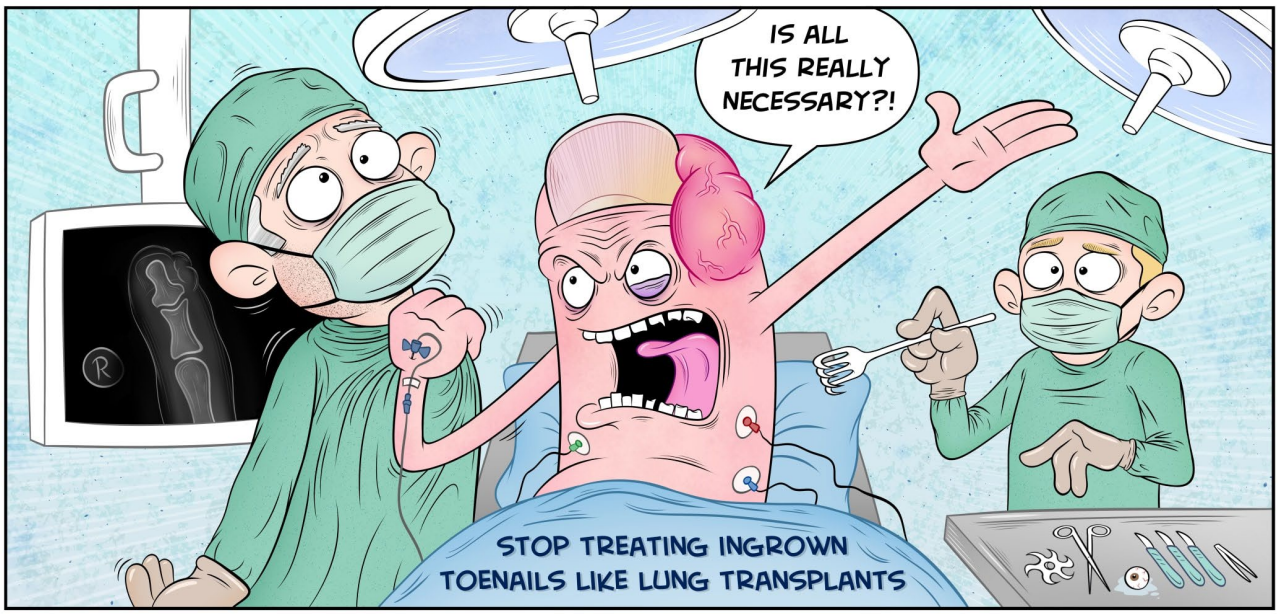

Transplant types

Graft	Features	Uses
Allograft	Transplant of tissue from genetically non identical donor from the same species	Solid organ transplant from non-related donor
Isograft	Graft of tissue between two individuals who are genetically identical	Solid organ transplant in identical twins
Autograft	Transplantation of organs or tissues from one part of the body to another in the same individual	Skin graft
Xenograft	Tissue transplanted from another species	Porcine heart valve

Organ Transplantation: Immunosuppressants

A number of drugs are available which help to mitigate the processes resulting in acute rejection. Cyclosporin and tacrolimus are commonly used drugs.

Example regime

- Initial: ciclosporin/tacrolimus with a monoclonal antibody
- Maintenance: ciclosporin/tacrolimus with MMF or sirolimus
- Add steroids if more than one steroid responsive acute rejection episode

Ciclosporin

- Inhibits calcineurin, a phosphatase involved in T cell activation
- **Nephrotoxic**
- Monitor levels

Azathioprine

- Metabolised to form 6 mercaptopurine which inhibits DNA synthesis and cell division
- Side effects include myelosupression, **alopecia** and nausea

Tacrolimus

- Lower incidence of acute rejection compared to ciclosporin
- Also less hypertension and hyperlipidaemia
- However, high incidence of impaired glucose tolerance and **diabetes**
- Tacrolimus is metabolised by the P450 enzyme system. This is inhibited by a number of naturally occurring substances, these include grapefruit, watercress and St. John's Wort. These should all be avoided in immunosupressed patients taking tacrolimus.

Mycophenolate mofetil (MMF)

- Blocks purine synthesis by inhibition of IMPDH
- Therefore inhibits proliferation of B and T cells
- Side-effects: GI and marrow suppression

Sirolimus (rapamycin)

- Blocks T cell proliferation by blocking the IL-2 receptor
- Can cause hyperlipidaemia

Monoclonal antibodies

- Selective inhibitors of IL-2 receptor
- Daclizumab
- Basilximab

Complications Following Renal Transplant

Renal transplantation is widely practised. The commonest technical related complications are related to the ureteric anastomosis. The warm ischaemic time is also of considerable importance and graft survival is directly related to this. Long warm ischaemic times increase the risk of acute tubular necrosis which may occur in all types of renal transplanation and provided other insults are minimised, will usually recover. Organ rejection may occur at any phase following the transplantation process.

Immunological complications

Types of organ rejection

- Hyperacute. This occurs immediately through presence of pre formed antibody (such as ABO incompatibility).
- Acute. Occurs during the first 6 months and is usually T cell mediated. Usually tissue infiltrates and vascular lesions.
- Chronic. Occurs after the first 6 months. Vascular changes predominate.

Type of rejection	Key features
Hyperacute	Occurs within minutes of clamp release Due to pre formed antibodies* Immediate loss of graft occurs
Accelerated acute	Occurs in first few days following surgery Involved both cellular and antibody mediated injury Pre-sensitisation of the donor is a common cause
Acute	Traditionally the most common type of rejection Seen days to weeks after surgery Predominantly a cell mediated process mediated by lymphocytes Organ biopsy demonstrates cellular infiltrates and graft cell apoptosis
Chronic	Increasingly common problem Typically; graft atrophy and atherosclerosis are seen. Fibrosis often occurs as a late event

** Episodes of hyperacute rejection are typically due to preformed antibodies.* ***ABO mismatch*** *is the best example. However,* ***IgG anti HLA Class I antibodies*** *are another potential cause. These events are now seen less commonly because the cross matching process generally takes this possibility into account*

Technical complications

Complication	Presenting features	Treatment
Renal artery thrombosis	Sudden complete loss of urine output	Immediate surgery may salvage the graft, delays beyond 30 minutes are associated with a high rate of graft loss
Renal artery stenosis	Uncontrolled hypertension, allograft dysfunction and oedema	Angioplasty is the treatment of choice
Renal vein thrombosis	Pain and swelling over the graft site, haematuria and oliguria	The graft is usually lost
Urine leaks	Diminished urine output, rising creatinine, fever and abdominal pain	USS shows perigraft collection, necrosis of ureter tip is the commonest cause and the anastomosis may need revision
Lymphocele	Common complication (occurs in 15%), may present as a mass, if large may compress ureter	May be drained with percutaneous technique and sclerotherapy, or intraperitoneal drainage

Post-transplant complications

- **CMV:** 4 weeks to 6 months post-transplant
- **EBV:** > 6 months post-transplant *(post-transplant lymphoproliferative disease)*

Renal Transplant: HLA Typing and Graft Failure

The human leucocyte antigen (HLA) system is the name given to the major histocompatibility complex (MHC) in humans. It is coded for on chromosome 6.

Some basic points on the HLA system

- Class 1 antigens include A, B and C. Class 2 antigens include DP, DQ and DR
- When HLA matching for a renal transplant the relative importance of the HLA antigens are as follows DR > B > A

Graft survival

- 1 year = 90%, 10 years = 60% for cadaveric transplants
- 1 year = 95%, 10 years = 70% for living-donor transplants

Post-op problems

- ATN of graft
- Vascular thrombosis
- Urine leakage
- UTI

Hyperacute acute rejection

- Due to antibodies against donor HLA type 1 antigens
- Rarely seen due to HLA matching

Acute graft failure (< 6 months)

- Usually due to mismatched HLA
- Other causes include cytomegalovirus (CMV) infection
- Management: give steroids, if resistant use monoclonal antibodies

Causes of chronic graft failure (> 6 months)

- Chronic allograft nephropathy
- Ureteric obstruction
- Recurrence of original renal disease (MCGN > IgA > FSGS)