Renal Failure

Renal failure can be either acute or chronic with various etiologies (nephrotoxins vs. HTN / DM / GN / PCKD) and various stages of dysfunction including decreased excretory function which can lead to volume overload, accumulation of products of catabolism (e.g. K^+, H^+), PLT dysfunction, impaired excretion of drugs and may ultimately require dialysis.

ANESTHETIC CONSIDERATIONS:

- Increased risk of aspiration due to delayed gastric emptying
- Dysregulation of electrolyte, acid-base & volume status.
  - Hyperkalemia – caution with succinylcholine; relative cardiac tolerance due to increased K
- Etiology of renal failure (acute vs chronic)
- End organ dysfunction:
  - **CVS**: accelerated CAD, LV dysfunction, HTN, IHD, CHF, pericarditis
  - **Neuro -** autonomic dysfunction (aspiration, hemodynamic instability), polyneuropathy
  - **Hematologic**: anemia, platelet dysfx; impaired immune response and increased infection risk
  - **Respiratory**: pulmonary edema
  - **Metabolic**: electrolyte and endocrine abnormalities
  - **GI**: delayed gastric emptying
- Altered pharmacokinetics - ↓ drug excretion, ↑risk drug/metabolite accumulation post-op (esp sedative/narcotics)
- Difficult IV access
- Increased perioperative mortality & morbidity – intermediate cardiac RF for non-cardiac sx; dialysis pts have 4% mortality following general surgery & morbidity ~50%

ANESTHETIC GOALS:

- Preoperative optimization of electrolytes, volume status, co-morbidities.
- Avoid precipitating or exacerbating RF (maintain adequate renal perfusion, avoid nephrotoxins)
- If on dialysis, co-ordinate timing of run ~24hrs before. If urgent can do quick 2 hr run with less volume removal & no heparin
- Have a treatment plan ready for RF sequelae (HD, CVVHD, diuretics, $CaCl_2$)
- Avoid compromise of HD access (AV fistulas, indwelling IV lines, PD ports)
- Recognize that certain surgeries (cardiac, aortic surgeries) are high risk for postoperative renal dysfunction and patients with borderline renal function are at risk

HISTORY

- Etiology and co-morbidities: HTN, CAD, DM
- Severity (see scale based on CrCl below)
- Normal u/o vs oliguric vs anuric
- End-organ dysfunction
  - CV and respiratory function
    - Exercise tolerance
    - Angina, syncope, palpitations, Sx of CHF
    - BP control
    - Bleeding (epistaxis, GI)
- Dialysis details (mode, frequency, complications, access, duration, dry weight)
  - Nutritional status (albumin) a measure of adequacy of dialysis
- GERD
- Glucose metabolism

PHYSICAL

- **VITALS -** Tilt table test: ↑ HR, ↓ BP when tilted (autonomic dysfunction)
- **GENERAL** – IV access, AV fistulae (avoid IVs and BP cuff), generalized edema
- **HEENT** – A/W exam (airway edema in ARF)
- **CNS** – uremic encephalopathy (asterixis, tremor, myoclonus), peripheral neuropathy, ANS dysfx
- **CVS** - Signs of LVH, dysrhythmias, pericardial rubs (effusions) and volume status (JVP)
- **RESP** - Pulmonary edema (CHF, effusions)

INVESTIGATIONS

- **Labs**
  - **CBC -** anemia, PLTs – may be normal but dysfunctional
  - **Lytes -** ↑K^+ , ↑ PO_4^{2-} , ↑Mg^{2+} , ↓Ca^{2+} , ↓Na^+
  - **Coags –** bleeding time prolonged, normal INR, PTT
  - Serum **glucose – HbA1C**
  - **Serum proteins** - (hypoalbuminemia)
  - **BUN** - not a reliable indicator of GFR unless protein catabolism is normal and constant
  - **Cr -** directly related to muscle mass and inversely to GFR, therefore can change with large protein loads, cachexia; also decreases with age and certain medications (e.g. cimetidine)
    - Best indicator of RF and etiology (despite sources of error)
  - **Cr clearance**
    - This is the eGFR (which has many formulas)

        - **Cockcoft-Gault formula** – Cr Clearance = [(140-age) x weight x 1.23 if male] / Cr
        - **Stages of ESRD based on CrCl**
            - Stage I > 90 (at risk, as in DM)
            - Stage II 60-89
            - Stage III 30-59 (less than 60 for > 3 months is the diagnosis of CKD)
            - Stage IV 15-29 (should be seeing a nephrologist)
            - Stage V < 15 (on dialysis)
    - **ABG -** (acid-base status)
    - **Urinalysis** - (SG, pH, crystals, casts, glucose can help in ID of etiology)
- **Imaging**
    - **ECG -** LVH is common, arrhythmias on the basis of electrolyte abnormalities ($\uparrow K^+$)
    - **CXR** - effusions, CHF
    - **+/- ECHO** and functional studies (recall: RF is an intermediate risk factor in the AHA guidelines)

OPTIMIZATION

- If ARF: cancel surgery if elective
- Aspiration prophylaxis (cut ranitidine dose in half – all H_2 blockers dep on renal excretion)
- Timing of dialysis & consider need for perioperative dialysis in consultation with nephrology
    - Dialysis immediately preoperatively, or starting dialysis in a patient for the first time preoperatively, is associated with hemodynamic instability
    - Best to dialyze the chronic patient the day before
    - Save dialysis for postoperative in the new patient, unless preoperative hyperkalemia / acidemia / uremia is at a dangerous level
    - Peritoneal dialysis patients should be empty, to reduce reflux risk
- Diabetes management
- Blood conservation strategies (esp. if major blood loss procedure, consider adjustment of EPO dosing)
- Uremic bleeding: Cryo (10 units IV), DDAVP (0.3 mcg/kg IV/SC), Conjugated Estrogen (Chestnut Pg 333)
- If borderline function and high risk surgery for postoperative RF: generous preoperative hydration, possible use of mannitol intraoperatively

ANESTHETIC OPTIONS

- Local, regional, general okay
- Reflux risk makes sedation or an LMA less attractive
- Neuraxial - potential risk of bleeding (plt dysfx)

ANESTHETIC SETUP

- **Drugs** (see drug tables below for more info)
    - **Nephrotoxic:**
        - **Antibiotics**: aminoglycosides (gentamicin, amikacin, tobramycin, streptomycin)
        - **Contrast dye**
            - N-acetylcysteine for renal protection with contrast dye
        - **NSAIDs** (especially if we dry our elderly patients out)
            - NSAIDs inhibit the formation of PGs which are needed for renal afferent arteriolar vasodilation
        - Others: probably not a great idea to keep a patient on their ACEi / metformin / digoxin at their preoperative doses if they have developed or are at increased risk of developing renal insufficiency
        - Byproducts of cellular breakdown (Hb and myoglobin):
            - E.g. crush injury, prolonged down time, wrong unit of pRBCs → need adequate fluids
        - Reperfusion: after the X-clamp is taken off, tourniquet taken down or the limb is re-attached → O_2 free radicals and cellular debris can cause renal damage
    - **Anesthesia drugs**
        - **Propofol** and **etomidate**: minimal effect
        - **Barbiturates**: free fraction of induction dose is doubled d/t decreased protein binding
        - **Ketamine**: minimally affected, some active metabolites are renally excreted
        - Benzodiazepines:
            - **Diazepam** has active metabolites that can accumulate
            - **Midazolam** has prolonged effect (renally eliminated active metabolites), apparent mostly with prolonged infusions or repeated doses
        - Opioids:
            - **Morphine:** greater free fraction available and renally eliminated active metabolite (morphine-6-glucuronide), which is only significant if administered chronically (use a smaller initial dose)
            - **Meperidine:** renally eliminated neurotoxic metabolite (don't use it!!)
            - **Hydromorphone**: hydromorphone-3-glucuronide is an active metabolite, and is renally eliminated, significant if administered chronically
            - **Oxycodone** and **codeine**: elimination prolonged, so beware if prolonged administration
            - **Fentanyl**: lacks active metabolites, has an unchanged free fraction, and maintains a short redistribution phase
                - In one study, however, a prolonged opioid effect was noted that correlated to preoperative BUN (titrate small doses)
            - **Sufentanil**: free fraction is unchanged; conflicting reports about possible prolonged effect
            - **Remifentanil**: has a renally eliminated metabolite, but this has no significant clinical implication
        - **Anticholinergics**: 50% of active metabolites are excreted in the urine and could accumulate with repeated doses (atropine and glycopyrrolate)
        - Volatiles: possible concern with **sevoflurane** (compound A and fluoride ion formation – no good evidence that compound A does anything in humans), **desflurane** and **isoflurane** minimal fluoride ion formation (even after lengthy MAC hour exposures)
        - Muscle relaxants: have variable renal elimination, but one must also consider prolonged activity due to **acidemia**, **electrolyte abnormalities ($\uparrow Mg^{2+}$)**, and drugs such as immunosuppressants, diuretics, and aminoglycosides:
            - **SCh**: safe as long as the K^+ is < 5 mmol/L

        - Serum K^+ rises about 0.5-0.7 mmol/L and is well tolerated, particularly in patients used to high K^+ levels who have been dialyzed to a normal level
        - An infusion should be avoided, since it has a renally eliminated, weakly active metabolite
        - Possible slightly longer effect, due to reduced pseudocholinesterase levels
    - **Mivacurium**: minimal effect (possible slightly longer effect, d/t reduced pseudocholinesterase levels)
    - **Cis-atracurium** and **atracurium**: minimal or no effect
    - **Vecuronium** and **rocuronium**: both are minimally eliminated by kidneys, but clinically, the effect can be prolonged in severe disease
    - **Pancuronium**: not a good idea (elimination $T_{½}$ is primarily dependant on renal elimination)
  - **Reversal agents**: renal excretion is the principal route of elimination for edrophonium and neostigmine, the $T_{½}$ of these agents will be prolonged
- **Equipment**
  - CAS monitors + 5 lead EKG – careful attention to placement
  - Low threshold for invasive monitoring (A. line and CVC)
  - Note that mixed venous O_2 can be falsely elevated, depending on flow through shunt

MANAGEMENT OF ANESTHESIA

- **Induction**
  - RSI if concerned about GERD / delayed gastric emptying
    - Note conflict of RSI with hTN d/t hypovolemia and autonomic dysfunction → modify for possible hemodynamic instability
    - Reduction of agents if unstable, SCh fine (if K^+ is okay)
    - Consider cis-atracurium
- **Maintenance**
  - For short cases any technique is probably okay, most important to maintain intravascular volume and avoid hypo- and hypertension (restrict maintenance fluids, but replace any losses appropriately guided by hemodynamic monitoring)
  - Cautious use and selection of opiates
  - Cautious use and selection of NMBs and use reversal
  - Increased minute ventilation to compensate for metabolic acidosis
    - Overall buffering capacity is decreased, so a little postoperative respiratory acidemia can be significant to pH (see table below)
  - Reduce local anesthetic doses in the setting of decreased protein binding and acidemia
  - For neuraxial techniques, note that platelet dysfunction can exist in the setting of normal coagulation profile
  - TIVA with Remi/Prop/Cis-atracurium is an attractive option
- **Emergence**
  - Anticipate delayed emergence
  - Ensure patient awake and reversed

DISPOSITION & MONITORING

- Avoid nephrotoxins
- Ensure euvolemia, euglycemia
- Call nephrology
- Monitor for frequent causes of postoperative morbidity (hyperkalemia, infections, hTN / HTN, bleeding, dysrhythmias, clotted fistulas)

COMPLICATIONS

- ARF
- Volume overload
- Electrolyte abnormalities
- Perioperative cardiovascular complications

PREGNANCY

- Ch 50 in Chestnut
- Mild renal disease is not usually affected by pregnancy. Women with moderate to severe disease often experience deterioration in renal fx & exacerbation HTN (23%)
- Effects on Fetus:
  - Mild disease – preterm delivery 20%, IUGR 24%, fetal survival 93%
  - Moderate to severe ds – preterm delivery 59%, IUGR 37%, fetal survival 89%

PATHOPHYSIOLOGY

- **Chronic renal failure**
  - Majority of the patients we are dealing with will have CRF
  - > 100 cases of ESRD/million population
  - Overall perioperative mortality 4%; morbidity 50% (hyperkalemia, infections, hTN / HTN, bleeding, dysrhythmias, clotted fistulas)
  - Most common causes include: **hypertensive sclerosis**, **DM nephropathy**, **chronic GN**, **PCKD, collagen vascular disease, pyelonephritis**
  - ESRD usually temporized with dialysis (PD or HD) each with their attendant concerns
    - HD: hypotension, AVF concerns, anemia, hypokalemia, myopathy, osteomalacia
    - PD: accelerated CAD, peritonitis, hypoalbuminemia
  - Renal Osteodystrophy: bone pathology characterized by bone demineralization. Result of hyperparathyroidism secondary to hyperphosphatemia combined with hypocalcemia, both of which are due to decreased excretion of phosphate by the damaged kidney. Low activated vitamin D_3 levels are a result of the damaged kidneys' inability to convert vitamin D_3 into its active form, calcitriol, and results in further hypocalcemia. Can get deposition of $CaPO_4$ in vessel wall & may see calciphylaxis (vascular calcification, thrombosis & skin necrosis seen in pts with Stage 5 CKD. Results in chronic non-healing wounds and is usually fatal)
    - Tx: Ca, Vit D suppl, restrict dietary PO_4, phosphate binders ($CaCO_3$ etc), HD, renal transpl.

- **Acute Renal Failure** is a concern with our ICU / sepsis / unstable patients
  - ARF exhibits rapid decline in function that is not immediately reversible (with volume, CO etc.) which usually presents with azotemia and oliguria (although oliguria is not always present)

- ARF is usually diagnosed by: increase in BUN and Cr in 24-72 hours
- **Etiology of ARF**:
  - Pre renal: kidney hypoperfusion
  - Renal: ATN from ischemia (50%) & nephrotoxins (35%), AIN and other nephrities (15%)
  - Post renal: urethral or bladder outlet obstruction
- Mortality for ARF is ~50% and treatment is mainly supportive
- If an underlying cause (GN) is found, specific treatment should be started
- Electrolytes should be monitored and kept within safe limits
- Dialysis can be used to treat / prevent complications (**volume overload / pulmonary edema, hyperkalemia despite maximum medical management, uremic bleeding diathesis or pericarditis, acidemia, and toxin accumulation, metabolic encephalopathy**)
- CVVHD / HF is hemodynamically better tolerated, but, does not improve mortality

- Know this chart for the MCQ exam:

Urinary Composition in Oliguria			
	Physiologic Oliguria	**Prerenal Failure**	**Acute Tubular Necrosis**
Urinary sodium	< 10 mEq/L	< 25 mEq/L	> 35 mEq/L
Urinary specific gravity	> 1.024	> 1.015	1.010–1.015
Urinary osmolality	> 700 mOsm/kg	> 500 mOsm/kg	< 350 mOsm/kg
Urinary / plasma osmolality	> 2.5:1	> 1.8:1	1.1:1
Urinary / plasma urea	> 100:1	> 20:1	3:1, rarely > 10:1
Urinary / plasma creatinine	> 60:1	> 30:1, rarely <10:1	< 10:1
Fractional sodium excretion	> 0.5	< 1	> 1

Metabolic Acidosis In Chronic Renal Failure				
	$PaCO_2$ (mmHg)	**pH**	**HCO_3^- (mEq/L)**	**K^+ (mEq/L)**
Preoperative	32	7.32	17	5.0
Intraoperative	40	7.25	18	5.3
Postoperative	44	7.21	19	5.6
	48	7.18	19	5.9

HCO_3^- = calculated bicarbonate; K^+ = serum potassium; $PaCO_2$ = arterial CO_2 tension

- Preoperatively, there is chronic metabolic acidosis (HCO_3^- 17 mEq/L) with partial respiratory compensation ($PaCO_2$ 32 mmHg, pH 7.32) and K^+ is high normal at 5.0 mEq/L
- Intraoperatively, "standard" mechanical minute ventilation with "normal" $PaCO_2$ (40 mmHg) which unmasks metabolic acidosis (pH 7.25) and K^+ climbs to 5.3 mEq/L
- Extubated at the end of the case, but metabolic acidosis remains unchanged
- With residual opioid-induced narcosis, moderate CO_2 retention occurs ($PaCO_2$ 44, 48 mmHg), pH falls further to 7.18, and a dangerous degree of hyperkalemia can develop (5.9 mEq/L)

TABLE #2 -- EMERGENCY TREATMENT OF HYPERKALEMIA

Mechanism	Treatment	Limitations
Antagonism of K effect on cell membranes	Calcium chloride, 1–2 g IV slowly	May exacerbate digitalis toxicity
Shift of K from extracellular to intracellular space	Mechanical hyperventilation	May induce hypotension
	Sodium bicarbonate, 50–100 mEq IV slowly	May induce pulmonary edema
	IV infusion of insulin 5 u,dextrose 50 g over 20 min	Short-lived (30–40 min)
Removal of K from body	Kayexalate (sodium polystyrene sulfonate) 0.5 g/kg PR	Exchanges for Na, may induce pulmonary edema
	Emergency peritoneal dialysis	Inefficient K removal, respiratory compromise
	Emergency hemodialysis	Hypotension, hemorrhage
IV = intravenous; K = potassium; NA = sodium; PR = per rectum.		

DRUGS PREDOMINANTLY DEPENDENT ON RENAL ELIMINATION	
Muscle relaxants:	gallamine, demethyltubocurarine (metocurine)
Antibiotics:	penicillins, cephalosporins, aminoglycosides, vancomycin
Cardiovascular drugs:	digoxin
Caveat: The loading dose is unaltered, but maintenance doses are drastically reduced.	

Alterations of Pharmacology:

DRUGS PARTIALLY DEPENDENT ON RENAL ELIMINATION	
Anticholinergic agents:	atropine, glycopyrrolate
Cholinergic agents:	neostigmine, pyridostigmine, edrophonium
Muscle relaxants:	pancuronium, pipecuronium, d-tubocurarine, vecuronium, doxacurium

Cardiovascular drugs:	milrinone, amrinone, amphetamines
Barbiturates:	phenobarbital
Caveat: The loading dose is unaltered, but maintenance doses should be decreased by 30–50%.	

DRUGS WITH ACTIVE OR TOXIC METABOLITES DEPENDENT ON RENAL EXCRETION		
Drug	Metabolites	Activity
Morphine	Morphine-3-glucuronide	Antanalgesic
	Morphine-6-glucuronide	Analgesic (40 × morphine)
Meperidine	Normeperidine	Neuroexcitatory
Diazepam	Oxazepam	Sedative
Midazolam	1-Hydroxy-midazolam	Sedative
Sodium nitroprusside	Thiocyanate	Neurotoxic
Enflurane	Fluoride	Nephrotoxic
Vecuronium	Desacetyl-vecuronium	Relaxant
Pancuronium	3-Hydroxy-pancuronium	Relaxant
Procainamide	n-Acetyl-procainamide (NAPA)	Neurotoxic
Caveat: These drugs should be avoided or used with caution in patients in renal failure.		

DRUGS WITH INCREASED UNBOUND FRACTION IN CHRONIC RENAL FAILURE	
Barbiturates:	thiopental, methohexital
Benzodiazepines	diazepam
Caveat: Decrease dosage 30%–50%.	

REFERENCES

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