

EFFECTS OF ANESTHESIA AND SURGERY ON RENAL FUNCTION



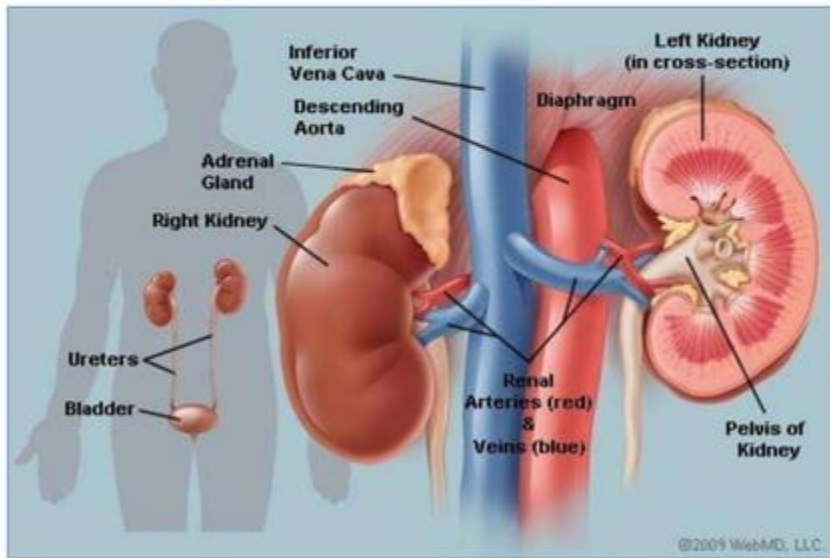
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INTRODUCTION

- Anaesthesia and surgical stress can affect renal function and body fluid regulation **indirectly** as well as **directly**.
- The **indirect effects**, through influences on **haemodynamics, sympathetic activity** and **humoral regulation**, are more pronounced than the direct ones.
- The **direct effects** of anaesthesia which are dose- and agent-dependent include **effects on renal autoregulation, tubular transport of sodium and organic acids** and **alteration in the effect of ADH**.

- **Normal renal function appears to be regulated by a balance between intrinsic autoregulation, tubuloglomerular balance, hormonal and neuronal influences.**
- **A comprehensive understanding of anesthetic drugs and their effects on renal function remains fundamental to the success of any surgery.**

KIDNEY: BLOOD SUPPLY AND ITS CIRCULATION?



Renal Circulation

- **Arterial supply:- Renal A. (br of Abdominal aorta)**
- **Venous drainage:- Renal vein into IVC.**
- **Both the kidneys weight around 0.4% of body weight, but the combined blood flow accounts for 20-25% of total cardiac output (CO).**
- **80% of renal blood flow goes to cortical nephrons. 10-15% goes to juxtamedullary nephrons.**
- **Autoregulation of renal blood flow occurs between MAP of 80 and 180 mm Hg.**

- **Clearance:-** volume of blood completely cleared of a substance per unit of time.
- **Renal Plasma Flow (RPF):-** measured by p-aminohippurate (PAH) clearance

$$\text{RPF} = \text{clearance of PAH} = \left(\frac{[PAH]U}{[PAH]P} \right) \times \text{Urine Flow}$$

- $[PAH]U$ = urinary concentration of PAH
- $[PAH]P$ = plasma PAH concentration

- **Renal Blood Flow (RBF)=**
$$\frac{RPF}{(1 - \text{Hematocrit})}$$

- Normally, RPF = 660mL/min and RBF = 1200mL/min

- **Glomerular Filtration Rate (GFR):-** Volume of fluid filtered from the glomerular capillaries into bowman's capsule per unit time.
- Calculated using inulin or creatinine clearance.

$$\frac{([Creatinine]_u \times \text{Urinary flow rate})}{[Creatinine]_P}$$

[Creatinine]U:- creatinine concentration urine.

[Creatinine]P:- creatinine concentration plasma.

- Normal:- 120 ± 25 ml/min (male), 95 ± 20 ml/min (female)

- **Filtration Fraction = GFR/RPF**

- Normally:- 20%

Volatile Anaesthetics And Renal Functions

- Volatile anesthetics cause a decrease in GFR by decreasing renal perfusion pressure either by **decreasing systemic vascular resistance** (isoflurane or sevoflurane) or **cardiac output** (halothane).
- This decrease in GFR is **exacerbated** by **hypovolemia** and the **release of catecholamines** and **antidiuretic hormone** as a response to painful stimulation during surgery.

Inhalation Agents

AGENT	PROPERTY	EFFECT
Halothane	Inorganic fluoride levels are less	No Nephrotoxicity
Isoflurane	Inorganic fluoride levels are less	No Nephrotoxicity
Desflurane	Inorganic fluoride levels are very less, highly stable & resists degradation by soda-lime & liver	No Nephrotoxicity
Sevoflurane	Inorganic fluoride levels are less but not stable , degraded by soda-lime to compound A & undergoes liver metabolism.	Compound A is Nephrotoxic
Enflurane	Biotransformed to inorganic fluoride levels after prolonged use (> 4hrs)	Nephrotoxic, after prolonged use
Methoxyflurane	Biotransformed to high inorganic fluoride levels	Highly nephrotoxic

SEVOFLURANE AND ITS RENAL EFFECTS?

- **Sevoflurane :-**
- Sevoflurane is degraded in basic carbon dioxide absorbents (Barium Hydroxide and Soda lime) into a vinyl ether called **compound A**.
- Compound A has been implicated to cause **renal injury** through fluoride toxicity (animal studies).
- High intra-renal fluoride concentrations **impair the concentrating ability of the kidney** and may theoretically lead to **non-oliguric renal failure**.

- **However, studies have failed to show a relevant effect in clinical practice.**
- **It is considered safe even in patients with renal impairment as long as prolonged low-flow anesthesia is avoided. (Minimum flow ≥ 2 L/min)**

METHOXYFLURANE AND ITS EFFECTS ON KIDNEYS?

- **Methoxyflurane** caused dose-dependent abnormalities post-surgery.
- It causes **vasopressin-resistant polyuria, serum hyperosmolality, hypernatremia, increased concentrations of serum urea nitrogen and inorganic fluoride, and decreased urinary potassium, sodium, osmolality, and urea nitrogen concentrations.**
- Therefore, clinically it is no longer used.

FLUORIDE INDUCED NEPHROTOXICITY

- Metabolism of sevoflurane, isoflurane, methoxyflurane, enflurane and halothane results in production of fluoride ions.
- **Isoflurane:** 20 MAC-hours of isoflurane could lead to serum fluoride levels above 50uM/L, however no postoperative renal dysfunction was detected.

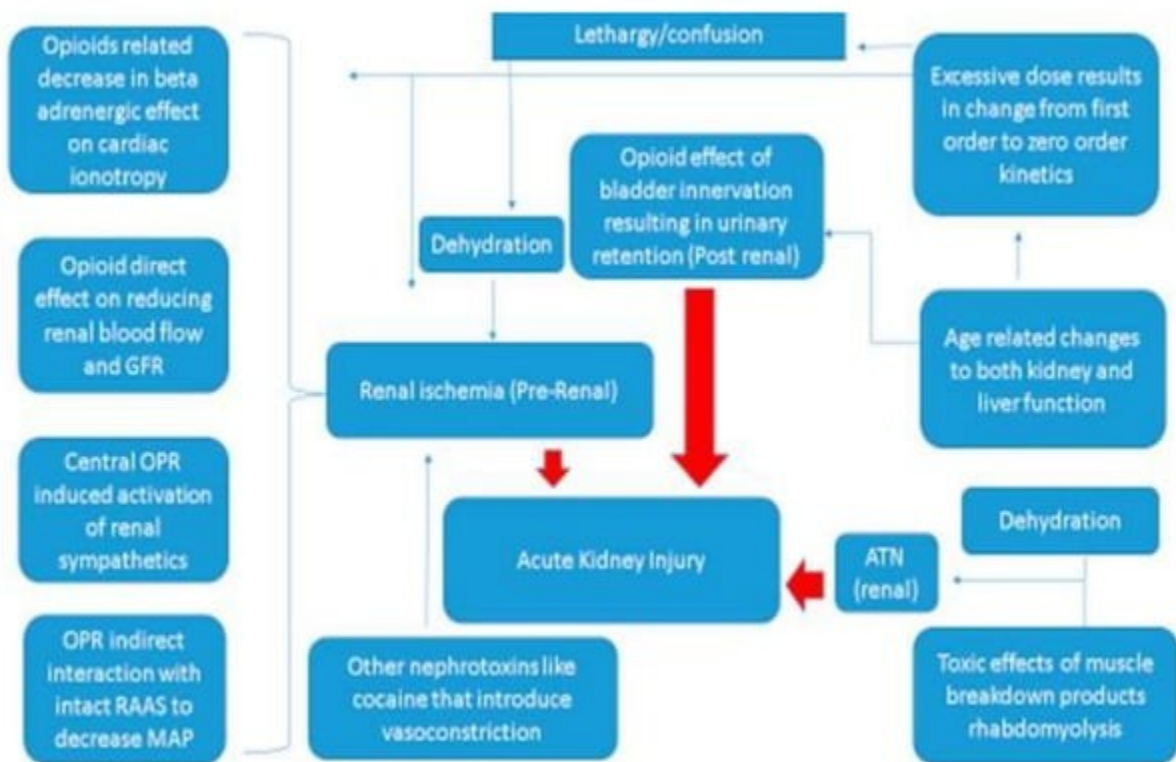
- **Sevoflurane**: around 7% of patients who receive sevoflurane will have serum fluoride levels above 50uM. Yet, no clinically significant renal dysfunction was detected.
- **Methoxyfluane** and **enflurane** might cause renal dysfunction especially when associated with hypovolemia, shock and renal vasoconstriction.

OPIOIDS AND ITS RENAL EFFECTS?

OPIOIDS AND RENAL FUNCTIONS

- Opioid are commonly used safely in anesthesia and pain control in the perioperative period.
- They decrease renal blood flow, GFR and urine output which is **minimal** and **transient**.
- **Ramifentanyl** pharmacokinetics are unaffected by renal functions due to rapid ester hydrolysis.
- With the exception of morphine and meperidine, significant accumulation of active metabolites do not occur.

- The **renal toxicity** appears in the context of inappropriate use:- either higher than needed doses, in the presence of other toxins, chronic use of opioids (accumulation of metabolites), deranged renal functions or with pre-existing dehydration.
- The accumulation of **morphine (morphine-6-glucuronide)** and **meperidine (normeperidine)** has been reported to prolong respiratory depression in patients with kidney failure.
- Increased level of normeperidine has been associated with **seizures**.

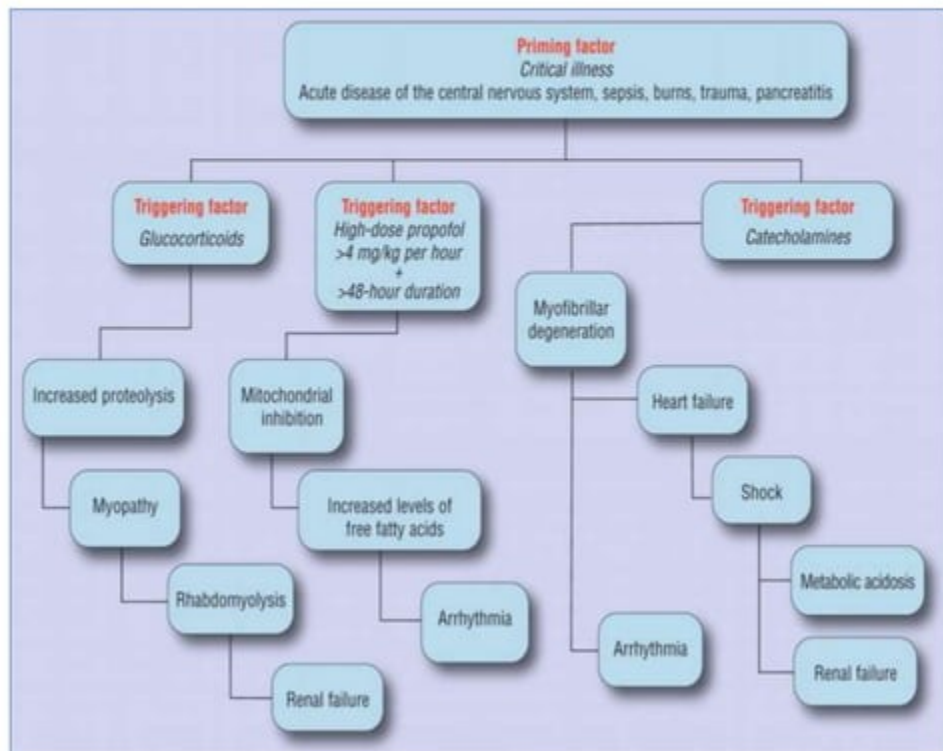


OPIOID RELATED RENAL INJURY

INTRAVENOUS AGENTS AND RENAL FUNCTIONS

- These exhibit minor effect on kidney when used alone.
- **Ketamine** minimally effects and preserves renal functions during haemorrhagic hypovolaemia. It is associated with tachycardia, increased blood pressure, and increased cardiac output; useful in the shocked, unwell patient.
- Propofol can be safely used. Its long term infusion use – ‘**Propofol Infusion Syndrome**’ is associated with renal failure.

WHAT IS PROPOFOL INFUSION SYNDROME (PRIS)?



- Life-threatening condition characterised by acute **refractory bradycardia** progressing to **asystole** and one or more of:-
 - (1) metabolic acidosis.
 - (2) rhabdomyolysis or myoglobinuria.
 - (3) hyperlipidaemia.
 - (4) enlarged or fatty liver.
- **Risk Factors:-**
 - $>4\text{mg/kg/hr}$ ($> 75\mu\text{g/kg/min}$) for 48 hours; but can occur at lower doses
 - younger age.
 - acute neurological injury.

- low carbohydrate intake.
- catecholamine/corticosteroids infusion.
- **Management:-**
 - Discontinue propofol immediately
 - Haemodynamic maintainance:-
crystalloid/colloids, vasopressors/inotropes.
 - Adequate carbohydrate intake (6-8mg/kg/min)
 - Hemodialysis & continuous renal replacement therapy (CRRT)
 - Transvenous pacing.
 - ECMO.

EFFECTS OF MUSCLE RELAXANT ON RENAL FUNCTIONS?

MUSCLE RELAXANTS AND KIDNEYS

- Upon administering histamine releasing muscle relaxants (mivacurium, atracurium, succinylcholine, d-tubocurarine), there is **transient fall in blood pressure, renal blood flow and cardiac output.**
- This hypotension has been attributed to **histamine release** and **autonomic ganglionic blockade.**

- Based on clinical and experimental data, it appears that muscle relaxants have only a **modest impact on RBF** and **no meaningful adverse influence** on postoperative Renal functions when Blood Pressure and Cardiac Output are adequately maintained.

EFFECTS OF COLLOID ON KIDNEYS?



COLLOIDS AND KIDNEY

- **Albumin** gives **renoprotection** which may be explained by **maintaining renal perfusion, promoting proximal tubular integrity and function, binding of endogenous toxins and nephrotoxic drugs, and preventing oxidative damage.**
- **Carbohydrate-based artificial colloids hydroxyethyl starch (HES) and dextran** were frequently associated with **acute kidney injury.**

- The **degradation products** of HES and Dextran cause **direct tubular injury** and **plugging of tubules**.
- Renal failure following HES and dextran use is more often reported when **renal perfusion is reduced** or when **pre-existing renal damage** is present.

EFFECT OF ANTI-DOPAMINERGIC DRUGS?

DRUGS WITH ANTI-DOPAMINERGIC ACTIVITY

- **Dopamine** and **fenoldopam** (selective D1 agonist) **dilate afferent and efferent arterioles** and increase renal perfusion.
- Drugs like **Metoclopramide, phenothiazines, and droperidol** may impair the renal response to dopamine and may precipitate AKI (in susceptible patients).

EFFECTS OF NSAIDS?

NSAIDS AND RENAL FUNCTIONS

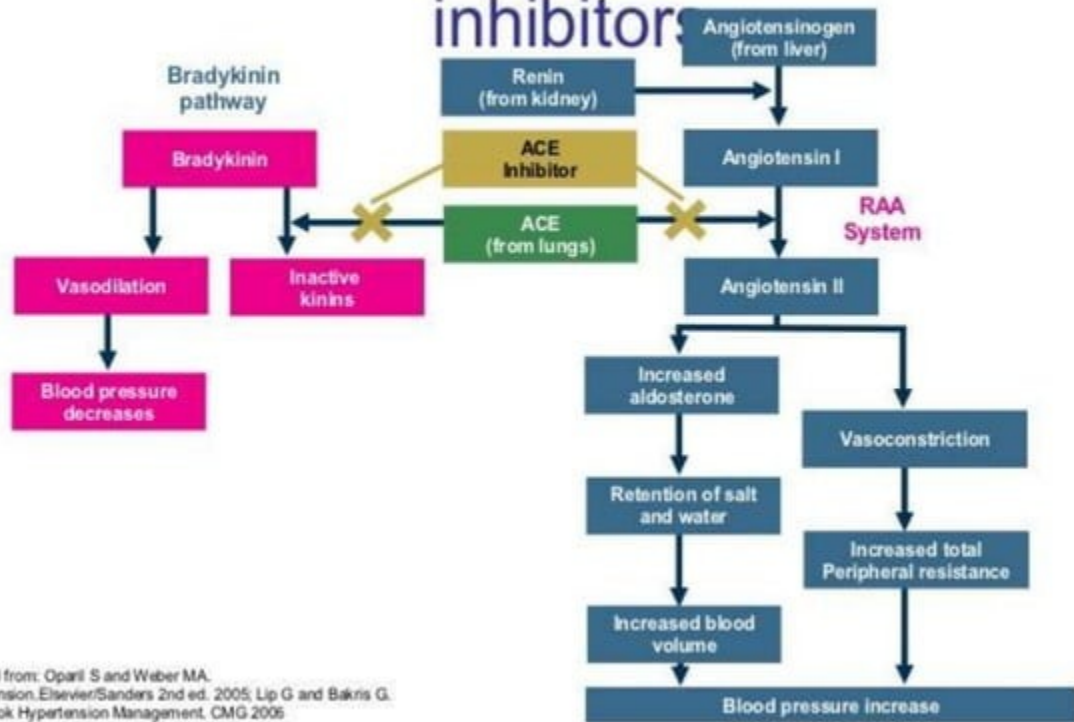
- Renal synthesis of **vasodilating prostaglandins (PGD₂, PGE₂ and PGI₂)** is an important protective mechanism during periods of systemic hypotension and renal ischemia.
- **Inhibition of prostaglandin synthesis** by NSAIDs impairs the renal autoregulation (the purpose of which was to maintain renal blood flow during systemic vasoconstriction eg In hypovolaemics).
- NSAIDs also cause **acute interstitial nephritis**.

RENAL EFFECTS OF ACE INHIBITORS?

ACE INHIBITORS AND ITS RENAL EFFECTS

- Angiotensin II causes **generalized arterial vasoconstriction** and secondarily reduces RBF.
- Both afferent and efferent glomerular arterioles are **constricted**, but because the efferent arteriole is smaller, its resistance becomes greater than that of afferent arteriole; GFR tends to be relatively preserved.
- ACE inhibitors **block** the **protective effects of Angiotensin II** and may result in reduction of GFR during anaesthesia.
- These prevent the local action of **bradykinins**, responsible for constriction of the efferent arteriole.

The Mechanism of Action of ACE-inhibitors



Adapted from: Oparil S and Weber MA. Hypertension. Elsevier/Sanders 2nd ed. 2005; Lip G and Bakris G. Handbook Hypertension Management. CMG 2005

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EFFECT OF POSITIVE PRESSURE VENTILATION ON KIDNEYS?

EFFECT OF POSITIVE PRESSURE VENTILATION (PPV)

- Positive-pressure ventilation used during general anesthesia can **decrease venous return, cardiac output, renal blood flow, and GFR.**
- Decreased cardiac output leads to release of **catecholamines, ADH, renin, and angiotensin II** with the activation of the **sympathoadrenal system** and resultant decrease in renal blood flow.

EFFECT OF REGIONAL ANAESTHESIA ON KIDNEYS?

REGIONAL ANAESTHESIA AND RENAL FUNCTIONS

- Spinal and epidural anaesthesia only **slightly decrease GFR and RBF** in proportion to the decrease in mean arterial pressure.
- The preexisting intravascular volume and the quantity of intravenous fluids given strongly influence the renal response to spinal and epidural anaesthesia.
- There is also **decreased diuresis** and a **marked fall in sodium excretion**.
- These trends are gradually reversed during recovery.

EFFECTS OF SURGERY ON **RENAL FUNCTIONS**

EFFECTS OF SURGERY ON RENAL FUNCTIONS

- Surgery influences renal functions by inducing **alterations in prerenal haemodynamics**.
- Operative stress leads to an increase in circulating **catecholamines** and **angiotensin**.
- Significant **fluid shifts, excessive blood loss** and **redistribution of third space** may lead to a prerenal oliguric state, **increasing secretion of vasopressin**.

EFFECTS OF PNEUMOPERITONEUM ON KIDNEYS?

PNEUMOPERITONEUM AND ITS EFFECT ON KIDNEY

- **Pneumoperitoneum** produced during laparoscopy creates an abdominal compartment syndrome like state.
- The increase in intra-abdominal pressure typically produces **oliguria (or anuria)** that is proportional to insufflation pressures.
- Mechanisms:- **central venous compression (renal vein and vena cava), renal parenchyma compression, decreased cardiac output; and increase in plasma level of renin, aldosterone and ADH.**

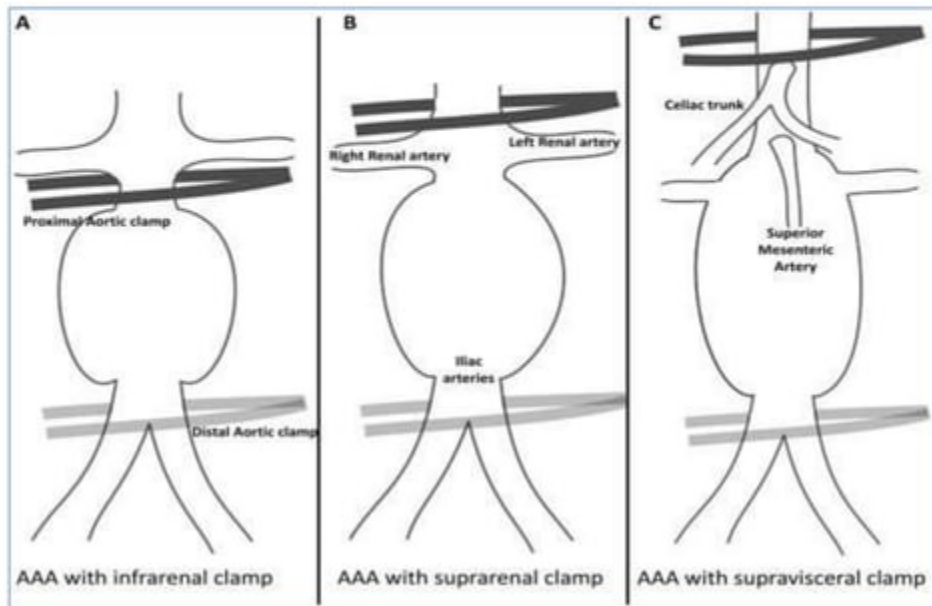
RENAL EFFECTS OF CARDIOPULMONARY BYPASS ?

CARDIOPULMONARY BYPASS (CPB) AND RENAL FUNCTIONS

- Initiation of CPB is associated with increase in **stress hormone** and **systemic inflammatory response**.
- Elevated levels of **catecholamine, cortisol, arginine vasopressin** and **angiotensin** are observed.
- These are influenced by depth of anaesthesia, blood pressure and type of surgical repair.

- Multiple **humoral systems** are also activated including **complement, coagulation and fibrinolysis**.
- Also, increased amount of **oxygen derived free radicals** are generated.
- These mediators can cause **decreased renal perfusion, direct tubular injury and renal vasoconstriction**.

WHAT ARE THE EFFECTS OF AORTIC CROSS CLAMPING ON KIDNEYS?

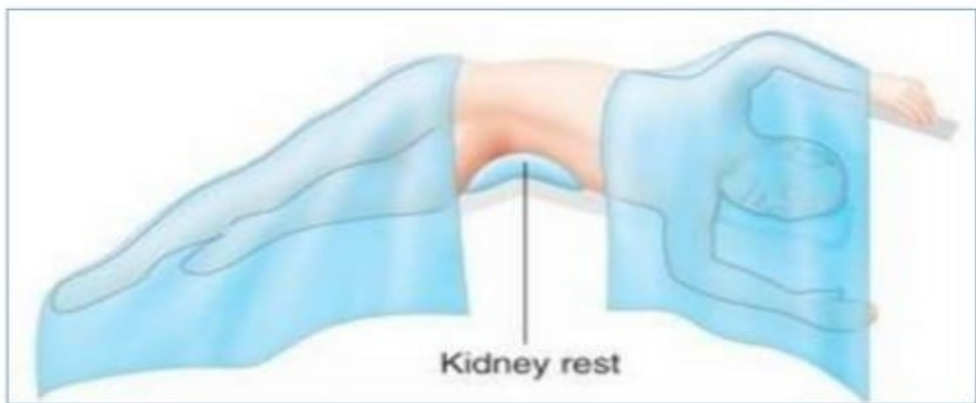


CROSS CLAMPING OF AORTA AND ITS RENAL EFFECTS

- Cross-clamping of the aorta is associated with **decreases in organ perfusion distal to occlusion** (spinal cord, kidneys, abdominal viscera, limbs).
- Clamping of **abdominal aorta** (suprarenal or infrarenal) is associated with transient renal insufficiency (Ischaemic perfusion injury).
- Cross-clamping of the **thoracic aorta** is associated with severe **decreases in renal blood flow, glomerular filtration rate, and urine output.**

- **Mediators:-** Prostaglandin imbalance, AT II, Sympathetic nervous system, catechalamine .
- **Renal Protective Measures:-**
 - Inj. **Mannitol** infusion (0.5 gm/kg) prior to cross clamping
 - Inj. **Dopamine** infusion (renal dose).
 - Preserve renal blood flow:- **Fenoldopam** infusion
 - **Maintainance** of intravascular volume and adequate cardiac functions.

EFFECTS OF POSITIONING ON KIDNEYS?



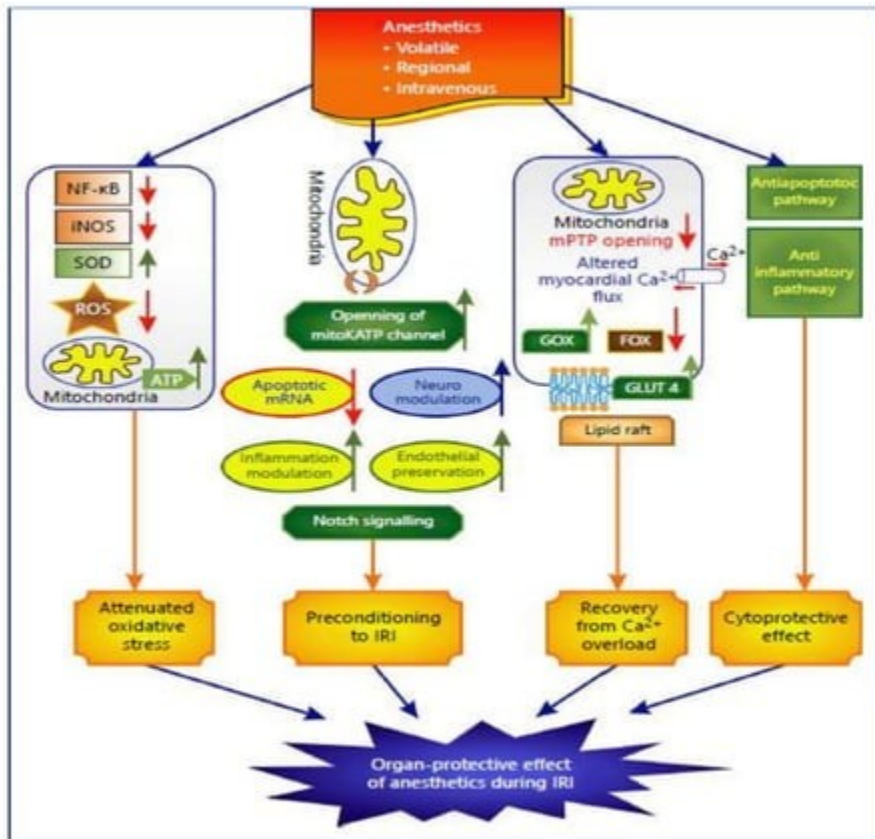
EFFECTS OF POSITIONING ON KIDNEYS

- Open procedures on kidney are carried out in **'kidney rest position'** – lateral flexed position.
- Dependant leg is flexed and the other is extended.
- **Axillary roll** – placed under dependant upper chest.
- Operating table is extended to achieve maximal separation between iliac crest and costal margin.
- **Kidney rest** is elevated to raise the non dependant iliac crest higher and increase surgical exposure.

- This position is associated with **adverse respiratory and circulatory effects.**
- It can significantly decrease the venous return to heart by **compressing the inferior vena cava.**
- Also, the **venous pooling in the legs** potentiates anaesthesia induced vasodilation.
- **Lithotomy position:-** Elevation of leg drain blood into central circulation acutely, mean BP and CO-↑
- Conversely, **rapid lowering of legs** from lithotomy/trendelenburg acutely **decreases venous return** and can result in **hypotension.**

**DOES ANAESTHESIA HAVE ANY RENAL
PROTECTION EFFECT AGAINST ISCHAEMIC
REPERFUSION (IR) INJURY?**

- **Renal ischemia/reperfusion (IR) injury** is a leading cause of **peri-operative acute kidney injury (AKI)**, which frequently complicates major vascular, cardiac transplant and liver surgeries.
- IR injury occurs due to **oxidative stress, inflammation, cellular necrosis and apoptosis.**
- Researchers found that **isoflurane** and **sevoflurane** provides **preconditioning reno-protective effects** through **anti-inflammatory, anti-apoptotic actions** and **altering myocardial calcium fluxes.**



Mechanism Of Protective Effect Of Anaesthesia

- **Sodium thiopentone** pretreatment reduced renal IR injury induced by free radicals.
- **Propofol** protected cells from apoptosis by **inhibiting oxidative and mitochondrial stress**; it also **attenuates tubular damage** after reperfusion.
- **Ketamine** ameliorated the upregulation of inflammatory pathways and reduction of metabolism caused by hypoxia.
- **Lidocaine** (epidural analgesia) may provide protection against IR injury by **preventing miRNA dysregulation**.

SUMMARY

- **The effects of anaesthetics on the kidney go beyond a simple change in basal haemodynamics and include, for some drugs, an alteration in the ability for the kidney to autoregulate its blood flow and glomerular filtration rate.**
- **Inhalational anaesthetics generally reduce glomerular filtration rate and urine output, mainly by extra-renal effects that are attenuated by pre-operative hydration.**
- **Opioids, barbiturates and benzodiazepines also reduce glomerular filtration rate and urine output.**

- **The effects of regional anaesthesia seem to be less than those of general anaesthesia and are related to changes in systemic haemodynamics.**
- **Mechanical ventilation decreases urine volume and sodium excretion to an extent that depends on the increase in intrathoracic pressure.**
- **Controlled hypotensive anesthesia, aortic cross-clamping, and cardiopulmonary bypass represent anticipated renal insults which should be carefully managed.**



THANK YOU