Approach to Common Problems in Dialysis Patients

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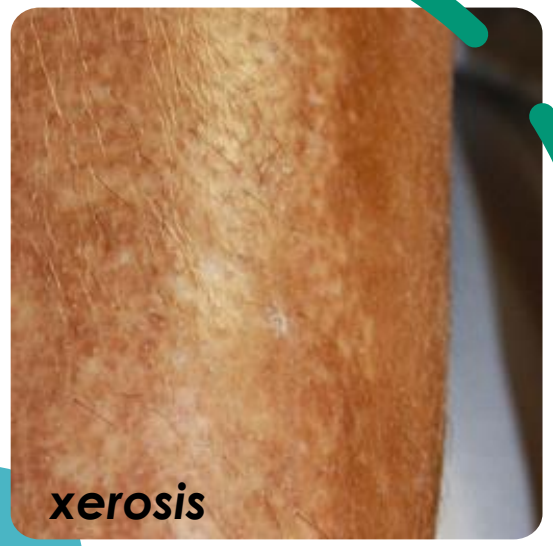
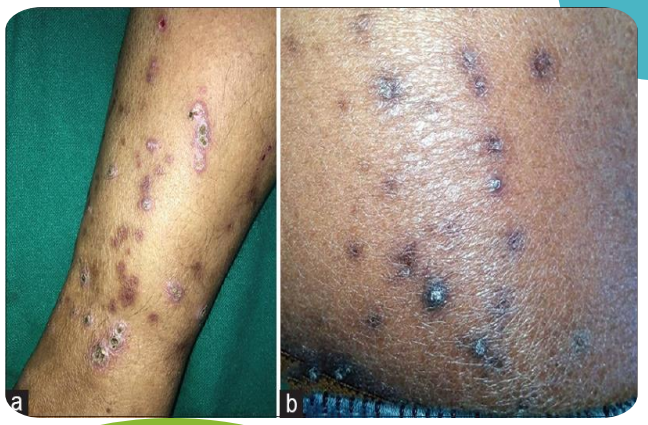
Uraemic pruritus

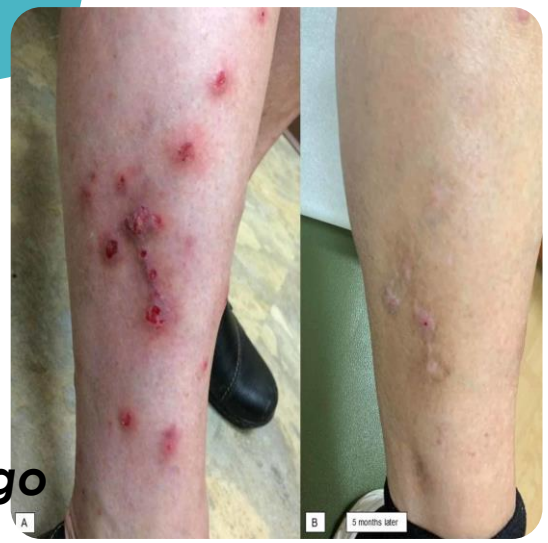
Scratch marks with linear excoriation



xerosis



Nodular prurigo



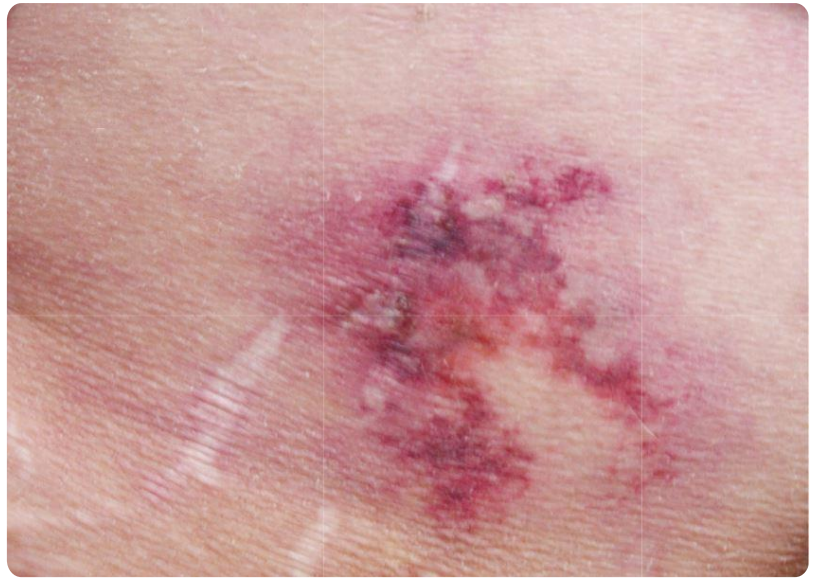
- Prevalence varies over the years
  - 1980 – 1993: 50 to 93%; 2000s: 22 – 57%
  - 1996 – 2001: extreme pruritus 28%; 2012 – 2015: 18%
- Poor sleep and a 15% higher mortality risk
- Pathophysiology is poorly understood
  - <u>*Immunologic*</u>
    - Systemic inflammation
    - Higher proinflammatory TH1 cells, IL6 and IL2
  - <u>*Opioidergic*</u>
    - Opioid mu-receptor activation and kappa-receptor blockade
  - Other contributing factors
    - Histamine release from mast cells, other pruritogens and xerosis
- Risk factors:
  - Inadequate dialysis, hyperparathyroidism, elevated CaxPO4 product, xerosis, elevated magnesium and aluminium concentration
- Differentials: lymphoma, cholestasis, hypersensitivity reactions

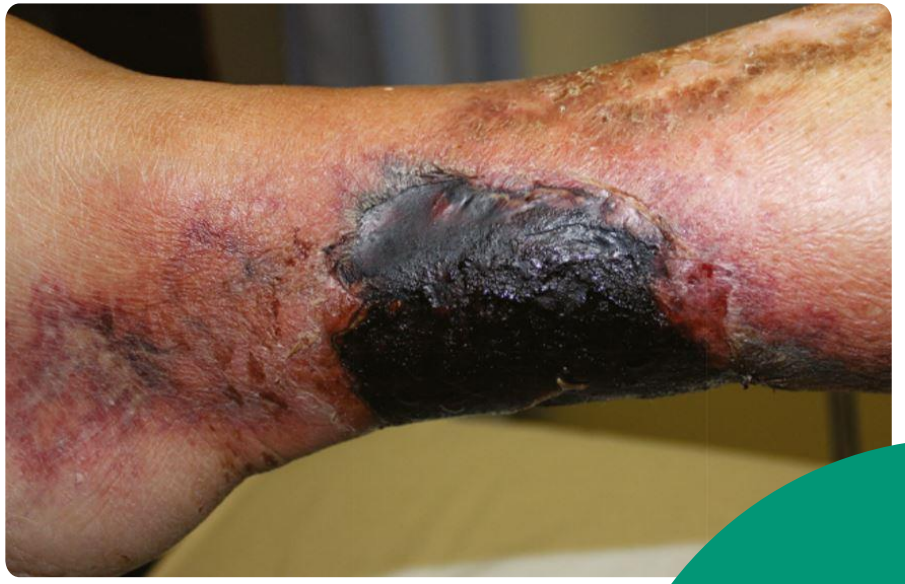
Uraemic Pruritus - Management

- Optimal dialysis treatment
- Optimal treatment of hyperparathyroidism and hyperphosphatemia
- Regular use of emollients and/or topical analgesics
  - Water content emollient: cetomacrogol + glycerol 10%
  - Capsaicin 0.025% for localised itch (*but, only funded for osteoarthritic pain*)
- *Resistant pruritus*
  - Gabapentin (max 300mg 3x/week) or pregabalin (max 75mg daily)
  - Oral anti-histamines
  - Sertraline 50mg daily
  - Montelukast 10mg daily
- *Refractory pruritus*
  - UVB phototherapy
  - Experimental:
    - Dupilumab - *a human monoclonal antibody*
    - Naltrexone: *opioid antagonist*
    - Difelikefalin: *kappa opioid receptor agonist*
    - Nalbuphine & Butorphanol: *mixed mu-antagonist/kappa-agonist*

Calciphylaxis (calcific uremic arteriolopathy)

- Rare and serious disorder
- Skin ischemia and necrosis
  - Histology: calcification of arterioles and capillaries in the dermis and subcutaneous adipose tissue
- Pathophysiology is poor understood. Factors involved
  - Mineral bone disorder and its treatment
  - Deficiencies of the inhibitors of vascular calcifications, and
  - Chronic inflammation
- Associated risk factors
  - **Warfarin use**, steroid use, obesity, diabetes, **recurrent skin trauma**, female, hypoalbuminaemia, longer dialysis vintage, inflammatory and autoimmune conditions, **hyperphosphatemia**, and **high PTH levels**
- ***High index of suspicion with following clinical features:***
  - *Painful subcutaneous nodules or plaques*
  - Non-healing ulcers
  - Cutaneous necrosis, particularly when present on the thigh and other areas of increased adiposity.
- Differential diagnosis:
  - atherosclerosis, embolization, warfarin necrosis, vasculitis, purpura fulminans, antiphospholipid antibody syndrome, radiation arteritis, Martorell hypertensive ischemic ulcer





Calciphylaxis – Management is multimodal

- Wound care and pain management
- Treatment of infected wounds
- Treatment of mineral bone disorder
  - Avoid parathyroidectomy unless tertiary
  - Avoid vitamin D analogs
  - Avoid calcium-based phosphate binders (use aluminum-based)
  - Cinacalcet (expensive, and funded only if calcium level > 3 mmol/L)
    - Avoid excessive suppression of PTH to prevent adynamic bone disease which may predispose patients to vascular calcification
- Warfarin cessation
- Dialysis optimization (not necessary)
- Vitamin K (limited evidence, but cheap)
- Sodium thiosulphate (limited evidence and expensive)
- Bisphosphonates (limited evidence)
- Hyperbaric oxygen therapy (limited evidence and expensive)

Sleep Disturbances

- Disruption of sleep-wake cycle is a characteristic feature of uraemia with both excessive daytime sleepiness and insomnia noted in clinical studies

- Daytime sleepiness: 30 to 67%

- Insomnia: 50 to 73%

Sleep Apnoea

- Prevalence 50% in ESKD, whereases 2 – 4 % in the middle-aged US population

- Pathophysiology
  - **Upper airway occlusion** from pharyngeal narrowing
    - volume overload
    - impaired upper airway muscle tone resulting from uraemic neuropathy
  - **Impairment of central ventilatory control**
    - a consequence of hypocapnia resulting from adaption to chronic metabolic acidosis

Sleep Apnoea - Management

- Epworth Sleepiness Score and Sleep Clinic referral
- CPAP
- Improved control of uraemia and fluid overload with nocturnal HD
- Kidney transplantation if suitable
- Weight loss if obese

Restless Leg Syndrome

- Prevalence 10 – 30%
- Impairs quality of life and an increased risk of all-cause mortality or dialysis withdrawal
- Disrupted dopaminergic function in the brain
- Risk Factors:
  - caffeine, antidepressants except bupropion, antipsychotics, dopamine-blocking antiemetics or centrally acting antihistamines

Restless leg syndrome - Management

- Lifestyle modifications: good sleep hygiene; exercise, walking, elimination of caffeine, nicotine, alcohol and antidepressant medications
- Iron infusion to replenish iron stores
- 1st line: Gabapentin (enacarbil) or Pregabalin
- 2nd line (dopaminergic therapy):
  - Ropinirole (max dose 4mg/day)
  - Pramipexole (max dose 0.75mg/day)
  - Pergolide
  - Levodopa (risk augmentation / avoid if used long term)
- Benzodiazepines for intermittent symptoms
- Rotigotine a non-ergot dopamine agonist – a 24h transdermal patch (not available in NZ)
- Renal transplantation

Periodic Limb Movements of Sleep

- Sudden and repetitive jerking movements of the lower extremities ***during sleep***
- Common, and associated with day time sleepiness and low quality of life, and an increased mortality
- Management is the same as that of RLS

Leg cramps

- Prevalence 35 – 86% of haemodialysis patients
- 74% during dialysis session, especially toward the end of a session

- Exact cause is unknown, but associated with:
  - Excessive ultrafiltration (UF)
  - Intradialytic hypotension
    - Multiple antihypertensive medications, incorrect dry weight, excessive UF within a short dialysis session, poor cardiac function
  - Electrolyte imbalances
    - Hyponatraemia, hypomagnesaemia, hypercalcaemia
    - Elevated PTH levels
    - L-carnitene deficiency
    - Vitamin C deficiency

Leg cramps – Management

- Assessment: structural foot/leg disorders, peripheral vascular disease, iron deficiency, electrolytes disturbances, statin use, hypothyroidism

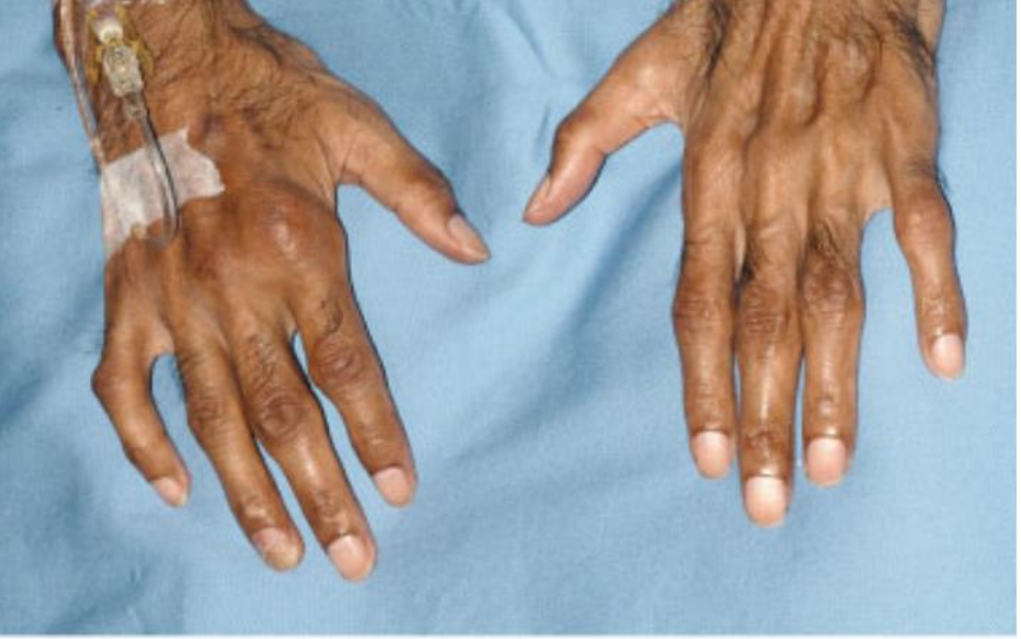
- Non-pharmacological strategies:
  - Daily stretch, stretch and light exercise before bedtime and haemodialysis treatment
  - Limit alcohol and caffeine
  - Wear comfortable shoes with proper support
  - Massage and stretch the cramped muscle
  - Avoid/easing during dialysis: low intensity exercise (e.g.. stationary bike) during dialysis, minimize inter-dialytic weight gain and intradialytic hypotension

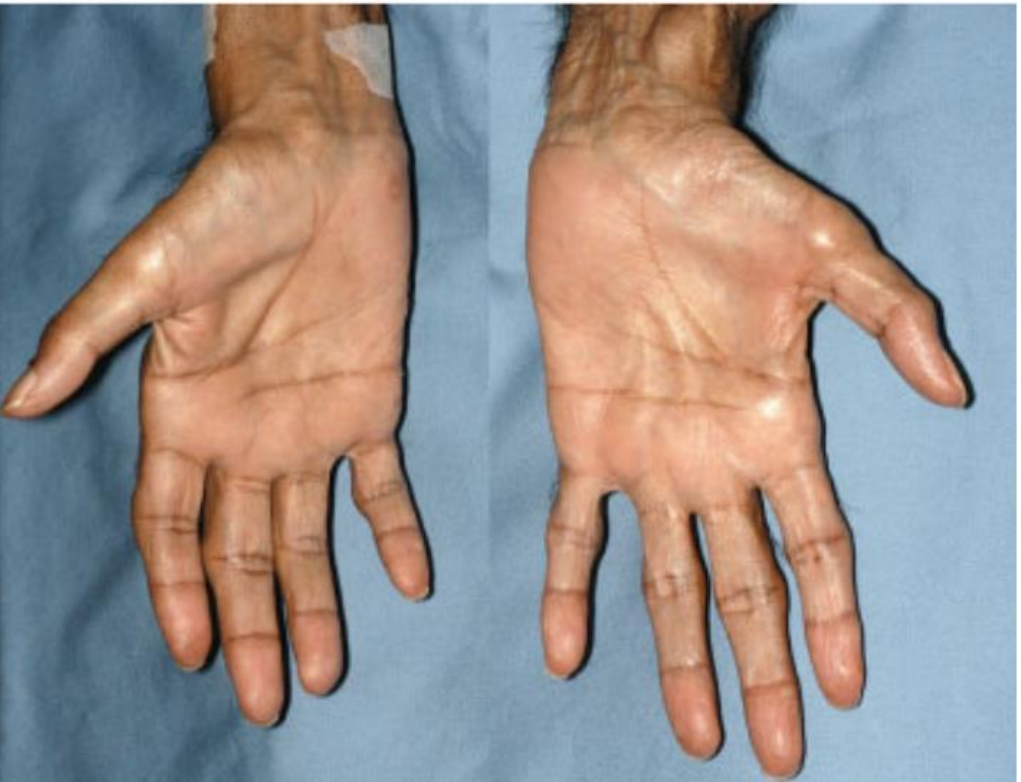
- Pharmacological options:
  - Vitamin E 400 IU daily (Clinicians renal vit does not contain vitamin E)
  - Gabapentin (up to 300m 3x/week)

- Avoid Quinine

Uraemic Polyneuropathy

- A distal, symmetrical, mixed sensorimotor neuropathy that is characterized by initial axonal degeneration followed by demyelination
- Often subclinical and detectable only by electrophysiologic studies
  - 60 – 100% have positive nerve conduction studies
  - 10% are symptomatic
  - Men > Women
- Contributing factors: deficiencies of thiamine, zinc, and biotin; increases in phenols, myoinositol, beta2-microglobulin and other middle-molecular-weight substances
- Clinical features: initially sensory symptoms include paraesthesia in a glove- and stocking distribution followed by motor weakness, areflexia and loss of vibratory sense
- Increased risk for developing foot ulcers
- Differential diagnosis: diabetes mellitus, SLE, vasculitides, multiple myeloma, amyloidosis, etc.





Uraemic polyneuropathy - Management

- Optimize dialysis treatment otherwise transplantation
- Gabapentin/pregabalin first, and then +/- TCA
- Proper foot and nail care

Atrial fibrillation

- Prevalence
  - 9 – 35 % of patients on HD
  - 7 % in patients on PD
  - 1 % age < 60 and 8% age > 80 in general population
- Anticipated mortality is doubled and the stroke risk is increased by +/- 6 fold
- CHA_2DS_2-VASc and HAS-BLED scoring systems
  - CrCl > 30: OK
  - CrCl 15 – 30: less robust, but the benefit outweighs the risk in most cases
  - CrCl < 15 not on dialysis: minimal data; treated as if patients in CKD stage 4
  - Dialysis patients: no evidence, risks and benefits are carefully assessed

Atrial fibrillation - Anticoagulation

- CrCl > 30: NOAC or warfarin (warfarin for mechanical heart valves)
- CrCl 15 – 30: Rivaroxaban 15mg daily or warfarin
- CrCl < 15, not on dialysis: Warfarin
- Dialysis:
  - Generally avoided (continue if already on warfarin before dialysis was started)
  - Give in high risk patients
    - mechanical heart valve, thrombotic events and cardio-embolic events
  - Warfarin only at this point, as apixaban is not available (? rivaroxaban 10mg)

Hypertension

- 50 – 60 % in HD and 30% in PD

- Volume expansion is the major cause
- Contributing factors: sympathetic overactivity, activation of RAS, arteriosclerosis, medications
  - Medications: Erythropoiesis-stimulating agents, OTC drugs include nasal decongestants, NSAIDs, illicit drugs, herbal remedies such as ma-huang and St. John's wort

- Target BP at midweek or interdialytic home BP < 140/80 mmHg

Hypertension – Management

- Fluid restriction to minimise interdialytic weight gain
- Salt restriction to 2 – 3g/day

- Avoid adding or starting an anti-hypertensive agent if volume overloaded, unless significantly hypertensive
  - Furosemide 250mg OD to BD if urine output > 200ml/day

- 1st line: B-blocker (carvedilol, but depending on circumstances)
- 2nd line: Dihydropyridine calcium-channel blocker (amlodipine)
- 3rd line: RAS blockade (ARB is preferred)
- 4th line: ? Mineralocorticoid receptor antagonist