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IFTM University, Moradabad, Uttar Pradesh

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IFTM University, Moradabad

A Presentation
On
Renal Transplantation

by
Km. Monika

Dept. of Pharmacy (Pharmacy Academy)
IFTM University, Moradabad

Defination

- A surgical process in which an organ is moved from donor to a recipients.
- Renal transplantation is the preferred treatment for patients with end-stage renal disease. It offers better quality of life and confers greater longevity than long-term dialysis
- The length of time donated organs and tissues can be kept outside the body vary: - Kidney: 48-72 hours.
- Over 54,000 patients currently awaiting cadaveric kidney transplants
- Over 5200 living donor transplants done in 2002
- Extremely successful
- 1-year graft survival rate
  - 90% for cadaver transplants
  - 95% for live donor transplants

History

- **1954** First successful kidney transplant performed.
- **1966** First simultaneous kidney/pancreas transplant performed..
- **1968** First successful isolated pancreas transplant performed. First successful heart transplant performed.
- **1977** Implementation of the first computer-based organ matching system, dubbed the "United Network for Organ Sharing.“
- **1984** The National Organ Transplant Act, passed by Congress (conference) in outlawed the sale of human organs and began the development of a national system for organ sharing and a . . . scientific registry to collect and report transplant data

- **1986** UNOS receives the initial federal contract to operate the Organ Procurement and Transplantation Network (OPTN).
- **1992** UNOS helps found Donate Life America to build public support for organ donation.
- **1995** UNOS launches its first Web site for all users with an interest in transplantation.
- **2001** For the first time, the total of living organ donors for the year (6,528) exceeds the number of deceased organ donors (6,081).
- **2006** UNOS launches Donor Netsm, a secure, Internet-based system in which organ procurement coordinators send out offers of newly donated organs to transplant hospitals with compatible (proper) candidates

The Donation Process

- When organs are donated, a complex process begins. UNOS maintains a centralized computer network, UNetSM, which links all organ procurement organizations (OPOs) and transplant centers.

- Transplant professionals can access this computer network 24 hours a day, seven days a week.

- UNet electronically links all transplant hospitals and OPOs in a secure, real-time environment using the Internet.

The Five Steps In Organ Matching

1. An organ is donated

OPO managing the donor enters medical information about the donor including organ size and condition, blood type and tissue type into the UNOS computer system.

2. A list of potential recipients is generated

The UNOS computer system generates a list of candidates who have medical and biologic profiles compatible with the donor's. The computer ranks candidates based upon how closely their medical Characteristics match the donor's, medical urgency, time spent waiting and *proximity (closeness)* of candidates to the donor.

3. The transplant center is notified of an available organ

Organ placement specialists at the OPO or the

UNOS Organ Center contact the transplant centers

whose patients appear on the ranked list.

4. The transplant team considers the organ for the patient

When the team is offered an organ, it bases its acceptance or refusal of the organ upon established medical criteria, organ condition, candidate condition, staff and patient availability and organ transportation. By policy, the transplant team has only one hour to make its decision.

5. The organ is accepted or declined

If the organ is not accepted, the OPO continues to offer it for patients at other centers until it is placed.

INDICATION

- ESRD GFR less than 15ml/L
- MALIGNANCY
- HYPERTENSION
- DIABETES MELLITUS
- GENETIC DISEASES- polycystic kidney diseases
- METABOLIC DISORDERS
- AUTO IMMUNE CONDITIONS- lupus ,good pastures syndrome
- CRF

Grafts Definations

- Allograft : graft between genetically dissimilar individuals of the same species.
- Autograft : graft in which donor and recipient are the same individual.
- Xenograft (heterograft): Donor and recipient belong to different species.

Graft Prognosis

- Directly related to source of donor kidney.
- Recipients of cadaveric kidneys have more episodes of rejection and lower graft survival rates.
- Graft survival rates for kidneys from living donor is 95% @ 1 yr and 76% @ 5 yrs vs graft survival from a cadaveric kidney donor is 89% @ 1 yr and 61% @ 5 yrs.

Kidney Transplant Step-By-Step

1. Getting the Green Light

- After receiving the call from the transplant team indicating they have a kidney for you, a patient needs to get to the hospital as quickly (and safely) as possible. A suggested list of things to bring to the hospital to ensure everything goes as quickly and smoothly as possible includes a list of current medications, a list of drug allergies, health insurance information and clothing for several days.

  It's also important for a patient to stop eating and drinking as soon as they get notice a kidney is available. A patient's stomach needs to be empty when the operation begins.

2. Arrival at the Hospital

- Once admitted, the patient will receive a physical exam, blood work, a chest x-ray, ECG and perhaps even other tests.

  While disappointing, there are some cases where surgery will be postponed and the patient will be sent home. These include:

- The patient has developed an infection or a medical problem that could cause problems with the surgery or recovery.
- The kidney being donated looks to be in bad shape or there is reason to believe it would have poor function

- ***3. PATIENT PREPARATION BEFORE SURGERY***
- To ensure the patient is ready for the operation, several things will be done. Hair on the chest and abdomen will be shaved, a laxative or enema may be administered to clean out the intestines and prevent constipation after surgery, and an intravenous line will be inserted to supply medicine and prevent dehydration. A sedative will also be administered to help the patient relax before surgery.

  There is a possibility a patient will need a transfusion of blood during the surgery. Today's donated blood is screened very carefully so the chance of contracting a disease from the transfusion is small. If you have concerns about transfusions, make sure you talk to the transplant team during the time you are waiting for a kidney.

- ***4. THE KIDNEY TRANSPLANT***
- The patient will be put “under” using a general anesthesia and will remain asleep for the duration of the surgery. Once asleep, the transplant surgeon will make an incision on the lower abdomen just above the groin.

  The donor kidney will be placed in the lower abdomen. The kidney's blood vessels will then be connected to the recipient's iliac artery and vein. The surgeons will then connect the ureter to the bladder. A small drain may be inserted into the abdomen to drain any excess fluid that may have accumulated during the operation.

- ***5. AFTER THE SURGERY***
- After the surgery, the patient will be taken to the intensive care unit or acute care unit where they will be monitored by medical personnel until the anesthesia wears off and they wake up. While recovering here are some things a patient can expect:
- Some pain and discomfort. Medication will be provided to help relieve this.
- To help keep the lungs clear, a patient will be asked to cough.
- Fluids and medications will be delivered through IV lines in the arm or neck for the first few days after surgery.

- A catheter to drain urine from the bladder will be inserted. While it may feel uncomfortable and create the feeling for the need for constant urination, it’s only temporary.
- If a drain was inserted near the incision during surgery to help with fluid removal, it will remain there for five to 10 days.
- In some situations, while waiting for the donated kidney to fully recover from the procurement/transplant process, dialysis may still be used to help remove excess fluid and toxins.
- Patients will be monitored for laboratory results, medications, eating and exercise. As soon as the patient is able, they will be prepared for going home.

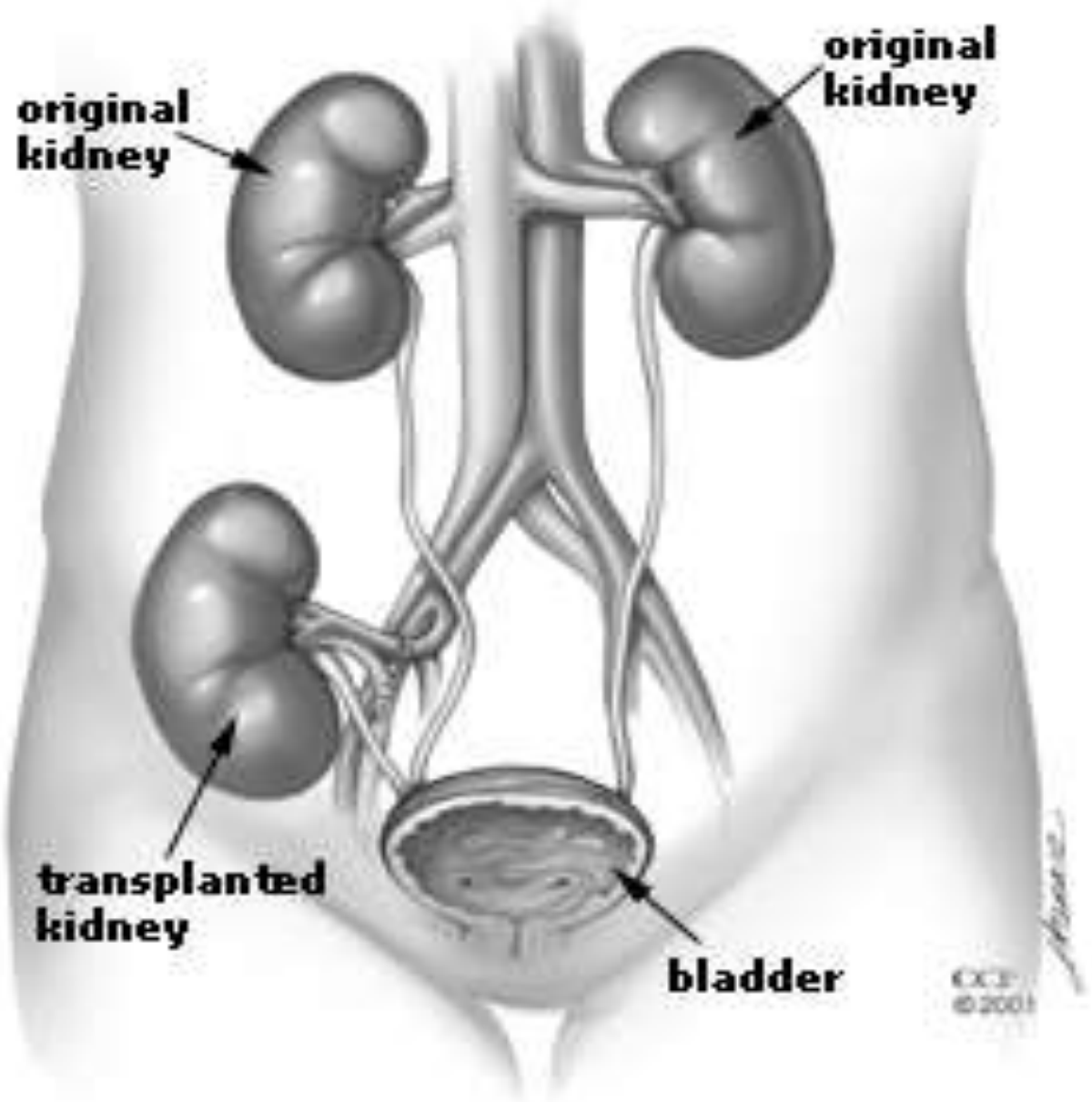
The Surgical Procedure

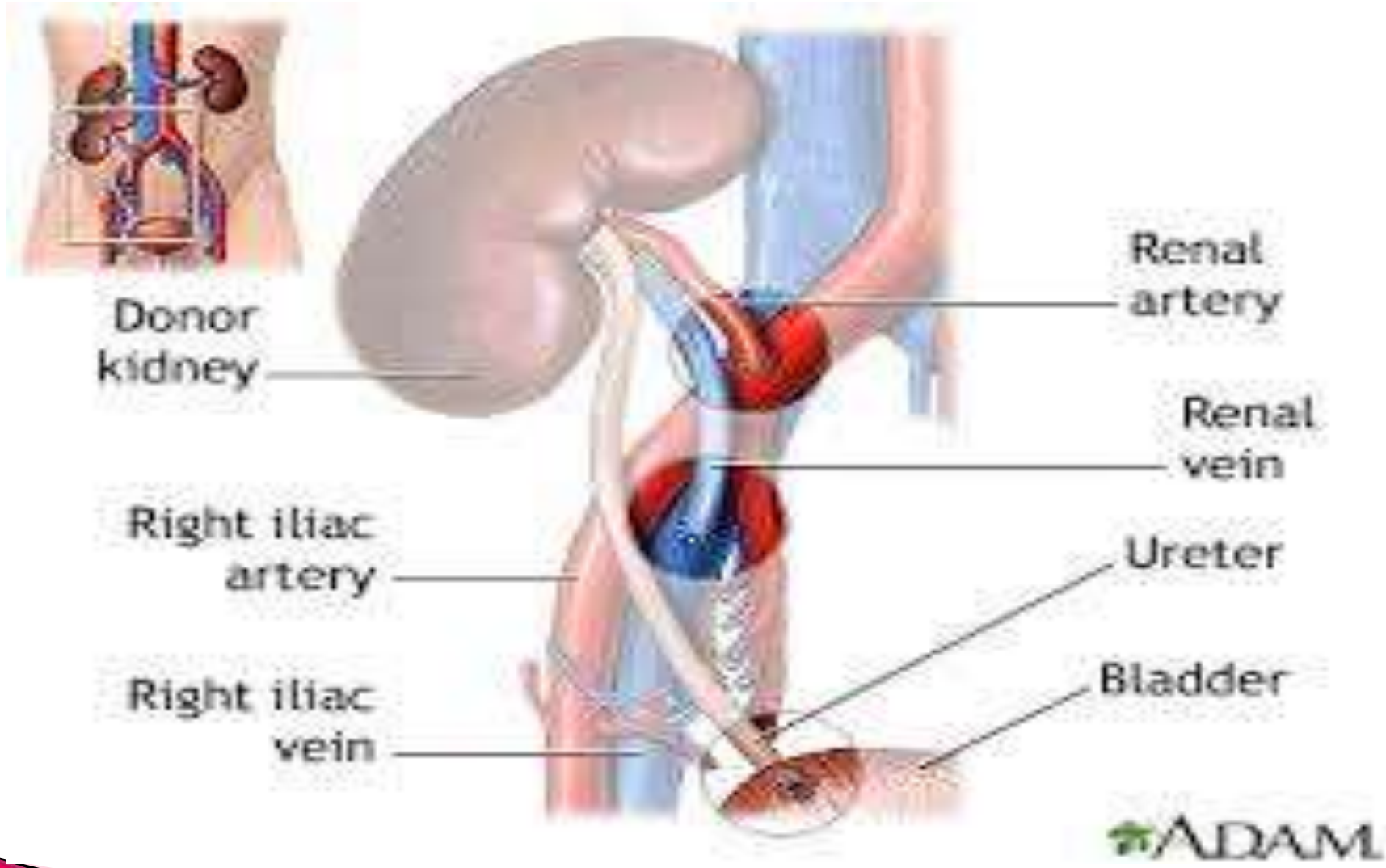
- Donor nephrectomy performed by a urologist or transplant surgeon
- Begins an hour or two before the recipient's surgery is started

- Wet ischemia time (time from cessation of circulation to removal of organ and its placement in cold storage) should not exceed 30 mins.
- Transplanted kidney is placed in the R or L lower quadrant of the abdomen in an extraperitoneal position. On examination, the transplant is easily palpable.
- The transplant renal a is anastomosed to the Epsilateral internal or external iliac a, the renal v to internal or external iliac v and the transplant ureter to the bladder.

- Generally a single kidney is transplanted.

- When small, paediatric or older cadaveric donor kidneys with age-related loss of renal fxn are transplanted, both kidneys from the donor might be placed in a single recipient to provide adequate fxnal renal mass.
- Living donor transplants fxn immediately after transplant, +/- 30% of cadaveric transplants have delayed graft fxn because of more prolonged ischaemic cold preservation. These pts need continued dialysis support until the kidney starts to fxn.


original kidney
original kidney
transplanted kidney
bladder


Donor kidney
Renal artery
Renal vein
Right iliac artery
Ureter
Right iliac vein
Bladder
A.D.A.M.

Types of Donors

- While the demand for kidneys continues to climb, currently, all transplanted kidneys only come from three sources:

1. **Deceased (or Cadaveric) Donor:** This is a kidney which comes from a person who has just died and the family has given permission for the kidneys to be donated for transplant.

- **2. Living Related Donor: ** A kidney which comes from a blood relative such as a parent, brother or sister.

Points to remember about related living donation:

- You have much more control over the timing of the transplant with a living donation. This may allow the transplant to occur before the recipient requires dialysis.
- Kidneys from close relatives (siblings, parents) tend to be better matches because of blood and antigen compatibility. This means there is less chance for rejection of the kidney, and the number and/or dose of anti-rejection medications which need to be taken may be lower.
- Waiting time is reduced. After the medical evaluation for health and compatibility, a transplant can take place almost immediately – unless the donor has medical issues which need to be resolved
- Living related donors have a reduced need for temporary dialysis after the transplant than with a deceased kidney donation.
- For those with genetic diseases, like PKD, other family members are often affected as well, making living related donation more difficult.

3. Living Unrelated Donor: A donated kidney from someone not related to the person who needs a transplant such as a spouse or friend.

Points to remember about unrelated living donation:

- You have much more control over the timing of the transplant with a living donation.
- Waiting time is reduced. After the medical evaluation for health and compatibility, a transplant can take place almost immediately – unless the donor has medical issues which need to be resolved.
- The need for temporary dialysis is less than with that of a deceased donor transplant.
- Since donor and recipient are not related, genetic factors usually are not problems.

BLOOD TYPE COMPATIBILITY CHART

If you have blood type...	You can normally receive a kidney from a donor with the blood type:	You can normally donate a kidney from a donor with the blood type:
O	O	O, A, B, AB
A	A, O	A, AB
B	B, O	B, AB
AB	O, A, B, AB	AB

Morbidity

- Infection (most common cause of M&M in first year post transplantation) and graft failure occur.
- HT occurs in 75-85% of all renal transplant recipients.
- Hyperlipidaemia 60%
- CVS disease 15.8 – 23%
- DM 16.9 – 19.9% (more likely to be present before transplantation and new onset DM after transplantation is related to corticosteroid use.)
- Osteoporosis 60%
- Malignant neoplasm 14% - related to the degree of immunosupression.

Advantages of kidney transplant compared with dialysis:

- Reverses many of the pathophysiologic changes associated with renal failure
- Eliminates the dependence on dialysis
- Less expensive than dialysis after the 1st year

Kidney Transplantation
Recipient Selection

- Candidacy determined by a variety of medical and psychosocial factors that vary among transplant centers

Contraindications to transplantation:

- Disseminated malignancies
- Cardiac disease
- Chronic respiratory failure
- Extensive vascular disease
- Chronic infection

Kidney Transplantation
Histocompatability Studies

- Purpose of testing is to identify the HLA antigens for both donors and potential recipients
- The pretransplantation workup of a potential donor includes testing for CMV, HSV, EBV, HIV, Hep A, B, C, D + E and HTLV type 1.

Kidney Transplantation
Donor Sources

- Compatible blood type cadaver donors
- Blood relatives
- Emotionally related living donors
- Altruistic(unselfish) living donors
- In general, donors must be:
- Healthy
- Free from disease, infection or injury that affects the kidney
- Usually of the same or a compatible blood type.
- Willing (ready) to give their kidney free from any mental, physical,

Kidney Transplantation
Kidney Transplant Recipient

Transplanted kidney

- Usually placed extraperitoneally in the iliac fossa
- Right iliac fossa is preferred

Before incision:

- Urinary catheter placed into bladder
- Antibiotic solution instilled
  - Distends the bladder
  - Decreases risk of infection

Nursing Management Preoperative Care

- Emotional and physical preparation
- Immunosuppressive drugs
- ECG
- Chest x-ray
- Laboratory

Nursing Management
Postoperative Care

Live donor

- Care is similar to laparoscopic nephrectomy
- Close monitoring of renal function

Recipient

- Maintenance of fluid and electrolyte balance is 1st priority

Kidney Transplantation
Complications

Rejection

- Hyper acute (antibody-mediated, humoral) rejection
  - Occurs minutes to hours after transplantation
- Acute rejection
- Occurs days to months after Transplantation
- Chronic rejection
  - Process that occurs over months or years and is irreversible

Kidney Transplantation
Complications

Infection

- Most common infections observed in the 1st month:
  - Pneumonia
  - Wound infections
  - IV line and drain infections
- Fungal infections
- Viral infections
  - CMV
  - Epstein-Barr virus
  - Herpes simplex virus

Cardiovascular disease

- Transplant recipients have ↑ incidence of atherosclerotic vascular disease

Malignancies

- Primary cause is immunosuppressive therapy

Recurrence (return) of original renal disease

Glomerulonephritis

- IgA nephropathy
- Diabetes mellitus

Corticosteroid-related complications

- Aseptic necrosis of the hips, knees, and other joints
- Peptic ulcer disease
- Glucose intolerance and diabetes
- Hyperlipidemia
- Cataracts
- Increased incidence of infections and malignancies

Surgical Complications affecting Allografts

- Usual postop generic complications: pneumonia, wound infection, ileus, bleeding and venous thromboembolism.
- 1. ***Acute occlusion of transplant renal a or v.***

  Occurs in first transplant week (0.5-8%). Causes oligoanuria and ARF. With renal vein thrombosis, there is graft tenderness, dark haematuria and decreased urine volume.

  Diagnosis is via doppler U/S or radioisotope scanning to demonstrate lack of blood flow.

  Rx is surgery.

- 2. ***Peritransplant haematoma***

  Early postop complication or in setting of perioperative anticoagulation (2-3%)

  Severe pain over allograft, decreased Hb or Hct, increased serum creatinine.

  Recurrent increased K due to lysis of RBC in haematoma. Diagnosis via CT.

  Rx is surgical and usually leads to allograft nephrectomy.

- 3. ***Urinary Leak***

  First transplant month. (2-5%)

  Presents with urine extravasation and ARF, fever, pain and distended abdomen.

  Diagnosis is via U/S which demonstrates a peritransplant fluid collection or via radioisotope scanning.

  Treatment is foley catheter insertion and surgery.

- 4. ***Lymphocoele***

  Occurs within the first 3 post transplant months and is due to lymph leaking from severed lymphatics (5-15%).

  Large collections cause pain, ARF, urinary frequency, ipsilateral lower extremity oedema, occasionally iliac vein thrombosis or PE. Most of the s&s are due to pressure effects. Diagnosis is via U/S.

- Treatment is percutaneous drainage.

- 5. ***Obstructive Uropathy***

  Occurs in early post transplant period (3-6%). The commonest causes are extrinsic compression of the ureter by a lymphocoele or due to a technical problem with the ureteric anastomosis to the bladder.

  Diagnosis is best achieved via U/S demonstrating hydronephrosis.

  Treatment is surgical.

6. ***Renal artery stenosis***

  Late presentation.

  Pts present with uncontrolled HT, allograft dysfunction and peripheral oedema.

  Diagnosis is via U/S or MRA.

Mortality

- Survival of pts after transplantation from a liver donor is 98% at 1 yr and 91% @ 5 yrs.
- Survival of pts who receive cadaveric organs is 95% @ 1 yr and 81% @ 5 yrs.

Long Term Complications in Renal Transplantation

- Infections
- Malignancy
- Bone Disease
- Cardiovascular Disease ,hypertention
- Post Transplant D.M
- Post Transplant Erythrocytosis
- Chronic Rejection

GIT Problems

- Abnormalities in LFTs occur frequently.
- The clinical presentation of acute cholecystitis may be blunted by immunosuppressive Rx (esp. by corticosteroid use).
- The incidence and severity of acute pancreatitis is increased.

Neurologic + Psychiatric Disorders

- Cyclosporine and tacrolimus cause similar neurological S/Es (headache, insomnia, tremors, parasthesias, cramp of extremities). The S/Es are dose + blood level related.
- Opportunistic CNS infections occur in 5-10% of renal transplant recipients.
- Meningitis: Listeria monocytogenes, cryptococcus + TB.
- Post transplant lymphoma commonly involves CNS.
- Depression and suicide are more prevalent.
- Remember steroid psychosis.

Haematological Disorders

- Anaemia, leukopaenia, thrombocytopaenia alone or in combination is common. Often due to drugs.

- HUS: anaemia, thrombocytopaenia, ARF, increased LDH, Decreased haptoglobin, schistocytes on peripheral blood smear. HUS in renal transplant pts has been associated with cyclosporine or tacrolimus Rx, acute vascular rejection + CMV infection.

Musculoskeletal Disorders

- Corticosteroids, and to a lesser extent cyclosporine + tacrolimus predispose to osteoporosis.
- Cyclosporine + tacrolimus cause hyperuricaemia which predisposes to gout.
- NSAIDs can worsen renal fxn + colchicine can interact with cyclosporin causing raised LFTs, leukopaenia, proximal muscle weakness and rhabdomyolysis
- With pts on azothioprine, the use of allopurinol can cause severe bone marrow suppression unless the azothioprine dose is reduced.

Electrolyte Abnormalities

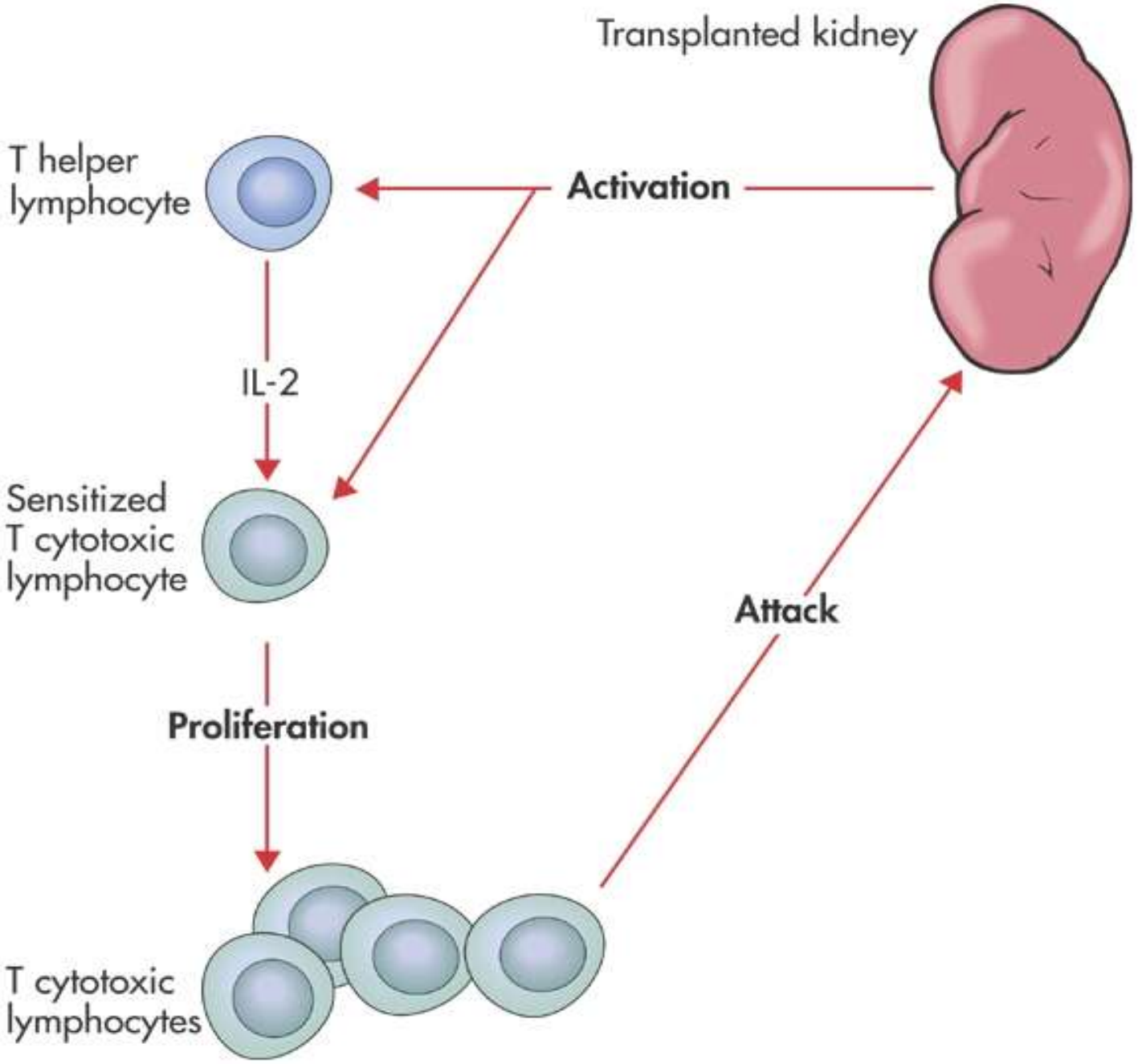
- Cyclosporin + tacrolimus cause hyperkalaemia (decreased K excretion in urine) and hypomagnesemia (increased Mg excretion in urine).
- Non anion gap metabolic acidosis can be due to tubular dysfunction due to acute or chronic rejection of kidney transplant.

New Onset DM

- De nova DM occurs in 5-20% of renal transplant recipients.
- Contributing to this complication are corticosteroids, cyclosporine + tacrolimus.

Acute Rejection

- Indirect pathway: soluble donor Ag that is processed by recipient APC + then presented to recipient T-cells in the groves of MHC I + II molecules.
- Direct pathway: donor APC presenting both class I + class II epitopes to recipient T cells.
- Hyperacute rejection occurs immediately in the operating room, when the graft becomes mottled and cyanotic. This type of rejection is due to unrecognised compatibility of blood groups A, AB, B, and O (ABO) or a positive T-cell crossmatch.



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Chronic Rejection

- Usually apparent from 3 months onwards and detected clinically by gradual deteriation in graft fxn.
- Factors associated with chronic rejection are both immunological + non-immunological.

Kidney Transplantation
Immunosuppressive Therapy

Goals:

- Adequately suppress the immune response
- Maintain sufficient immunity to prevent overwhelming infection

Medications:

- Cyclosporine
- Prednisone
- Prografin FK 506 (Tacrolimus)
- Mycophenolate Mofetil (CellCept)

Immunosuppressive Therapy

- Renal transplant pts require lifelong immunosuppression to prevent rejection.
- Current “triple” regimes include cyclosporine-microemulsion or tacrolimus, mycophenolate mofetil or azathiopine and corticosteroids.
- Sicrolimus became available in 1994 and has become incorporated into protocols.

- **Cyclosporine**: inhibits both cellular and humoral immunity by binding to cyclophilins which block cytokine transcription and production resulting in the inhibition of lymphocyte signal transduction.

  Results in potent immunosuppression of helper T cells, without affecting suppressor T cells.

Azathioprine: antimetabolite derivative of 6-mercatopurine. Inhibits DNA + RNA synthesis, resulting in suppression of lymphocyte proliferation.

- **Corticosteroids**: wide range of effects on immune system specifically the T lymphocytes. Because of long-term toxic effects, every effort is made to minimise the dosage of glucocorticoids.

- **Tacrolimus**: newer macrolide compound that binds to lymphocyte proteins and inhibits cytokine synthesis. Used as either primary or rescue therapy for allograft rejection.

- Immunosuppressant minimisation protocols are becoming more popular.

- Triple Rx for 3-12 months after transplantation followed by withdrawal of 1 of the 3 drugs to minimise long term side effects (most commonly withdrawn drug is corticosteroid).

- Antilymphocyte Abs are also widely used in the pts (polyclonal & monoclonal Abs are available).

- The initial Rx of rejection involves the administration of IVI corticosteroids (methylpred 250-1000mg daily for 3/7 or dexamethasone 100mg daily for 3/7).

Take Home Massage

- 1. If a transplant pt presents the ED, always consider the possibility of organ rejection, infection or drug toxicity.
- 2. The signs + symptoms of medical problems are often subtle.
- 3. Inability of the pt to not take their oral immunosuppressants even for one day should be considered an emergency.
- 4. When prescribing in the ED, always be careful to avoid drug interactions + toxicity.