. Particular attention should be paid to immunosuppressive agents with regard to the importance of taking these in a regular manner, not missing doses, and when to delay morning doses of twice-daily drugs to allow measurement of trough drug levels. Patients need to know not to take additional drugs without prior discussion with the transplant unit because of the risk of drug interactions.

The recently transplanted kidney often takes several weeks to acquire the ability to regulate urine concentration adequately, and patients will often be discharged during a polyuric phase with high volume, low concentration urine. They need to understand the importance of identifying and reacting to developing fluid depletion (or overload) which can be most accurately anticipated after discharge by asking patients to check a daily weight and adjust their salt and water intake accordingly. Recipients who were oliguric or anuric prior to transplantation (especially if they have been on dialysis for many years) will often find it difficult to cope with the sudden switch from fluid restriction to having to drink several litres daily, often with associated reduced appetite and urinary frequency, and need to be warned about this.

Patients transplanted pre-emptively need to understand that the early post-discharge period will involve much more frequent hospital attendance with disruption to their day-to-day activities than they were experiencing in the pre-transplant period (those who were on dialysis when transplanted will be able to set this intensity of supervision off against the time they gain from being dialysis independent), but need to understand that early surveillance in the transplant clinic may be much less predictable and regular than dialysis treatments.

A clear and brief summary of the postoperative course, including whether graft function was immediate or delayed; details of any surgical complications, rejection episodes, or infections; and the patient's weight, graft function, and CNI trough levels at discharge, is necessary to ensure effective transfer of care to the transplant clinic.

Tips and Tricks: Five Common Mistakes and How to Avoid Them

1. Missing retroperitoneal haemorrhage

   Ultrasound is the main traditional form of imaging for the recent renal transplant, providing confirmation of graft perfusion, early (if non-specific) warning of problems from changes in resistive index, and identification of lymphocoeles and other surgically related fluid collections. It is not however a sensitive modality for the identification of retroperitoneal haemorrhage which, if progressive, can lead to pressure on the renal vessels (with associated risk of venous thrombosis or in extreme cases avulsion of the vascular anastomoses) or circumferential pressure on the graft itself with associated reduced function.

   In cases where the patient's Hb is dropping without an obvious reason, a CT scan with contrast is required to exclude significant haemorrhage around or behind the graft. This is not an easy request to submit because (especially in the context of delayed or suboptimal graft function) of the risk of nephrotoxicity from X-ray contrast.

Remember, contrast nephrotoxicity is a transient phenomenon; kidney transplant vein thrombosis is usually forever.

2. Failing to anticipate changes in Tacrolimus absorption

   Tacrolimus is absorbed throughout the GI tract (even from the oral mucosa, although this is not a reliable route). As well as first-pass metabolism in the liver, there is significant degradation of tacrolimus within small bowel mucosa, so that intercurrent events which prevent the drug from reaching the small intestine, or reduce the time it spends there, will lead to increased tacrolimus levels. Two common scenarios are:

   (i) A postoperative ileus following transplantation is associated with high tacrolimus levels due to reduced transit of the drug through to its sites of metabolism in the small bowel combined with efficient absorption from the gastric mucosa. This leads to reduction in the dose around postoperative day 4–5, just as the ileus is resolving. The patient then goes home about day 7 with tacrolimus levels which are falling sharply and is underdosed during the second post-transplant week, a period of high risk of acute cellular rejection in grafts undertaken without the cover of induction therapy.

   (ii) Diarrhoeal episodes are frequently associated with decreased tacrolimus breakdown (due to reduced exposure to the small intestinal mucosa combined with efficient absorption within the large intestine). When combined with the metabolic consequences of intravascular volume depletion, this may commonly present with significant hyperkalaemia (overriding the effects of gastrointestinal K^+ loss) and significant graft dysfunction.

   Cyclosporin is predominantly absorbed from the small intestine and is less prone to these effects than tacrolimus.

3. Not knowing important interactions with Calcineurin inhibitors

   Calcineurin inhibitors (cyclosporin and tacrolimus) have a narrow therapeutic index and are principally metabolised by the cytochrome P450 3A4 enzymes, and drugs which affect this system can significantly alter blood levels.

   The commonest interactions leading to high levels and toxicity are from CYP 3A inhibition by macrolide antibiotics (especially erythromycin, with clarithromycin exerting a smaller but still significant effect), azole antifungal agents (most commonly fluconazole), and the now rarely prescribed Cimetidine. There is a clinically significant effect of co-administration of CNI's with grapefruit juice (presumably via inhibition of enteric CYP3A4).

   Less commonly, reduction in CNI levels can follow induction of cytochrome P450 by phenytoin, carbamazepine, or rifampicin.

4. Overfilling the recipient with delayed graft function

   Delayed graft function is not a life-threatening complication of transplantation. Fluid overload in a renal patient, who may well have impaired cardiac performance commonly due to coronary vascular disease or chronic uraemic myocardial dysfunction (often diastolic ventricular relaxation impairment), rapidly results in pulmonary oedema which is life-threatening and in this context will require dialysis/ultrafiltration as an emergency which is always best avoided postoperatively. Less medically concerning, although uncomfortable for the recipient, is severe peripheral tissue salt and water accumulation as a result of overenthusiastic fluid administration in pursuit of a reassuringly high initial urine volume.

5. Failure to react fast enough to sudden oligoanuria

   The first rule of thumb is always get a US as it rarely proves unhelpful and often is reassuring if not diagnostic.

   (i) Obstruction.

   (ii) Antibody-mediated rejection. Can be detected clinically with pain over the allograft and/or macroscopic haematuria. More prevalent in sensitised recipients (commonest causes of sensitisation being pregnancy and previous transplantation, particularly when re-transplantation occurs across a repeat mismatch) and associated with graft loss as well as suboptimal outcomes both acute and chronically.

   (iii) Renal artery or vein thrombosis. A relatively rare but highly important cause of allograft loss and more commonly seen in those with a prothrombotic tendency (be wary if arteriovenous access for dialysis has proved difficult to maintain or previous other thrombotic events occurred). Early anticoagulation is likely to be protective but this needs careful consideration and negotiation with the surgical team postoperatively. Often its presentation is dramatic with sudden anuria and only suspicion (with or without the assistance of a Doppler USS revealing reversed flow in diastole) may result in the correct management which is immediate surgical exploration and examination of the venous anastomosis.

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