# ANAESTHESIA FOR RENAL TRANSPLANTATION

# INTRODUCTION

- In 1954, Dr Joseph Murray performed the first successful renal transplantation on identical twins
- Organ survival rate has increased significantly, mainly due to improvements in immunosuppressant therapy
- The 5 year survival rate in patients with transplanted kidneys is 70% compared to 30% in patients on hemodialysis

# INTRODUCTION

- Even recipients of marginal kidney transplants enjoy higher survival and quality of life compared to patients who stayed on dialysis
- Marginal transplants are considered to be grafts from older donors, HTN/DM, non-heart-beating cadaver donors and grafts with prolonged cold preservation time.

Lemmens HLM (2004) Kidney transplantation: recent developments and recommendations for anesthetic management. Anesthesiol Clin North America 22: 651-662. . Kapoor HS, Kaur R, Kaur H (2007) Anaesthesia for renal transplant surgery. Acta Anaesthesiol Scand 51: 1354-136

# INTRODUCTION

- Minority of patients are selected for kidney transplantation after exhaustive evaluation.
- Of these, most transplantation occurs in patients receiving donated kidneys from living related donors (23 per million people) compared to patients receiving deceased donor transplantation (2.5 per million people)

# INTRODUCTION

- Median wait time - 2.3 years .
- During this period, patients are thoroughly evaluated and medically optimized. Medical optimization is one of the requirements to remain on the transplantation list

ThDrury N (2010) Anaesthesia for renal Transplantation. Anaesthesia tutorial of the week 174: 12 e Organ Procurement Transplantation network.
United States renal data system, 2011 USRDS annual data report Vol 2. National Institutes of Health, National Institutes of Diabetes and Digestive and Kidney Diseases, Division of Kidney, Urologic and Hematologic Diseases– accessed 11/20/2012

# CHRONIC RENAL FAILURE

- Chronic renal failure (CRF) and end-stage renal disease (ESRD) are functional diagnoses characterised by a progressive decrease in glomerular filtration rate (GFR).

- CRF occurs when GFR is reduced to 10% of normal function (20 ml min–1) and ESRD when GFR falls below 5% (10 ml min–1).

- Diabetes mellitus (31%),
- Chronic glomerulonephritis (28%),
- Cystic kidney disease (12%),
- Hypertension (9%),
- Interstitial nephritis (3%)
- And other diseases such as obstructive uropathy, lupus nephritis and human immunodeficiency virus

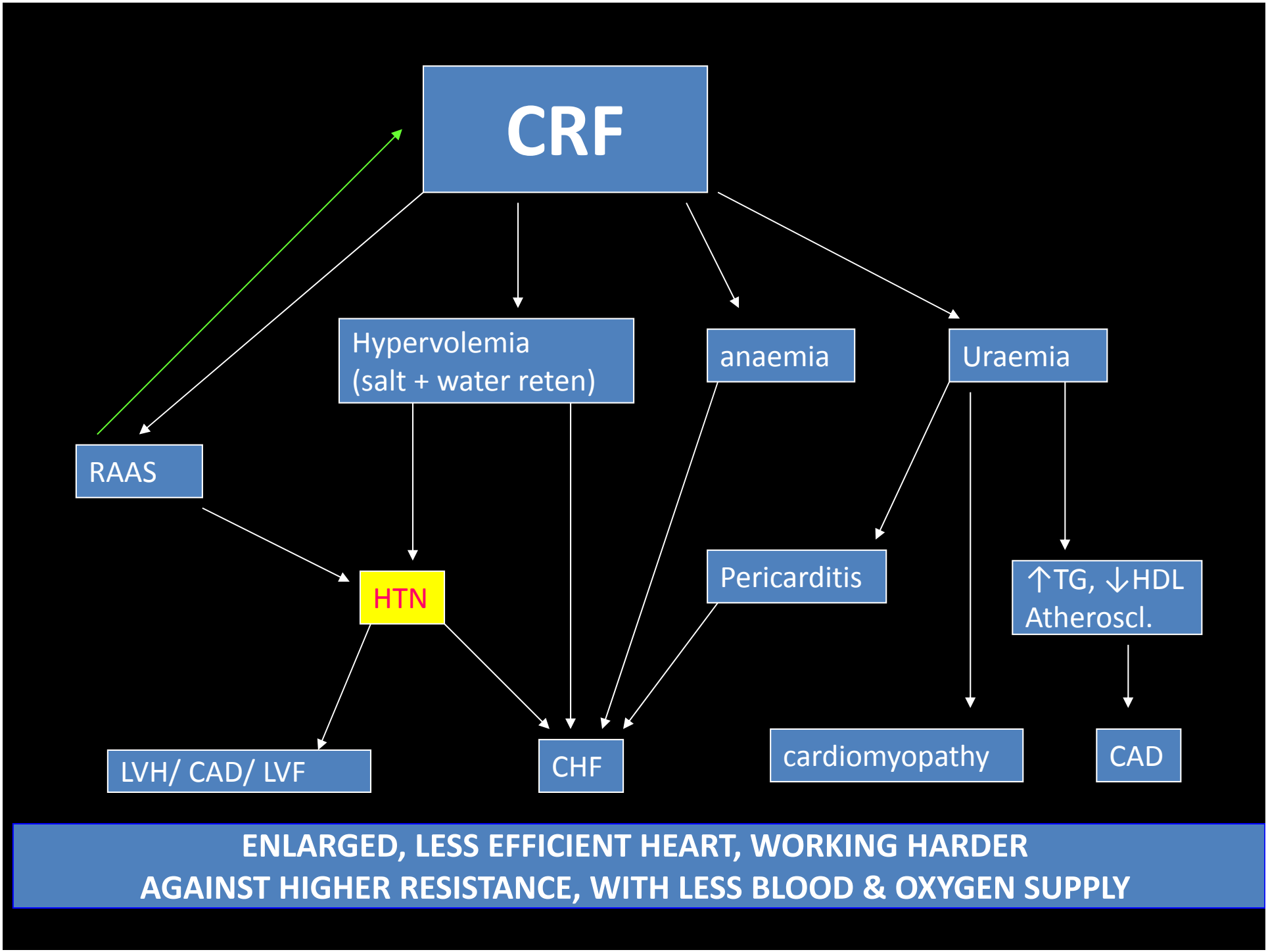
# CLASSIFICATION OF CKD

| STAGE | GFR ( ml/min/1.73m2 | KIDNEY FUNCTION |
|---|---|---|
| STAGE 1 | >90 | NORMAL |
| STAGE 2 | 60-89 | MILD IMPAIRMENT |
| STAGE 3 | 30-59 | MODERATE IMPAIRMENT |
| STAGE 4 | 15-29 | SEVERE IMPAIRMENT |
| STAGE 5 | <15 | END STAGE RENAL DISEASE |

# PATHOPHYSIOLOGICAL CONSEQUENCES OF CHRONIC RENAL FAILURE

# CARDIOVASCULAR SYSTEM

- IHD leading cause of morbidity and mortality
- CAD- 25% incidence in CKD patients
- Hypertension 80% (Na, H2O retention, altered RAAS )
- Accelerated atherosclerosis (decreased plasma triglyceride clearance, HTN, fluid overload →LVH & failure.↑ plasma TG concentrations is a defect in lipoprotein lipase activity and reduced lipolysis)
- ↑ metastatic calcific valvular heart lesions( Aortic 55%→ aortic stenosis 13%, MV 40%→mitral stenosis 11%)
- Uraemic pericarditis


CRF
Hypervolemia
(salt + water reten)
anaemia
Uraemia
RAAS
HTN
Pericarditis
↑TG, ↓HDL
Atheroscl.
LVH/ CAD/ LVF
CHF
cardiomyopathy
CAD
ENLARGED, LESS EFFICIENT HEART, WORKING HARDER
AGAINST HIGHER RESISTANCE, WITH LESS BLOOD & OXYGEN SUPPLY

# ELECTROLYTE ABNORMALITIES

- Hyponatremia, hypocalcemia, , hyperkalemia hyperchloremia, hypermagnesemia ( muscle weakness, potentiates NDMR)
- Severity related to the timing of last dialysis session

# ELECTROLYTE ABNORMALITIES

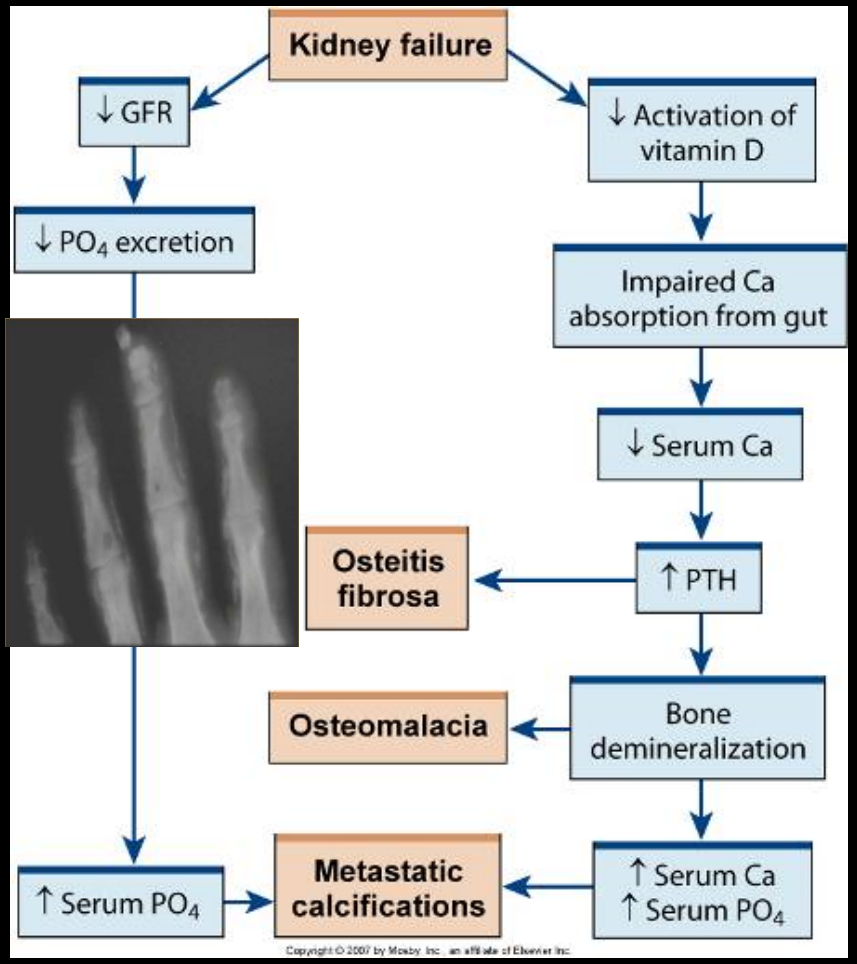
- Perioperative hyperkalemia most concerning. Patients are usually chronically hyperkalemic.Periodic checks to detect hyperkalemia
- ECG changes may not be present until much higher values are reached (peaked t-waves, flat P waves, increased PR interval or widening QRS)
- Rx- insulin, sodium bicarbonate, and beta-agonist if the potassium is greater than 5.5 meq/L
- Routine preoperative electrolyte evaluation should be obtained prior to surgery

# METABOLIC ACIDOSIS

- **Usually chronic**
  - Inability to excrete acid load
  - Initially non anion gap acidosis then later high anion gap metabolic acidosis(due to retained sulfates and phosphates).
  - Corrected by Hemodialysis

# CALCIUM AND PHOSPHATE METABOLISM

- Patients usually tolerate hypocalcaemia remarkably well
- Oral calcitriol is prescribed and calcium carbonate is used both as an intestinal phosphate binder and a source of calcium



# HEMATOLOGICAL ABNORMALITIES

- **Anaemia – normocytic normochromic**

✓ **due to**

- ↓ EPO
- BM depression
- ↓ survival of RBC
- Nutritional deficiency of iron ,folates
- ↑ bleeding
- ↑ PTH – BM – Fibrous tissue

✓ **Treatment**

- Supplement iron + FA
- Introduction in 1989 of synthetic erythropoietin

✓ **leads to**

- ↑ C.O.
- ↓ blood viscosity
- ↑ 2,3 DPG
- Acidosis (shifts ODC → right)

***Improved tissue oxygenation and anemia is well tolerated***

# COAGULOPATHY

- Platelet count is wnl **platelet activity is deranged with decreased adhesiveness and aggregation**
- Inadequate vascular endothelial release of a von willebrand factor/factorviii complex which binds to and activates platelets
- Tendency to excessive bleeding is present
- Standard tests of coagulation are normal (i.E pt,appt , inr)

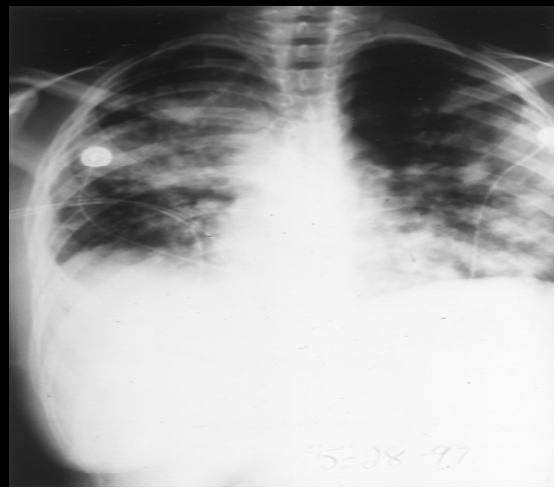
# COAGULOPATHY

Thrombocytopathy is not corrected by platelet transfusion but by

1. Dialysis
2. Cryoprecipitate or Desmopressin (which enhances release of von Willebrand factor). DDAVP 0.3 µg kg–1 is effective within 1–2 h but has a duration of only 6–8 h
3. Intravenous conjugated oestrogens - slower onset but a longer duration of action (5–7 days )

# PULMONARY ABNORMALITIES

- ✓ Volume overload → pulm.Congestion → hypoxemia and hypercarbia
- ✓ Pleural effusion →poor compliance
- ✓ Hyperventilation – chronic metabolic acidosis
- ✓ Patients undergoing peritoneal dialysis intraperitoneal fluid results in diaphragmatic splinting → basal lung atelectasis → arterio-venous shunting
- ✓ Improved by dialysis



# GIT

- N, V, anorexia, hiccups
- Delayed gastric emptying – risk of regurgitation and aspiration
- Diabetes autonomic neuropathy
- Preoperative treatment with a Histamine2 blocker and metoclopramide are recommended

# CNS

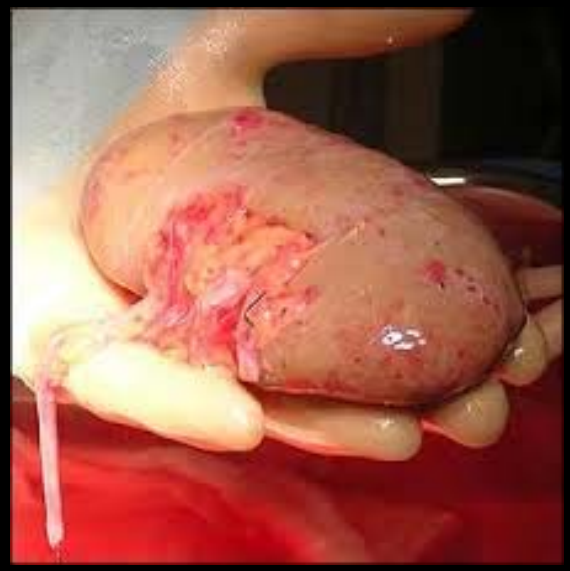
- Memory loss, drowsiness, myoclonus, seizure, stupor, coma
- Peripheral & autonomic neuropathy- risk of delayed gastric emptying, postural hypotension and silent myocardial ischaemia
- Both dialysis and renal transplantation may improve the neuropathy
- Dialysis dementia related to aluminium toxicity
- Dialysis disequilibrium syndrome- associated with rapid initial reduction in plasma urea concentrations at the start of dialysis

# Immune

- Inhibition of cell-mediated immunity and humoral defence mechanisms occurs, with little improvement following dialysis
- Increased production of pro-inflammatory cytokines
- Superficial infections common in fistula ,catheter sites
- Wound healing is poor

# ANAESTHESIA FOR KIDNEY TRANSPLANT PATIENTS (KTP)

- Donor & Nephrectomy
  - Living donor
  - Cadaveric donor
- Preservation of harvested kidney
- Transplant recipient
  - why is AV fistula created?
  - anaesthetic management
- Immunosupressants and KTP
- Paediatric  kidney transplantation
- Transplant patients for non transplant surgery



# DONOR AND NEPHRECTOMY

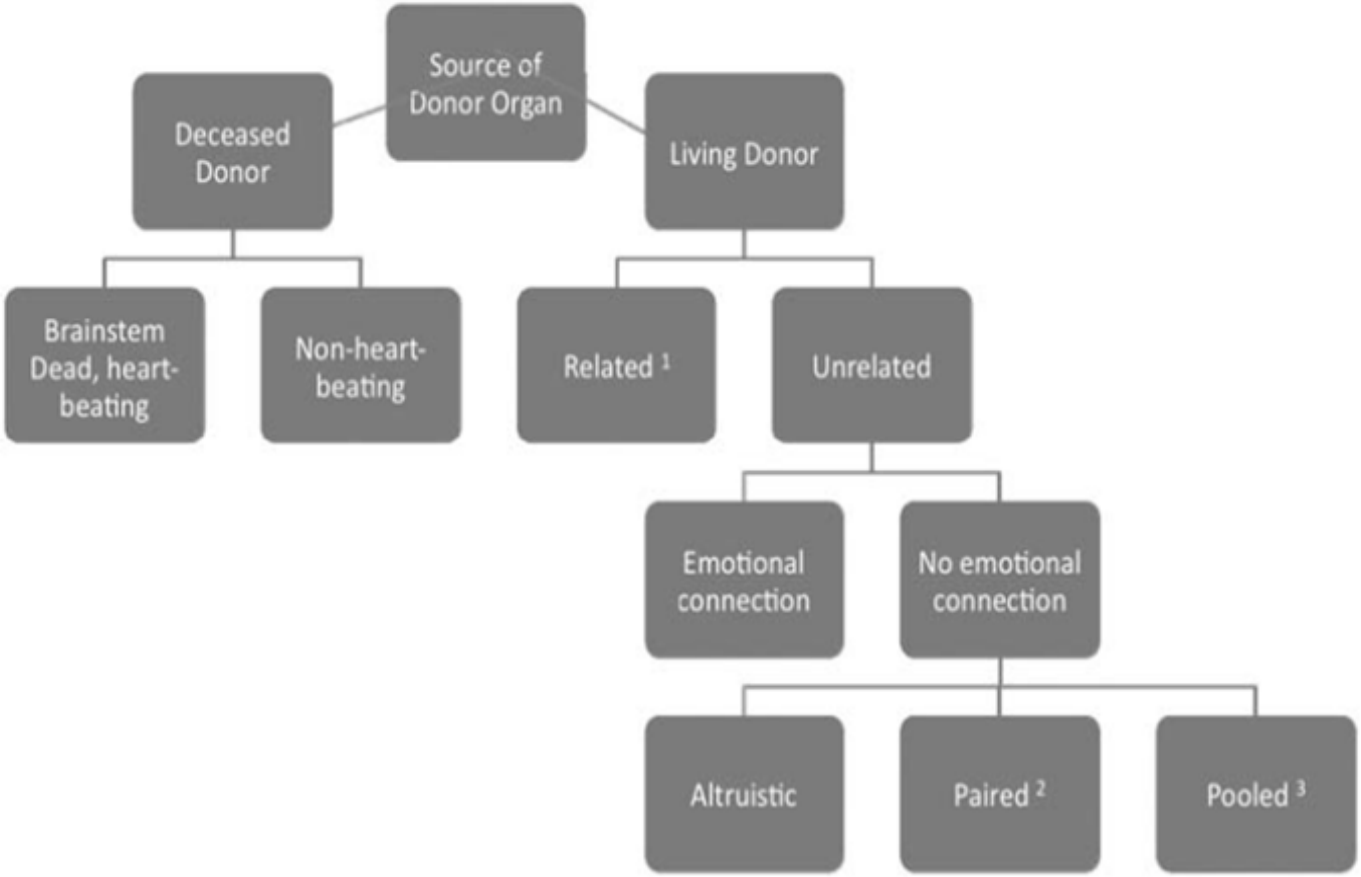



**Fig 1** Classification of renal transplants by donor organ source. (1) Related: the donor is genetically related to the recipient (parent, child, sibling, half-sibling, aunt, uncle, niece, nephew, first cousin). (2) Paired: when a donor agrees to give one of their healthy kidneys to a known recipient, the donor and recipient will be assessed to find out if they are suitable for an exchange. In some cases, the donor and recipients' blood groups or tissue types are mismatched or incompatible. If so, as a pair, they can be put forward for 'paired donation', where they will be matched up with another donor and recipient in the same situation. (3) Pooled: occasionally, more than two donors and two recipients will be involved in a swap. Each recipient gains from a transplant that they would not otherwise have had. The donors might not have given their kidney to the person they know, but that person will have received a kidney from one of the other pooled donors.

# Advantages of live donation

- Elective procedure
- Timing of an operation flexible
- Kidneys transplanted from living donors show an increased graft survival

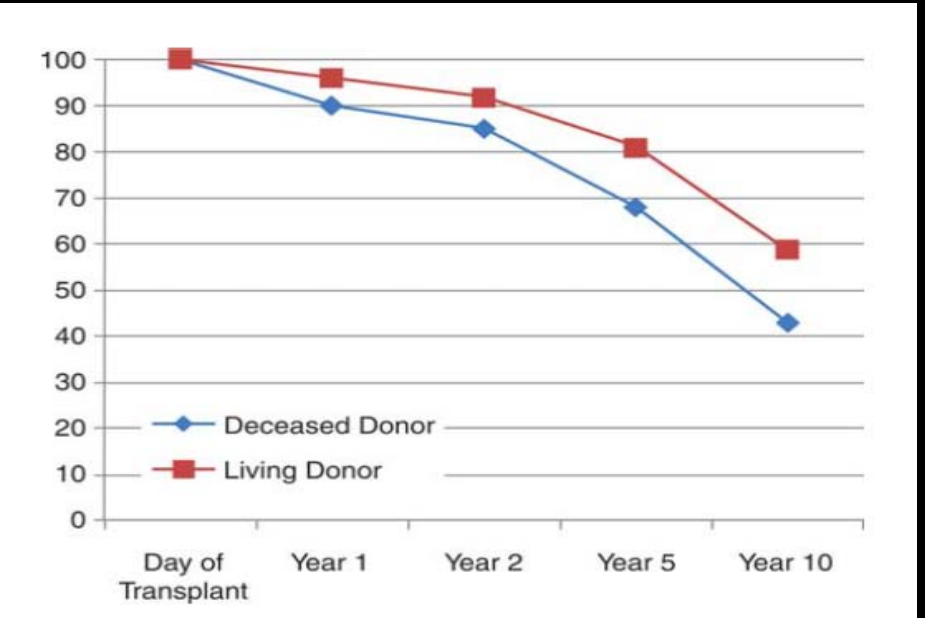



Fig 3 Graft survival after living-donor *vs* deceased-donor renal transplant. Data from NKUDIC.[4]

**Anaesthesia for living donor renal transplant nephrectomy Continuing Education in Anaesthesia, Critical Care & Pain j Volume 12 Number 6 2012**

# Evaluation of potential living donors

- Carefully evaluated **both psychologically and medically**.
- Psychological assessment -to ensure the donor gives fully informed consent and is not being coerced
- Donor must be fit for surgery ,no disease state that increases the risk of a poor outcome for either the donor or the recipient.
- Extremes of age not contraindications to donation(individuals <18 yrs never considered as potential living kidney donors, biological age is considered more important than chronological age i.E donors as old as 70–80 yr been successfully recruited)

# Evaluation of potential living donors

- ASA 1 and 2
- Full preoperative asessment - ABO blood group, tissue typing, leucocyte crossmatch ,History, GPE,INV – CBC , coag profile RFT , FBS , viral markers to rule out HBsAg , HCV, CMV, lipid profile, urine R/M & C/S , cxray , ECG
- Donors are classified as 'complicated' -if they are older, with comorbidities obese (BMI >30), refuse blood products, have vascular abnormalities (e.g. multiple renal arteries), or are required to have a right nephrectomy (which is surgically more demanding).

# ANAESTHESIA FOR LDN-KEY MESSAGES

- Careful positioning, prevent pressure damages
- Wide bore i/v access
- Non invasive monitoring
- *Keep renal perfusion pressure/ MAP at preop values*
- Positive fluid balance and preloading post induction
- Heparin before application of vascular clamps
- U.O 1-2ml/kg/hr (mannitol 0.5g/kg
- Avoid hypothermia

**General anaesthesia is the only practical option for laparoscopic LDN as it involves a pneumoperitoneum and a head-down position**

**Surgical techniques used for Living Donor Nephrectomy (LDN)**

1. **open**
2. **laparoscopic LDN**
3. **hand assisted laparoscopic LDN**
4. **robot assisted laparoscopic LDN**

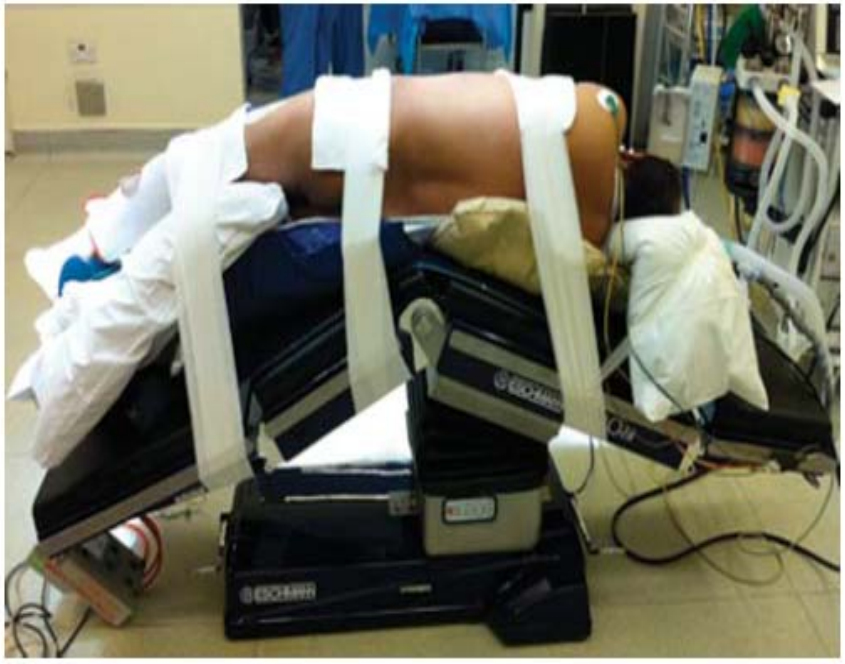


Fig 4 Near full lateral position with extension break at the waist.

# LAPAROSCOPIC VS OPEN LDN

Advantages

- Reduced blood loss,
- Decreased tissue trauma
- Lower analgesic requirements
- Faster resumption of food intake
- Shorter hospitalization, quicker return to work
- Better postoperative cosmetic appearance

Disadvantages

- Technically more demanding
- Twice as long as an open procedure

# POSTOPERATIVE CONSIDERATIONS

- Postoperative pain -In laparoscopic LDN, pain is due to port pain, abdominal incision (to extract kidney), diaphragmatic irritation, ureteric colic, urinary catheter discomfort
- Multimodal analgesia- PCA with fentanyl, epidural analgesia , TAP block
- Avoid NSAID's

# POSTOPERATIVE CONSIDERATIONS

- Perioperative mortality- 0.03-0.06%
- Causes – PE, hepatitis, MI, arrythmias
- Morbidity- 20%,  1-2% significant
- Transient increase in serum creatinine level ,usually return to normal within 1 month
- ***Remaining kidney tends to hypertrophy, long-term renal function remains at 75%. No adverse affect on long-term mortality***

# CADAVERIC DONOR NEPHRECTOMY

- Donation after circulatory death  (DCD)
- Donation after brain death (DBD)

# Cadaveric donors- **Donation after Circulatory Death (DCD)**

- Donation after cardiac arrest or non-heart beating donation
- Two broad categories -

  1.Uncontrolled DCD -when death occurs suddenly and unexpectedly.

  2. Controlled DCD - when death occurs after the planned withdrawal of life-sustaining treatment.
- Upto 1976 majority of organs were retrieved from dcd
- Drawback – increased warm ischemia time

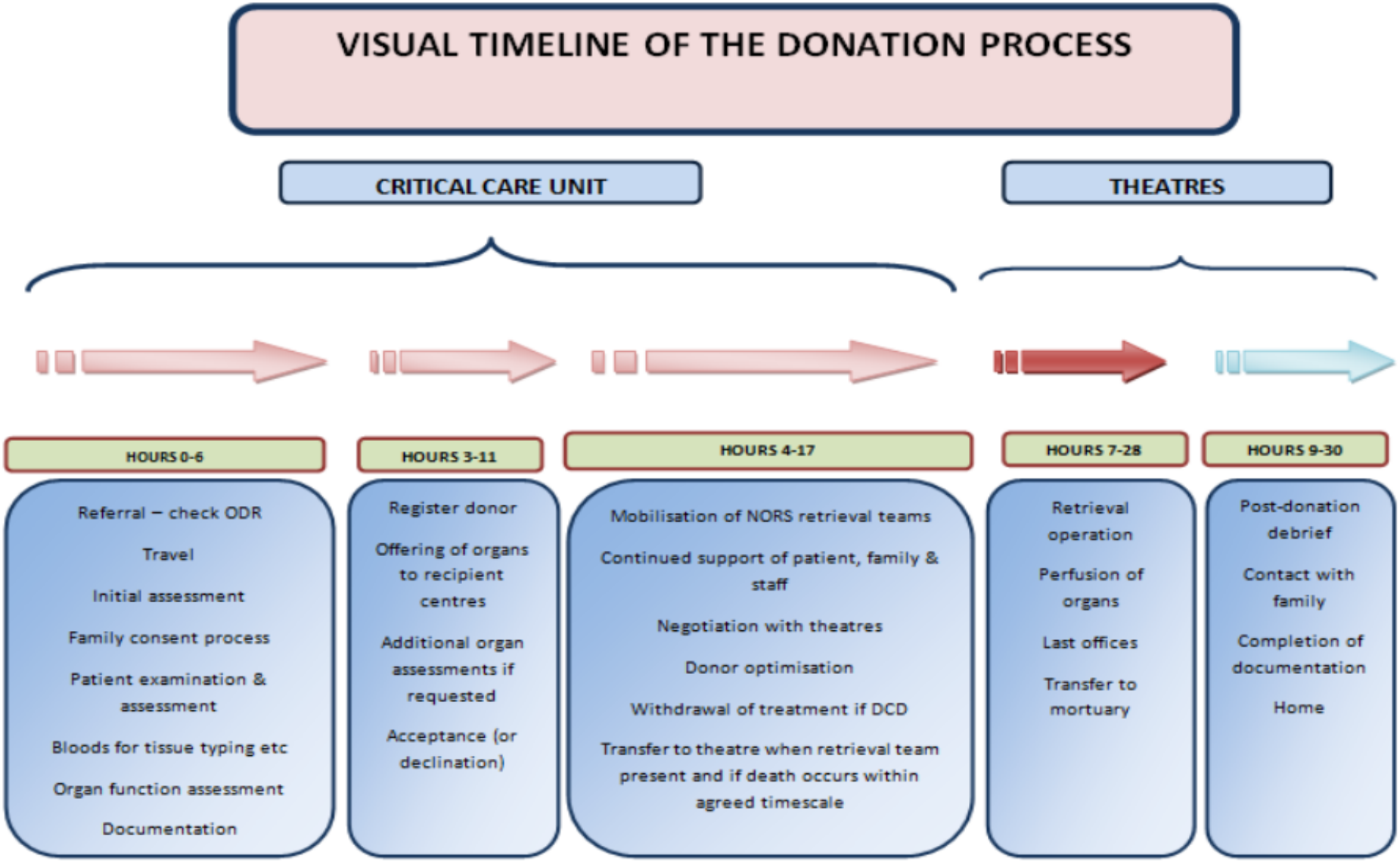
**Table 1**: Modified Maastrict Classification of DCD

| Category | Circumstances | Controlled/Uncontrolled | Location of care |
|---|---|---|---|
| Category 1 | Dead on arrival | Uncontrolled | ED in a transplant centre |
| Category 2 | Unsuccessful resuscitation | Uncontrolled | ED in a transplant centre |
| Category 3 | Anticipated cardiac arrest | Controlled | ICU and ED in transplant and non-transplant centres |
| Category 4 | Cardiac arrest in a brain-dead donor | Controlled | ICU and ED in transplant and non-transplant centres |
| Category 5 | Unexpected arrest in ICU patient | Uncontrolled | ICU in a transplant centre |

# CADAVERIC DONOR- DBD

**Donation after Brain Death**

- Donation after brain death, previously known as heart beating organ donation or donation after brain stem death, is retrieval of organs after confirmation of death using brain stem death testing criteria
- After 1976, most transplant centres switched rapidly to transplantation of organs from DBD donors




There are many different steps and staff groups involved in achieving successful organ donation and transplantation following death

# CADAVERIC DONOR DBD

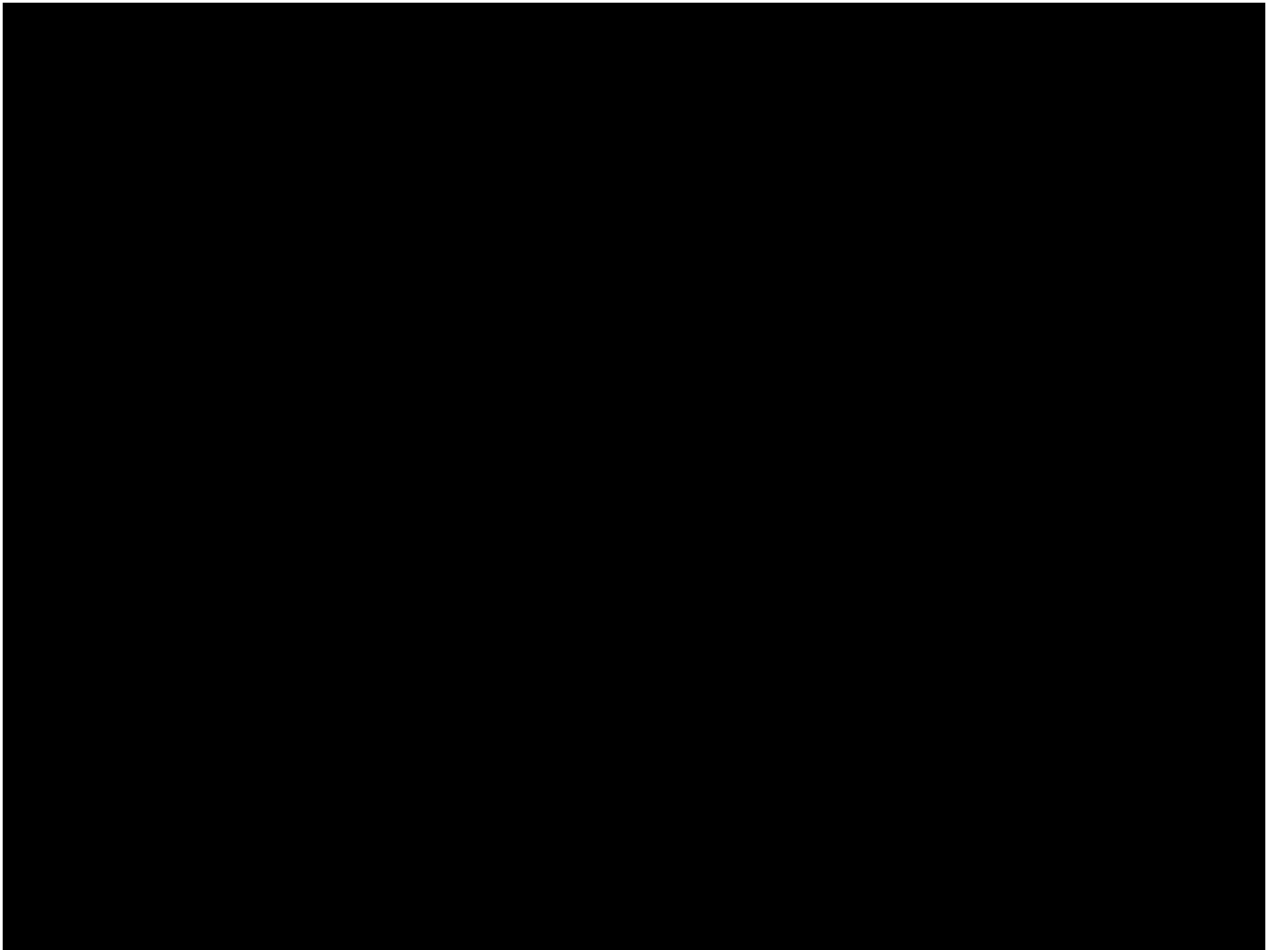
Goal of management

1. achieve physiological stability to ensure that organs retrieved are in the best possible condition for transplantation
2. Invasive monitoring
3. Close medical attention
4. Donors should be cared for in the intensive care unit

Anaesthesia is not required for brain dead patients, these procedures can be associated with significant blood loss and marked haemodynamic instability and are best managed by a senior anaesthetist

## Management of the brain stem dead donor

| | Targets | Monitoring | Management |
|---|---|---|---|
| **Cardiovascular** | HR 60—120 bpm<br>SBP >100 mmHg<br>MAP ≥70 mmHg<br>CVP 6—10 mmHg<br>PAWP 6—10 mmHg<br>CI ≥2.4 l/min/$m^2$<br>SVR 800—1200 dynes/s/$cm^5$<br>$SvO_2$ >60% | ECG, Arterial and CVP line. Flow monitoring<br>±PA catheter<br>±TTE[a]<br>±coronary Angiography[a] | Short acting agents for initial hypertension<br>Isoprenaline for ↓HR (atropine ineffective)<br>Restore circulating volume (avoid excess volume)<br>Minimize catecholamine dose (high doses associated with myocardial damage)<br>Vasopressin (see below)<br>Consider hormonal therapy[a] |
| **Respiratory** | $P_aO_2$ ≥8 kPa<br>$SpO_2$ ≥92%<br>$P_{AW}P$ ≤30 cm $H_2O$ | CXR, $SpO_2$,<br>Serial ABG<br>± Bronchoscopy[a] | $V_t$ 5—8 ml/kg<br>PEEP 5 cm $H_2O$<br>Head up positioning<br>Recruitment manoeuvres<br>Limit excess fluid — diuretics if overload |
| **Renal & Electrolyte** | Urine 0.5—2.5 ml/kg/hr<br>Normal electrolyte conc. | Urine output<br>Serum electrolytes | Maintenance fluids<br>If urine output > 4ml/kg/h then DDAVP (1—2 μg) or vasopressin infusion |
| **Other** | | | Active warming if temp <35 °C<br>Maintain feeding/glucose |
| | Temperature >35 °C<br>Blood glucose 4—8 mmol/l<br>Infection free | Core temperature<br>Full blood count<br>Coagulation screen | Manage in critical care environment<br>Treat coagulopathy ± anaemia<br>Stop unnecessary drugs<br>Treat identified infections<br>Continue thromboprophylaxis |
| **Hormonal** | Pathophysiological changes during brain stem death result in pituitary failure.<br>Current evidence suggests that hormonal therapy **may** be beneficial<br>• Methylprednisolone: 15 mg/kg bolus<br>• Vasopressin: 1 IU bolus then 0.5—5 IU/h infusion (titrate to SVR 800—1200 dynes/s/$cm^5$) | | |



# Intraoperative management

- Certain guidelines can be summarized as follows: **RULE of 100**
  - Systolic blood pressure greater than 100 mm Hg (mean 70 to 110 mm Hg)
  - $P_{O_2}$ greater than 100 mm Hg
  - Urine output greater than 100 mL/hr (1 to 1.5 mL/kg/hr)
  - Hemoglobin concentration greater than 100 g/L
  - Central venous pressure (CVP) 5-10 cm h20

THE MATCHING PROCESS -Three distinct areas

1.Blood group matching - ABO matching

2. HLA type matching

- Six antigens (MHC), at three loci _ A, B and DR

-six antigen match – best outcome

-immunosuppression ensures favuorable outcome for fully mismatched organs.

3. Testing donor T cells against recipient serum

- final crossmatch

- lymphocytotoxicity cross-match between donor lymphocytes and recipient serum

-If positive _ risk of hyperacute rejection , consider next potential recipient

# Preservation of the Harvested Organ: Warm Ischemia Time

- Preservation of a viable kidney depends on minimizing ischemia time
- Warm ischemia begins when the donor vessels are clamped, and is interrupted when the kidney is perfused with cold preservation solution
- Warm ischemia is particularly deleterious
- Incidence of acute tubular necrosis increases with its duration
- Should not exceed 3- 5 minutes for live donors
- Warm ischemia resumes when the kidney is placed in the recipient, and terminates when the vascular anastomosis is complete and perfusion by the recipient begins

# Preservation of the Harvested Organ - cold Ischemia Time

- During cold ischemia, the kidney is preserved by storing it at **4°C.**
- Ideally, cold ischemia time is 20 – 30 minutes
- Although cold ischemia times greater than 36 hours are associated with poorer results, cold ischemia times of as long as 72 hours have occurred with successful kidney transplants

# COLD STORAGE SOLUTIONS

Oxygen radical scavengers , improve organ storage conditions

- Collins
- Euro-Collins
- Histidin-Tryptophan-Ketogluterat (HTK) –cheaper, commonly used
- Celsior
- Perfadex
- University of Wisconsin (UW)

# ANAESTHESIA FOR RECIPIENT

# RECIPIENT

- According to the recent ESA guidelines (2009) renal transplantation is an intermediate-risk surgical procedure
- Transplant patients are often among the most complex patients that an anesthesiologist may encounter
- Extensive preoperative 'work-up' should be done to identify risk factors but not just for risk stratification but also for the ***development of a tailored perioperative treatment regime***

# PREOPERATIVE ASSESSMENT

- Detailed history and examination
- Evaluation of dialysis (How long? How often? When was the last dialysis? Any diuresis left?)
- Full preoperative assessment - CBC , coag profile, SE, RFT , FBS , lipid profile, urine R/M & C/S
- ECG and chest X-ray
- ABG

# CARDIOVASCULAR EVALUATION

Used in high risk, symptomatic patients

- diagnose active or chronic CAD
- determine the patient's functional status
- optimize therapy prior to renal transplantation

Guidelines published in July 2012 by ACC/AHA:

- "Cardiac Disease Evaluation and Management among Kidney and Liver Transplantation Candidates" - focus on obtaining a

  **1. Thorough history**

  **2. Physical examination to identify any active cardiac condition** *unstable coronary syndrome, severe valvular disease, decompensated heart failure, and significant arrhythmias*.

  **3. Assessment of functional status**

# CARDIOVASCULAR EVALUATION

- Noninvasive stress testing should be considered without active cardiac disease but who have 3 or more risk factors associated with coronary artery diseases (CAD)
  - diabetes mellitus
  -prior cardiovascular disease
  -duration of dialysis greater than 1 year
  -left ventricular hypertrophy
  -age greater than 60 years
  - hypertension
  -dyslipidemia.

- Noninvasive testing used for further risk stratification (dobutamine stress echocardiography versus myocardial perfusion scintigraphy), is at the discretion of the perioperative evaluator

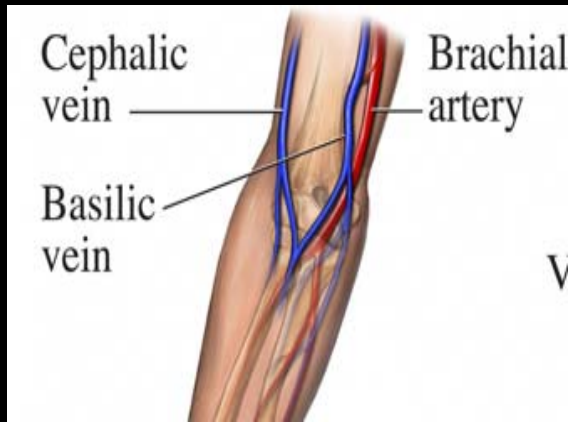
Abbud-Filho M, Adams PL, Alberu J, Cardella C, Chapman J, et al. (2007) A Report of the Lisbon Conference on the Care of the Kidney Transplant Recipient. Transplantation 83: 1-22.

# Patients waiting on the transplant list beyond one year

- Screened annually with 12 lead ECG and resting TTE
- Recipients found to have PAH on TTE should have right heart catheterization to confirm the diagnosis and full evaluation

# Why is AV fistula created????

- Required for long term vascular access for haemodialysis
- Veins of the arms can be cathetrized easily and repeatedly, too low blood flow to support HD
- Peripheral arteries have high blood flow , too small for repeated cathetrization
- **Creation of av fistula produces an arterialized venous channel – which yield combined adv of large diameter and higher blood flow**
- Arteriovenous fistula must be protected
- Wrapped padded palpated at intervals
- Bp cuffs and venous and arterial lines must be placed on opp arm



# HAEMODIALYSIS

- Most RT patients are established on haemodialysis
- Nowadays, preoperative dialysis 24 h before surgery is routine for this patient population
- Important for the management of potassium levels, acid–base status and overall volaemic status
- Preoperative dialysis reduces perioperative mortality and delayed graft function
- Studies show reduced perioperative mortality rate among RT patients from 16% to almost 0%

Anaesthesia for renal transplant: recent developments and recommendations
Zorica jankovic, chunda sri-chandana current anaesthesia & critical care (2008) 19, 247–253

# MONITORING

- Standard ASA monitoring - Five-lead ECG with ST segment analysis , NIBP , pulse oximetry ,capnography
- Invasive BP - restricted for patients with marked cardiovascular compromise.
- CVP monitoring-

  - routine use of ultrasound guidance is advocated as distorted anatomy from previous central lines, hypovolaemia following dialysis make traditional landmark technique difficult.

  - 30% patients
- Temperature & Urine output monitoring
- Neuromuscular junction monitoring - essential owing to decreased clearance and potential residual neuromuscular blockade.

When is immunosuppression is started?

a. Pre-operatively

b. Intra-operatively

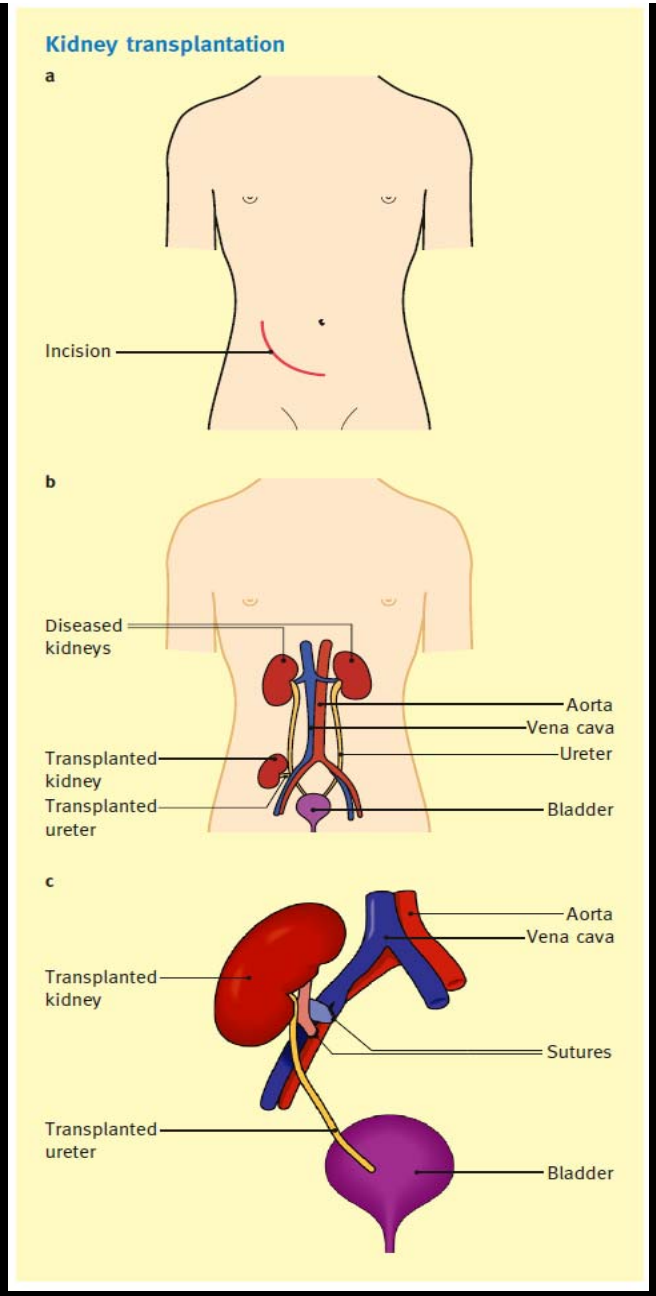
c. Post-operatively

**A state of immunosuppression is induced immediately after anaesthesia, just prior to the operation. Different units have different regimens**

**Anesthesiologists must communicate with the transplant team to obtain the schedule of immunosuppressive agents**

**immunosuppression is then maintained postoperatively.**

**Antibiotics are also given before incision.**




- Curvilinear incision is made from above the symphysis pubis to the anterior superior iliac spine.
- The donor kidney is placed in the iliac fossa, below the native kidney, which is typically left in situ.
- Anastomoses are made between
  -renal vein and the external iliac vein
  -renal artery and the common, external or internal iliac artery
  -ureter of kidney to the bladder

**IMMEDIATE URINE PRODUCTION IS SEEN IN 90% OF LIVING DONOR KIDNEY AND 40-70% OF CADAVERIC TRANSPLANT**

# Anaesthetic perioperative management

- General anaesthesia - technique of choice.
- However extraperitoneal procedure - combined spinal epidural technique without sedation can be used successfully in patients considered to be high risk for GA
- Concerns with routine use of regional anaesthesia

✓ increased risk of epidural haematoma (uraemic thrombasthenia and thrombocytopathy, residual dialysis anticoagulation)

✓ infection (long-term immunosuppression).

# PREOPERATIVE ORDERS

- Anxiolysis- midazolam drug of choice distribution and clearance relatively unchanged
- Aspiration prophylaxis- $H_2$ blocker
  - Metaclorpromide
- Care during transfer to OT table as prone to pathological fractures

# Altered Renal Function and the Effects of Anesthetic Agents

- Most drugs employed during anesthesia partly dependent on renal excretion
- The systemic effects of azotemia potentiate the pharmacological actions
  - ✓ Low albumin levels → increase in free fraction of available drugs
  - ✓ Uremia → altered BBB → increase the levels of unbound drug crossing the BBB into CNS
  - ✓ Depressent effects of metabolic toxins on CNS have synergistic effect with anaesthetic drugs.

*Dose of agents may need to be adjusted according to the volume status, acidic pH and increased sensitivity of the nervous system to these drugs*

# Induction agents

- Propofol and thiopental - safe for induction of anaesthesia
- Etomidate - not recommended as it induces adrenal  insufficiency and increases mortality in critically ill patients

# Neuromuscular blocking drugs

- Rapid sequence induction can be performed in order to reduce the risk of aspiration in pts with decrease bowel motility ( DM , uremia) but it is not recommended for every patient undergoing transplantation
- Succinylcholine can be used for rapid sequence induction , Avoid when serum K > 5.5 mmol/l

# Neuromuscular blocking drugs

- Rocuronium - equally effective, non-depolarising, alternative when used at a dose of 1.2 mg/kg
- Recently, sugammadex has been introduced for reversal of rocuronium induced neuromuscular blockade.
- Due to the 100% renal excretion pathway of the sugammadex and rocuronium complex, its use is not recommended in patients with end-stage renal disease

# Neuromuscular blocking drugs

- If a rapid sequence induction is not necessary, nondepolarising muscle relaxants can be used.
- Atracurium and cis-atracurium - recommended as they are inactivated by Hofmann elimination and hydrolysis by esterases independent of renal function
- Hofmann elimination is influenced, however, by blood pH.
- Acidosis  in ESRD may prolong the effects of atracurium and cis-atracurium.

# Neuromuscular blocking drugs

- Laudanosine a potentially toxic metabolite
- Undergoes renal elimination. At high concentrations it can cause convulsions. Although concentrations at toxic levels have never been seen in humans
- Cis-atracurium may be a safer choice, as it is about four times as potent as atracurium resulting in lower laudanosine levels

# Neuromuscular blocking drugs

- Vecuronium and rocuronium - eliminated relatively independent of kidney function
- Duration of action slightly prolonged and a cumulative effect has been noted with repetitive administration.
- Avoid pancuronium 80% eliminated through kidneys

# Inhalational agents

- Isoflurane  desflurane can be safely used
- Safety concerns use of sevoflurane - compound A generation, nephrotoxic in  rats
- However, this effect has never been shown in humans. In contrast, many studies have shown no negative effect on renal function
- Sevoflurane can be used safely for renal transplant surgery
- Enflurane- fluoride ions , should be avoided

# ANALGESICS

- Morphine – morphine-6-glucuronide is an active degradation product of morphine, renal excretion , monitor for postop respiratory depression.
- Fentanyl analogues (including alfentanil sufentanil and remifentanil) can be used safely.
- Nsaids – containdicated

# Avoidance of potentially nephrotoxic agents

**Table 2 Suitability of drugs commonly used during renal transplantation surgery**

| | Use | Avoid |
|---|---|---|
| **Volatile anaesthetics** | Sevoflurane<br>Isoflurane<br>Desflurane | Enflurane |
| **Neuromuscular blocking drug** | Cis-atracurium<br>Atracurium | Pancuronium<br>Sugammadex |
| **Rapid sequence induction** | Rocuronium 1.2 mg kg$^{-1}$<br>Succinylcholine | |
| **Opioids** | All fentanyl analogues | Morphine |
| **Intravenous induction agents** | Propofol<br>Thiopental | Etomidate |
| **Diuretics** | Mannitol | Furosemide |

European Journal of Anaesthesiology 2012, Vol 29 No 12

# FLUID THERAPY

- Postdialysis patients- intravascular volume depletion.
- Liberal hydration policy is employed intraoperatively.
- To optimize cardiac output and renal blood flow.

SBP - 130-160 mm hg

CVP - 10-15 mm hg

Mean PA pressure -18-20 mm hg

**It is critical that patients are well hydrated, as renal function is critically dependent on renal perfusion.**

# FLUID THERAPY

- Normal saline- controversial due to hypercholemic metabolic acidosis leading to hyperkalemia
- Preferred approach - balanced crystalloids to be alternated with NS
- Fluids are warmed before administration Larger volumes may be required and patients should be kept normothermic

# Diuretics

- Mannitol- 200 to 250 ml of 20% immediately before reperfusion , improve renal perfusion pressure , acts as a free radical scavenger, decreased incidence of impaired renal function immediately after transplant
- Furosemide role is controversial.
- Two large RCTs did not show any benefit of furosemide on the recovery from renal failure in patients with oliguria.

Anaesthesia for renal transplant surgery: an update Sebastian Schmid Bettina Jungwirth Eur J Anaesthesiol 2012; 29

# Colloids

- Albumin -Authors suggest an improvement in short-term and long-term outcome in renal transplant surgery patients after volume expansion with human albumin , routine use not recommended
- HES should be used with caution and reserved for special indications, such as the need for large volumes of fluid or for an increase in colloid osmotic pressure

Anaesthesia for renal transplant surgery: an update Sebastian Schmid Bettina Jungwirth Eur J Anaesthesiol 2012; 29

# Blood Transfusion

- Transfusion trigger for these patients is not known, but is probably lower than in patients without renal failure
- Many patients undergoing renal transplant surgery are treated with erythropoietin, haemoglobin values are increased and blood transfusion is not required before the operation
- Most patients have become accustomed to anaemia for some years and significant blood loss during the operation is rare, transfusion should be performed reluctantly
- Investigations have shown higher incidence of acute graft rejection

# Vasopressors

- Optimised volume therapy is essential and hypotensive episodes to be avoided , especially after reperfusion
- However, when volume loading is not tolerated, such as in patients with pulmonary oedema, vasopressors should be considered despite the risk of renal vasoconstriction.
- Use of noradrenaline in donors does not have a negative effect on graft function in recipient

# Dopamine

- Two large meta-analyses have shown a detrimental effect of dopamine on renal function in acute renal failure
- Another study showed a higher mortality and prolonged length of icu stay in patients receiving dopamine after renal transplant surgery
- Therefore, the use of dopamine in renal transplant surgery cannot be recommended

Anaesthesia for renal transplant surgery: an update sebastian schmid bettina jungwirth eur j anaesthesiol 2012; 29

# Dobutamine

- Can be used as a positive inotrope for patients with a low cardiac output
- However, in these patients advanced haemodynamic monitoring may help to optimise volume and drug therapy

# POSTOPERATIVE MANAGEMENT

- Renal transplant recipients should be reversed and extubated once the established criterion for extubation is fulfilled and there is no concern for airway protection
- In general, renal transplant patients are postoperatively nursed in a high-dependency unit
- Rarely require intensive care unit admission unless there is fluid overload, a cardiac event or sepsis

# POSTOPERATIVE MANAGEMENT

- Supplemental O2
- Avoid hypotension and hypovolemia( continuous monitoring of cvp and bp)
- Strict monitoring of urine output

  decrease strongly suggests mechanical impingement of graft , vessel or ureter
- Sudden decrease in UO may require surgical reexploration
- Nephrotoxic agents should be avoided
- Postoperative pain is usually mild to moderate after kidney transplantation.
- PCA with fentanyl or sufentanil is the choice.

# IMMUNOSUPPRESIVE THERAPY

- Immunosuppression strategies aim to prevent graft rejection
- Form a vital part in the management of renal transplant patients
- Immunosuppression regimens differ from center to center, anesthesiologists must communicate with the transplant team to obtain the schedule of immunosuppressive agents used for each patient

# DRUGS


- Steroids
- Calcineurin inhibitors(CNI) –Cyclosporin , Tacrolimus
- Target of rapamycin(TOR)inhibitors- Sirolimus, Everolimus
- Polyclonal antibodies- Antilymphocyte globulin
- Monoclonal antibodies- IL-2, Daclizumab, Basiliximab ,OKT 3
- Purine synthesis inhibitors- Azathioprine

# IMMUNOSUPPRESSION

Three phases.

1. Induction therapy -started before surgery and during first week post transplant and involves marked immune suppression. Induction agents are- Thymoglobulin, OKT3, daclizumab, or basiliximab.
2. Maintenance therapy- involving drug administration continuously for three to six months to prevent acute graft rejection and induce tolerance.
3. Long-term therapy - immunosupression maintained for the rest of the life.

# IMMUNOSUPPRESSION

- **Conventional regimen -**consists of a calcineurin inhibitor (cyclosporine or tacrolimus), a corticosteroid, and an antimetabolite (mycophenalte mofetil or azthoprine).

- **Antibody induction regimen -** uses lower doses of the conventional medications with the addition of an antibody directed at T-cells antigens: anti-lymphocyte antibodies (i.e. Thymoglobulin, alemtumzumab, OKT3) or interleukin-2 receptors antagonist: Basiliximab (trade name Simulect) or Daclizumab (trade name Zenapax)

- The antibody induction regimen has been shown to result in better graft outcomes

# COMPLICATIONS OF CHRONIC IMMUNE SUPRESSION

- CNS- Lower siezure threshold
- Hematologic/Immune- increased risk of infections, increased risk of tumours, pancytopenia
- Endocrine – poor wound healing, impaired glucose tolerance, osteoporosis
- CVS- HTN, Hyperlipidemia

# RENAL TRANSPLANTATION - ABSOLUTE CONTRAINDICATIONS

1. Active infection
2. Untreated malignancy
3. Predicted patient survival less than 5 years
4. Risk of transplant graft loss greater than 50% at 1 year
5. Inability to comply with immunosuppression regimen, and immunosuppression predicted to cause a life threatening complication

Miller's Anesthesia by Churchill Livingstone, 7th edition: 2161-2166

# Paediatric patient undergoing renal transplant

- Renal transplantation has been a successful treatment modality in children with chronic renal failure or end-stage renal disease (ESRD)

- One-year survival of 89% and 3-year survival of 80% seen with grafts from living related donors

**Box 1. Diseases leading to renal transplantation in children**

Alpert's syndrome
Anaphylactoid purpura
Bladder neck obstruction
Congenital nephrotic syndrome
Corticosteroid-resistant nephrotic syndrome
Cystinosis
Glomerulonephritis
Hemolytic uremic syndrome
Hereditary interstitial nephritis
Hypoplasia-dysplasia
Lupus nephritis
Medullary cystic disease
Membranoproliferative glomerulonephritis
Neurogenic bladder
Oxalosis
Pyelonephritis

# ANAESTHESIA

- General management same
- Special consideration should be given to the small child receiving an adult-sized kidney or in patients in whom the aorta is cross-clamped. The blood volume required to fill the new kidney may constitute a significant proportion of the child’s total intravascular volume.

# TRANSPLANT PATIENT FOR NON TRANSPLANT SURGERY

# TRANSPLANT PATIENT FOR NON TRANSPLANT SURGERY

General considerations-

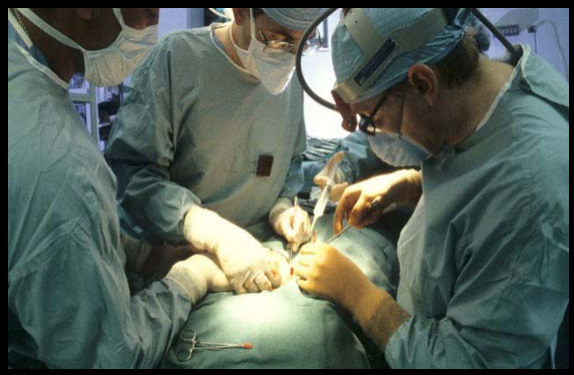
- Physiological and pharmacological problems of allograft denervation
- Side effects of immunosuppression
- Risk of infection
- Potential for rejection

# ASSESSMENT OF TRANSPLANTED KIDNEY

- Interval since transplant
- Organ source ( living / cadaveric)
- Previous episodes of rejection
- H/O fever, infection, exposure to ill patients(chickenpox, CMV , HCV)
- Immunosuppressive therapy, route, any recent change in dose , compliance
- Need for dialysis, frequency , interval since last HD

# ANAESTHESIA TECHNIQUES

- GA / RA
- Special precautions?
- Regional containdicated if –
  - hypovolemia
  - platelet dysfunction
  - coagulation abn
  - uremic/Diabetic cardiomyopathy



# ANAESTHETIC TECHNIQUE

- Use sterile circuits, laryngoscope, air filters
- Choose drugs that do not rely on the kidney for excretion (e.g., atracurium).
- Nephrotoxic drugs should be avoided.
- Diuretics should not be given without careful evaluation of the patient’s volume status.
- Renal hypoperfusion from inadequate intravascular volume should be prevented

# Immunosupressive agents

- Immunosuppressive drugs may modify the pharmacological behavior of many drugs used in anesthesia.
- Cyclosporine – enchances effect of Fentanyl, NDMR (small dose required)
- Azathioprine- antagonizes NDMR- increase req
- Withdrawl of azathioprine with warfarin therapy ppts bleeding
- OKT3- anaphylaxis, seizures( hyperventilation)

# Immunosuppressive agents

- All recipients are immunocompromised
- Immune competence altered by acute illness, stress of surgery, disruption of regimen predisposing them to infection

# Infection

- Maximum during first six months
- Bacterial, viral, fungal,protozoal
- Signs of abdominal sepsis are not obvious- high index of suspicion required for postop infection
- Give antibiotic prophylaxis
- Use aseptic techniques
- Invasive lines to be avoided, Remove at the earliest

# Rejection

- Late cause of mortality
- Surgery during period of rejection increases morbidity and mortality
- Treated by increasing dose, adding new drugs, steroids

# SUMMARY

- Patients with CRF have multiple medical problems which require careful assessment before anesthesia
- Perioperative fluid balance needs close monitoring & adjustment
- Altered pharmacodynamics & pharmacokinetics of anesthetic drugs should be taken into consideration
- Renal transplantation should be recommended as the preferred mode of RRT for most patients with ESRD in whom surgery and subsequent immunosuppression is safe and feasible

Thank you