EMERGENCIES IN RENAL FAILURE AND DIALYSIS PATIENTS

END-STAGE RENAL DISEASE IS THE IRREVERSIBLE LOSS OF RENAL FUNCTION THAT RESULTS IN THE ACCUMULATION OF TOXINS AND THE LOSS OF INTERNAL HOMEOSTASIS

URAEMIA → THE CLINICAL SYNDROME THAT RESULTS FORM ESRF, IS UNIVERSALLY FATAL WITHOUT SOME FORM OF RENAL REPLACEMNT THERAPY → EITHER DIALYSIS OR TRANSPLANT

NEARLY HALF OF NEW CASES OF ESRF ARE IN THOSE >65 AND THE MAJOR CAUSES ARE DIABETES AND HYPERTENSION

THE FIVE YEAR SURVIVAL RATE OF ESRF IS 35%, WITH MOST DEATHS BEING FROM CARDIAC DISEASE

PATHOPHYSIOLOGY OF URAEMIA:

- URAEMIA = CONTAMINATION OF THE BLOOD WITH URINE
- AZOTAEMIA → build up of nitrogen in the blood

CONSISTS OF EXCRETORY FAILURE, BIOSYNTHETIC FAILURE AND REGULATORY FAILURE:

- EXCRETORY FAILURE:
  - Leads to elevated levels of >70 chemicals
  - Limiting protein intake markedly improves symptoms of uraemia
  - Urea, the major breakdown product of proteins reproduces a few of the neurobehavioural uraemic symptoms → many others implicated
- BIOSYNTHETIC FAILURE:
  - Refers to aspects of uraemia caused by loss of renal hormones → cholecalciferol (vitamin D mediated calcium absorption → leads to decreased GI calcium absorption therefore leading to secondary hyperparathyroidism and renal bone disease) and EPO → anaemia (85% of EPO is produced in the kidneys)
- REGULATORY FAILURE:
  - Results in oversecretion of hormones → disruption of normal feedback mechanisms
  - Results in free oxygen radicals that accelerate atherosclerosis and amyloidosis

CLINICAL FEATURES OF URAEMIA:

- URAEMIA IS A CLINICAL SYNDROME → no single symptom, sign or lab value reflects all aspects (urea and creatinine are inaccurate markers of the syndrome of uraemia)
- Clinical features are outlined in the table below and then summarised thereafter:

Table 93-1 Clinical Features of Uremia and Dialysis
Neurologic
Uremic encephalopathy: cognitive defects, memory loss, decreased attentiveness, slurred speech, reversal of sleep-wake cycle, asterixis, seizure, coma, symptomatic improvement with dialysis
Dialysis dementia: progressive neurologic decline, failure to improve with dialysis, fatal
Subdural hematoma: headache, focal neurologic deficits, seizure, coma
Peripheral neuropathy: singultus (hiccups), restless leg syndrome, sensorimotor neuropathy, autonomic neuropathy
Cardiovascular
Coronary artery disease
Hypertension: essential hypertension, glomerulonephritis, renal artery stenosis, fluid overload
Heart failure: fluid overload, uremic cardiomyopathy, high-output arteriovenous fistula
Pericarditis: uremic, dialysis related, pericardial tamponade
Hematologic
Anemia, decreased red blood cell survival, decreased erythropoietin levels
Bleeding diathesis
Immunodeficiency (humoral and cellular)
GI
Anorexia, metallic taste, nausea, vomiting
GI bleeding
Diverticulosis, diverticulitis
Ascites
Renal bone disease
Metastatic calcification (calciphylaxis)
Hyperparathyroidism (osteitis fibrosa cystica)
Vitamin D_3 deficiency and aluminum intoxication (osteomalacia)

NEUROLOGIC COMPLICATIONS OF URAEMIA:

- STROKE OCCURS IN ~6% OF HAEMODIALYSIS PATIENTS → most ICH
    - Subdural occurs 10x more frequently in dialysis patients than in general population → consider in any ESRF patient with altered mental state
- URAEMIC ENCEPHALOPATHY → constellation of nonspecific central neurologic symptoms that respond to dialysis → DIAGNOSIS OF EXCLUSION
- DIALYSIS DEMENTIA → 4% of dialysis patients → progressive and eventually fatal (unlike uraemic encephalopathy)
- PERIPHERAL NEUROPATHY → one of the most frequent manifestations in ESRF (60-100%) poorly responsive to dialysis but can be reversed by transplantation

CARDIOVASCULAR COMPLICATIONS OF URAEMIA:

- Mortality from cardiovascular disease is 10-30x higher in dialysis patients than in the general population → high prevalence of IHD, and CCF (~40%)
- Aetiology is multifactorial → HT, DM, uraemia, dialysis related hypotension all contribute

- The diagnosis of ischaemia in ESRF patients often has been clouded by misconception that the traditional serum markers of myocardial damage are unreliable in dialysis patients → TROPONIN IS NOT SIGNIFICANTLY ELEVATED IN THOSE REGULARLY UNDERGOING DIALYSIS
- HT is very common → 80-90%. Management begins with control of blood volume (i.e. dialysis) and add ACE-I
- CCF → most commonly results form HT → IHD → valvular problems
    - Causes unique to dialysis population → uraemic cardiomyopathy, fluid overload, AV fistula-related high output failure
    - Pulmonary oedema is commonly ascribed to fluid overload, but other causes should always be investigated → AMI can lead to APO even BELOW DRY WEIGHT. Diuretics can still be effective, even with minimal urine output. Dialysis is the ultimate treatment for fluid overload.
- CARDIAC TAMPONADE → complication of uraemic pericarditis → rarely present with classic Beck's triad → consider in those with altered mental state, hypotension or SOB
- PERICARDITIS → usually due to uraemia and occurs in 20% of patients requiring chronic dialysis. Can get dialysis-related pericarditis (less common). Uraemic pericarditis has been linked to fluid overload, platelet dysfunction and increased fibrinolysis. INFLAMMATORY CELLS DO NOT PENETRATE THE MYOCARDIUM IN URAEMIC PERICARDITIS, HENCE TYPICAL ECG CHANGES ARE ABSENT! Mortality rates for ESRF patients with pericarditis are as high as 8% and average survival without dialysis is ~one month → management is INTENSIVE DIALYSIS, with other standard treatments being of questionable value.

HAEMATOLOGIC COMPLICATIONS:

- ANAEMIA → multifactorial → ↓EPO, blood loss form dialysis/phlebotomy, ↓red cell survival time. Treated with regular recombinant EPO
- BLEEDING DIATHESIS → produces ↑d risk of subdural, GIT bleeding → ↓d platelet function, abnormal platelet-vessel wall interactions, altered vWF all contribute to uraemic bleeding. Bleeding risk increased by taking warfarin and aspirin. Bleeding time can be improved with DESMOPRESSIN, CRYOPRECIPITATE AND EPO.
- IMMUNOLOGIC DEFICIENCY → results in high morbidity and mortality → leukocyte chemotakxis and phagocytosis are depressed in uraemic patients secondary to anaemia, malnutrition and zinc/selenium/vitamin deficiency
    - Dialysis does not appear to improve immune function and may even exacerbate by complement loss

GI COMPLICATIONS:

- Anorexia, N+V are common symptoms of uraemia → there is an increased incidence of gastritis and UGI bleeding in ESRF with higher mortality rates
- Chronic constipation is common → decreased fluid intake combined with phosphate binders

- Increased rate of diverticular disease and colonic perforation → especially those with polycystic kidneys

RENAL BONE DISEASE:

- SYSTEMIC CALCIFICATION → as GFR ↓s ➔phosphate excretion falls and thus when the calcium-phosphate product is higher than 4 → risk of METASTATIC CALCIFICATION INCREASES → RESULTS in skin and finger necrosis with life-threatening calcification within the cardiac and pulmonary system → treat with low-calcium dialysate and phosphate binders
- HYPERPARATHYROIDISM ➔ combination of calciphylaxis an dvitamin D deficiency results in DEPRESSED IONISED CALCIUM → STIMULATION OF PARATHYROID GLAND → results in high burn turnover → weakened bones that are highly susceptible to fracture → can be treated with vitamin D replacement and parathyroidectomy.
- ALUMINIUM INTOXICATION → rare but can come from dialysate diluent and phosphate-binding gels. Can be treated with desferrioxamine.
- BETA-2 MICROGLOBULIN AMYLOIDOSIS → chronic inflammatory state

HAEMODIALYSIS AND ITS COMPLICATIONS

HAEMODIALYSIS SUBSTITUTES A HAEMODIALYSER FILTER FOR THE GLOMERULUS TO PRODUCE AN ULTRAFILTRATE OF PLASMA

COMPLICATIONS OF VASCULAR ACCESS:

- The fistula can of NATIVE VESSEL vs GRAFT → grafts have higer complication rates and shorter functional life expectancies. Other form of access is TUNNELED CATHETERS (permacath, vascath, Hickman)
- Complications of vascular access account for more inpatient hospital days than does any other complication of haemodialysis!
- FAILURE TO PROVIDE ADEQUATE FLOW (<300mL/min):
    - THROMBOSIS AND STENOSIS → most common causes
        - Grafts have higher rate of stenosis than do fistulas
        - Both present with LOSS OF BRUIT AND THRILL OVER THE ACCESS
        - Can be treated with angiographic clot removal or angiography
- VASCULAR ACCESS INFECTIONS:
    - Occur in 2-5% of fistula and ~10% of grafts
    - Patients present with systemic sepsis without classic signs of pain, erythema, swelling and discharge from the access site
    - Dialysis-catheter-related bacteraemia is very common and potentially life-threatening (after 6 months in situ ~48% patients develop bacteraemia) → a serious complication occurs in 5-10% (death, endocarditis, osteomyelitis, septic arthritis, epidural abscess)
        - Most authorities recommend a trial of IV antibiotics over catheter-removal followed by removal if fever persists for 2-3 days

        - Staph aureus most commonly → cover with VANCOMYCIN (long-half life of 5-7 days in dialysis, give 1g IV or 15mg/kg). Add an aminoglycoside if gram-negative organisms are suspected
- HAEMORRHAGE:
    - Rare but potentially life-threatening
    - Can result from aneurysms, anastomosis rupture and over-anticoagulation
    - Control immediately with point-pressure for 5-10 minutes
    - Aneurysms result form repeated punctures (most are pseudoaneurysm that result from subcutaneous extravasation of blood from puncture sites → signs are bleeding and infection at the access site)
- VASCULAR INSUFFICIENCY OF THE LIMB DISTAL TO THE ACCESS SITE:
    - Occurs in ~1%
    - This "steal syndrome" is result of preferential shunting of arterial blood away from nutrient arteries to the low-pressure venous side of the access
    - Signs/symptoms are exercise pain, nonhealing ulcers, cool/pulseless digits
    - Diagnosed by US → operative repair indicated
- HIGH OUTPUT CARDIAC FAILURE → can occur when >20% of the cardiac output is diverted through the access

COMPLICATIONS <u>DURING</u> HAEMODIALYSIS:

- HYPOTENSION → most frequent complication and occur during 20-30% of treatments. Maintenance of normal blood pressure is dependent on CV compensatory mechanisms and refilling the vascular space by fluid shifts from the interstitial and intracellular compartments. EXCESSIVE ULTRAFILTRATION due to underestimation of the patient's ideal blood volume (dry weight) is the most common causes of intradialytic hypotension. Refilling of the vascular tree can be inhibited by hypoalbuminaemia and concurrent removal of solutes with ultrafiltration

Table 93-3 Differential Diagnosis of Peridialytic Hypotension
Excessive ultrafiltration
Predialytic volume loss (GI losses, decreased oral intake)
Intradialytic volume loss (tube and hemodialyzer blood losses)
Postdialytic volume loss (vascular access blood loss)
Medication effects (antihypertensives, opiates)
Decreased vascular tone (sepsis, food, dialysate temperature >37°C or 98.6°F)
Cardiac dysfunction (left ventricular hypertrophy, ischemia, hypoxia, arrhythmia, pericardial tamponade)
Pericardial disease (effusion, tamponade)

- The TIMING of intradialytic hypotension is often helpful in formulating a differential diagnosis
    - If early → usually due to pre-existing hypovolaemia
    - If late → usually the result of excessive ultrafiltration, but pericardial or cardiac disease is still a possibility. Give saline bolus and reassess
    - When patient is transferred to ED, assess for immediate and potential life-threats
        - ASSESS FOR ADEQUACY OF VOLUME STATUS, IMPAIRMENT OF CARDIAC FUNCTION , PERICARDIAL DISEASE, INFECTION AND GI BLEEDING
- DIALYSIS DISEQUILIBRIUM → **RARE** → N+V THAT CAN PROGRESS TO SEIZURE, COMA AND DEATH. Need to distinguish from other CNS disorders and is believed to be due to CEREBRAL OEDEMA from an osmolar imbalance between the brain and the blood ➔ treat with IV mannitol and stop dialysis
- AIR EMBOLISM → always a risk when blood is pumped through and extracorporeal circuit
    - If patient sitting → goes to cerebral circulation → ↑ICP and neurologic symptoms
    - If patient recumbent → air goes to right ventricle and pulmonary circulation → pulmonary HT and systemic hypotension.
    - Can lodge in pulmonary circulation
    - Symptoms are acute SOB, chest tightness, altered consciousness and sometimes → cardiac arrest
    - Treat by clamping the venous blood line and placing patient supine → traditionally in Trendelenburd with left side down → no specific benefit
        - Apply 100% O2
- ELECTROLYTE ABNORMALITIES → can occur due to errors in mixing the dialysate concentrate with water → lead to rapid osmolar shifts
- HYPOGLYCAEMIA ➔ drugs, malnutrition, sepsis all can contribute → significant mortality associated

ED EVALUATION OF HAEMODIALYSIS PATIENTS:

- Patients treated with haemodialysis may develop complications related to ESRF or form dialysis or these conditions may be coincidental to their presentation
- Main questions to ask are outlined below:

Table 93-4 Key Historical Elements for Hemodialysis Patients
Cause of end-stage renal disease
Dialysis schedule: any missed dialysis sessions?
Recent complications of hemodialysis
Dry weight, baseline laboratory values, and vital sign values
Average intradialytic weight gain
Does patient usually make dry weight by end of hemodialysis?
Does patient experience intradialysis hypotension? (Timing of hypotension?)
Which vascular access is currently functioning?
Symptoms of uremia
Retention of native kidneys?
Still producing urine?

- Repeated episodes of intradialytic hypotension may provide important early clues to pericardial tamponade or myocardial ischaemia
- EXAMINATION → always examine the access point and cardiac exam deserves special notice (see below) → NB Branham sign is suggestive of high output failure and relates to decrease in HR with occlusion of vascular access

Table 93-5 Key Elements of Physical Examination of Hemodialysis Patients
Vital signs
Vascular access: bruit, thrill, erythema, warmth, swelling, tenderness, discharge, bleeding, Branham sign
Cardiac: signs of heart failure, murmurs, muffled (distant) heart sounds
Neurologic: mental status changes, peripheral neuropathy, asterixis

PERITONEAL DIALYSIS AND ITS COMPLICATIONS:

- In PD, the peritoneal membrane is the blood-dialysate interface and the amount of ultrafiltration is determined by osmotic pressure differences between the blood and dialysis → manipulated by altered the dialysate-fluid glucose concentration
- Typical PD regimens use four exchanges daily, instilling 2L and draining a few hours later (CAPD) vs multiple exchanges at night → continuous cyclic PD

COMPLICATIONS OF CAPD:

- PERITONITIS ➔ most common complication of PD → incidence is about one episode every 15-18 patient months → mortality ranges form 2.5-12.5%
    - Symptoms/signs similar to anyone else with peritonitis → fever, abdominal pain and rebound tenderness
    - CLOUDY EFFLUENT suggests the diagnosis → send for gram stain, cell count and culture → cell count is usually >100 leukocytes/mm3 with >50% neutrophils. Results of gram-staining are positive in 10-40% → Staph epidermidis (40%), S aureus (10%), strep, gram negative and fungi (5%)
    - EMPIRIC THERAPY STARTS WITH RAPID EXCHANGE TO DILUTE NUMBERS OF MICRO-ORGANISMS
        - Intraperitoneal administration is preferred and systemic antibiotics NOT REQUIRED as reasonable absorption is achieved
    - CONSIDER SURGICAL CAUSE OF PERITONITIS (I.E. PERFORATION)
    - INDICATIONS FOR REMOVAL OF CATHETER:

Indications for catheter removal include:

- refractory peritonitis (failure to respond to appropriate antibiotics within 5 days)
- relapsing peritonitis
- refractory exit-site and tunnel infection
- fungal peritonitis.

Also, consider catheter removal if not responding to therapy in cases due to mycobacteria or multiple enteric organisms.

Vancomycin is not generally recommended for empirical therapy because of concerns with the development of vancomycin-resistant enterococci. Although many coagulase-negative staphylococci test resistant to cephalosporins in the laboratory, outcomes of clinical treatment with cephazolin are usually satisfactory.

If **Gram-positive organisms** are seen in the dialysate, use:

cephazolin (adult and child) 15 mg/kg added to 1 bag per day (intermittent)
or cephazolin (adult and child) 500 mg/L as a loading dose in the initial bag, then 125 mg/L (continuous with each bag exchange).

If the patient is colonised with methicillin-resistant *S. aureus* or there is evidence of systemic sepsis, and in patients with immediate hypersensitivity to penicillin (see Table 2.2), instead of cephazolin, use:

vancomycin 2 g (child: 50 mg/kg up to 2 g) added to 1 bag every 5 to 7 days (intermittent)
or vancomycin (adult and child) 1 g/L as a loading dose in the initial bag, then 25 mg/L (child: 30 mg/L) (continuous with each bag exchange).

If **Gram-negative organisms** are seen in the dialysate, use:

gentamicin (adult) 0.6 mg/kg up to 50 mg added to 1 bag per day (intermittent)
or gentamicin (adult and child) 8 mg/L as a loading dose in the initial bag, then 4 mg/L (continuous with each bag exchange) to a maximum of 40 mg/day.

If the Gram stain is not helpful, use gentamicin plus cephazolin (see above for dosages).

There is no convincing evidence that short courses of aminoglycosides harm residual renal function. However, an alternative to gentamicin for patients who are not anuric, in an effort to preserve residual renal function, is:

ceftazidime 1 to 1.5 g (child: 15 mg/kg up to 1 g) added to 1 bag per day (intermittent)
or ceftazidime 500 mg/L (child: 250 mg/L) as a loading dose in the initial bag, then (adult and child) 125 mg/L (continuous with each bag exchange).

If diverticular disease or bowel involvement is suspected, **add** to all of the above regimens:

metronidazole 500 mg (child: 12.5 mg/kg up to 500 mg) IV, 12-hourly
or metronidazole 400 mg (child: 10 mg/kg up to 400 mg) orally, 12-hourly.

ED EVALUATION OF PERITONEAL DIALYSIS PATIENTS:

Table 93-6 Key Historical Elements for Peritoneal Dialysis Patients
Cause of end-stage renal disease
Type of peritoneal dialysis (continuous ambulatory peritoneal dialysis vs. continuous cyclic peritoneal dialysis)
Peritoneal dialysis parameters: concentration, number of exchanges per day
Recent complications of peritoneal dialysis
Baseline weight, laboratory values, and vital sign values
Symptoms of uremia
Retention of native kidneys?
Still producing urine?

Table 93-7 Key Elements of Physical Examination of Peritoneal Dialysis Patients
Abdominal examination: inspection for hernia, auscultation of bowel sounds, test for rebound tenderness
Peritoneal catheter: examination of surrounding skin, palpation of tunnel

- DATE OF LAST EPISODE OF PERITONITIS IMPORTANT, AS FREQUENT RELAPSES MAY SUGGEST FUNGAL PERITONITIS OR TUNNEL INFECTION