ACUTE AND CHRONIC PYELONEPHRITIS, NEPHROLITHIASIS, ACUTE AND CHRONIC RENAL FAILURE

Acute pyelonephritis

Symptoms
Develops quickly over an interval lasting from hours to a day. Fever with shaking chills, vomiting, diarrhea. Marked tenderness on deep pressure in one or both costovertebral angles or on deep abdominal palpation.

Diagnosis
- Urine cultures $\geq 10^5$ bacteria/mL of urine.
- Bacteriuria from suprapubic aspirates or $\geq 10^2$ bacteria/mL of urine.
- The presence of bacteria in Gram-stained uncentrifuged urine indicates infection and correlates with $\geq 10^5$ bacteria/mL in urine cultures.
- Urinalysis:
  - Pyuria is a highly sensitive indicator of infection.
  - Leukocyte esterase “dipstick” positivity is useful when microscopy is not available.
  - Pyuria without bacteriuria may indicate infection with unusual organisms such as C. trachomatis or Mycobacterium tuberculosis or may be due to noninfectious causes such as calculi.
  - Leukocyte casts are pathognomonic of acute pyelonephritis.

Specific recommendations
- Acute pyelonephritis in pregnancy should be managed with hospitalization and parenteral antibiotic therapy.
- Urologic evaluation should be considered in patients with relapsing infection, a history of childhood infection, stones, or painless hematuria and in women with recurrent pyelonephritis.
- Most men with UTIs should have a urologic evaluation.
- Anyone with signs or symptoms of obstruction or stones should undergo prompt urologic evaluation.

Treatment

Principles
A quantitative urine culture with susceptibility testing should precede empirical treatment. Factors predisposing to infection should be identified and corrected if possible (nephrolithiasis, diabetes). Most community-acquired infections are due to antibiotic-sensitive strains, despite increasing antibiotic resistance. Antibiotic-resistant infections should be suspected in patients with recurrent infections, instrumentation, or recent hospitalization.

Antibiotic treatment

<table>
<thead>
<tr>
<th>Condition</th>
<th>Characteristic pathogens</th>
<th>Mitigating circumstances</th>
<th>Recommended empirical treatment</th>
</tr>
</thead>
</table>

1
Acute uncomplicated pyelonephritis in women

<table>
<thead>
<tr>
<th>Pathogens</th>
<th>Course</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. coli, P. mirabilis, S. saprophyticus</td>
<td>Mild to moderate illness, no nausea or vomiting: outpatient therapy</td>
<td>Oral quinolone for 7–14 d (initial dose given IV if desired); or single-dose ceftriaxone (1 g) or gentamicin (3–5 mg/kg) IV followed by oral TMP-SMX for 14 days</td>
</tr>
<tr>
<td>Severe illness or possible urosepsis: hospitalization required</td>
<td>Parenteral quinolone, gentamicin (± ampicillin), ceftriaxone, or aztreonam until defervescence; then oral quinolone, cephalosporin, or TMP-SMX for 14 days</td>
<td></td>
</tr>
</tbody>
</table>

Complicated UTI in men and women

<table>
<thead>
<tr>
<th>Pathogens</th>
<th>Course</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. coli, Proteus, Klebsiella, Pseudomonas, Serratia, enterococci, staphylococci</td>
<td>Mild to moderate illness, no nausea or vomiting: outpatient therapy</td>
<td>Oral quinolone for 10–14 days</td>
</tr>
<tr>
<td>Severe illness or possible urosepsis: hospitalization required</td>
<td>Parenteral ampicillin and gentamicin, quinolone, ceftriaxone, aztreonam, ticarcillin/clavulanate, or imipenem-cilastatin until defervescence; then oral quinolone or TMP-SMX for 10–21 days</td>
<td></td>
</tr>
</tbody>
</table>

Prognosis
Repeated symptomatic UTIs with obstructive uropathy, neurogenic bladder, structural renal disease, or diabetes progress to chronic renal disease with high frequency.

Special forms
- Papillary necrosis
- Emphysematous pyelonephritis

Nephrolithiasis
Affects ~1% of the population, and recurrent in more than half of patients. Stone formation begins when urine becomes supersaturated with insoluble components due to:
- low urinary volume, or
- excessive or insufficient excretion of selected compounds, or
- other factors (e.g., urinary pH) that diminish solubility.

Composition
- ~75% Ca-based (the majority Ca oxalate; also Ca phosphate and other mixed stones)
- 15% struvite (magnesium-ammonium-phosphate)
- 5% uric acid
- 1% cystine, reflecting the metabolic disturbance(s) from which they arise.

Signs and symptoms
Stones in the renal pelvis:
- asymptomatic or cause hematuria alone
- with passage, obstruction may occur at any site along the collecting system.
Obstruction related to the passing of a stone leads to:

- severe pain, often radiating to the groin, sometimes accompanied by intense visceral symptoms (i.e., nausea, vomiting, diaphoresis, light-headedness)
- hematuria, pyuria, urinary tract infection (UTI), and,
- rarely, hydronephrosis.

Staghorn calculi, associated with recurrent UTI with urea-splitting organisms (Proteus, Klebsiella, Providencia, Morganella, and others), may be completely asymptomatic, presenting with loss of renal function.

**Calcium stones**
Mostly Ca oxalate.

- Hypercalciuria: very high-Na diet, loop diuretic therapy, distal (type I) renal tubular acidosis (RTA), sarcoidosis, Cushing’s syndrome, aldosterone excess, or conditions associated with hypercalcemia (e.g., primary hyperparathyroidism, vitamin D excess, milk-alkali syndrome), idiopathic.
- Hyperoxaluria: intestinal (especially ileal) malabsorption syndromes (e.g., inflammatory bowel disease, pancreatitis), due to reduced intestinal secretion of oxalate and/or the binding of intestinal Ca by fatty acids within the bowel lumen, with enhanced absorption of free oxalate and hyperoxaluria.
- Deficiency of urinary citrate, an inhibitor of stone formation that is underexcreted with metabolic acidosis
- Hyperuricosuria

Ca phosphate - much less common

- Abnormally high urinary pH (7–8), usually in association with a complete or partial distal RTA.

**Uric acid stones**

- Develop when the urine is saturated with uric acid in the presence of an acid urine pH
- Underlying metabolic syndrome and insulin resistance, associated with a relative defect in ammoniagenesis and urine pH that is <5.4 and often <5.0
- Myeloproliferative disorders (esp. after treatment with chemotherapy), gout, acute and chronic renal failure, and following cyclosporine therapy
- Hyperuricosuria without hyperuricemia: certain drugs (e.g., probenecid, high-dose salicylates).

**Struvite stones**

- Form in the collecting system when infection with urea-splitting organisms is present.
- Are the most common components of staghorn calculi and obstruction.
- Risk factors: previous UTI, nonstruvite stone disease, urinary catheters, neurogenic bladder (e.g., with diabetes or multiple sclerosis), and instrumentation.

**Cystine stones**

- Rare inherited defect in renal and intestinal transport of several dibasic amino acids
- The overexcretion of cystine (cysteine disulfide), which is relatively insoluble, leads to nephrolithiasis.
- Stones begin in childhood and are a rare cause of staghorn calculi; they occasionally lead to end-stage renal disease.
- Are more likely to form in acidic urinary pH.
Workup for an outpatient with a renal stone
1. Dietary and fluid intake history
2. Careful medical history and physical examination, focusing on systemic diseases
3. Imaging: ultrasound, noncontrast helical CT, with 5-mm CT cuts
4. Routine urine analysis: presence of crystals, hematuria, measurement of urine pH
5. Serum chemistries: BUN, creatinine, uric acid, calcium, phosphate, chloride, bicarbonate, PTH
6. Timed urine collections (at least 1 day during week, 1 day on weekend): creatinine, Na, K, urea nitrogen, uric acid, calcium, phosphate, oxalate, citrate, pH

Specific therapies for nephrolithiasis

<table>
<thead>
<tr>
<th>Stone Type</th>
<th>Dietary Modifications</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium oxalate</td>
<td>Increase fluid intake*</td>
<td>Citrate supplementation (calcium intake or potassium salts &gt; sodium) Cholestyramine or other therapy for fat malabsorption Thiazides if hypercalciuric Allopurinol if hyperuricosuric</td>
</tr>
<tr>
<td></td>
<td>Moderate sodium intake</td>
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<tr>
<td></td>
<td>Moderate oxalate intake</td>
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</tr>
<tr>
<td></td>
<td>Moderate protein intake</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Moderate fat intake</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcium phosphate</td>
<td>Increase fluid intake*</td>
<td>Thiazides if hypercalciuric</td>
</tr>
<tr>
<td></td>
<td>Moderate sodium intake</td>
<td>Treat hyperparathyroidism if present</td>
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<tr>
<td></td>
<td></td>
<td>Alkali for distal renal tubular acidosis</td>
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<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uric acid</td>
<td>Increase fluid intake*</td>
<td>Allopurinol</td>
</tr>
<tr>
<td></td>
<td>Moderate dietary protein intake</td>
<td>Alkali therapy (K+ citrate) to raise urine pH to 6.0–6.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Struvite</td>
<td>Increase fluid intake*; same as calcium oxalate if evidence of calcium oxalate nidus for struvite</td>
<td>Methenamine and vitamin C or daily suppressive antibiotic therapy (e.g., TMP/SMX)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cystine</td>
<td>Increase fluid intake*</td>
<td>Alkali therapy, penicillamine</td>
</tr>
</tbody>
</table>

*to at least 2.5–3 L/d. Note: Sodium excretion correlates with calcium excretion.

Acute renal failure

Definition
Measurable increase in the serum creatinine concentration. Usually relative increase of 50% or absolute increase by 44–88 μmol/L (0.5–1.0 mg/dL)

Decreased urine output:
- Oliguria (200-500 mL/d)
- Anuria (<200 mL/d)

Classification
- Prerenal
- Renal (intrinsic)
- Postrenal (urinary tract obstruction)

Common causes of acute renal failure- prerenal

Volume depletion
- Blood loss
- GI fluid loss (e.g., vomiting, diarrhea)
- Overzealous diuretic use
Volume overload with reduced renal perfusion
- Congestive heart failure
- Low-output with systolic dysfunction
- “High-output” (e.g., anemia, thyrotoxicosis)
- Hepatic cirrhosis
- Severe hypoproteinemia

Renovascular disease

Drugs
- NSAIDs, cyclosporine, amphotericin B, ACE inhibitors, ARBs

Other
- Hypercalcemia, “third spacing” (e.g., pancreatitis, systemic inflammatory response), hepatorenal syndrome

Common causes of acute renal failure – intrinsic renal

Acute tubular necrosis (ATN)
- Hypotension or shock, prolonged prerenal azotemia, postoperative sepsis
- syndrome, rhabdomyolysis, hemolysis, drugs
- Radiocontrast, aminoglycosides, cisplatin

Other tubulointerstitial disease
- Allergic interstitial nephritis
- Pyelonephritis (bilateral, or unilateral in single functional kidney)
- Heavy metal poisoning

Atheroembolic disease
- after vascular procedures, thrombolysis, or anticoagulation

Glomerulonephritis
- ANCA-associated: Wegener’s granulomatosis, idiopathic pauci-immune GN, PAN
- Anti-GBM disease; isolated or with pulmonary involvement (Goodpasture’s syndrome)
- Immune complex–mediated: Infective endocarditis, SLE, cryoglobulinemia (with or without HCV infection), postinfectious GN (classically poststreptococcal)

IgA nephropathy and Henoch-Schönlein purpura

Glomerular endotheliopathies

Other
- Hemolytic uremic syndrome (HUS), thrombotic thrombocytopenic purpura (TTP), malignant hypertension, scleroderma, antiphospholipid syndrome, preeclampsia

Common causes of acute renal failure- postrenal

Bladder neck obstruction, bladder calculi

Prostatic hypertrophy

Ureteral obstruction due to compression
- Pelvic or abdominal malignancy, retroperitoneal fibrosis
Nephrolithiasis

Papillary necrosis with obstruction

Clinical and laboratory findings in acute renal failure - prerenal

- Hypovolemia: orthostatic hypotension, tachycardia, low jugular venous pressure, and dry mucous membranes.
- If CHF is present: jugular venous distention, an S3 gallop, and peripheral and pulmonary edema.
- BUN/creatinine ratio tends to be high (>20:1), more so with volume depletion and CHF than with cirrhosis.
- Uric acid may also be disproportionately elevated in noncirrhotic prerenal states (due to increased proximal tubular absorption).
- Low urine [Na+] (<10–20 mmol/L, <10 with hepatorenal syndrome) and a fractional excretion of sodium (FENa) of <1%
- The urinalysis (UA) typically shows hyaline and a few granular casts, without cells or cellular casts.
- Renal ultrasonography is usually normal.

Clinical and laboratory findings in acute renal failure – intrinsic renal

Glomerulonephritis

- Hypertension and mild to moderate edema (associated with Na retention and proteinuria, and sometimes with hematuria).
- If GN occurs in systemic illness, e.g., vasculitis or SLE; these may include hemoptysis or pulmonary hemorrhage (vasculitis and Goodpasture’s syndrome), arthralgia/arthritis (vasculitis or SLE), serositis (SLE), and unexplained sinusitis (vasculitis).
- Urine sediment: RBC, WBC, and cellular casts
- Increased renal echogenicity on ultrasonography.

Pyelonephritis

- WBC casts, pyuria

Allergic interstitial nephritis

- >10% of urinary eosinophils with Wright’s or Hansel’s stain.

Ischemic or toxic acute tubular necrosis

- Pigmented “muddy-brown” granular casts and casts containing tubular epithelial cells.

Clinical and laboratory findings in acute renal failure – postrenal

Urinary tract obstruction

- Patients are usually less severely ill than patients with prerenal or intrinsic renal disease, and their presentation may be delayed until azotemia is markedly advanced, i.e. BUN >54 μmol/L (150 mg/dL), creatinine >1060–1325 μmol/L (12–15 mg/dL).
- Urinary electrolytes typically show a FENa >1%, and microscopic examination of the urinary sediment is usually bland.
- Ultrasonography is the key diagnostic tool: >90% of patients with postrenal acute renal failure show obstruction of the urinary collection system on ultrasound (e.g., diluted ureter, calyces).

Acute renal failure - therapy

Treatment should focus on providing etiology-specific supportive care.
Prerenal failure
- due to GI fluid loss: IV fluid to expand volume.
- CHF: vasodilators and/or inotropic agents.

Intrinsic renal causes
- GN associated with vasculitis or SLE: high-dose glucocorticoids and cytotoxic agents (e.g., cyclophosphamide);
- Goodpasture’s syndrome: plasmapheresis and may be useful in other selected circumstances
- HUS/TTP: plasma exchange
- Pyelonephritis or endocarditis: antibiotic therapy
- Allergic interstitial nephritis: glucocorticoids

Urinary tract obstruction
- Urologic interventions: Foley catheter placement, multiple ureteral stents and/or nephrostomy tubes.

Dialysis for acute renal failure and recovery of renal function
If nonprerenal ARF continues to progress, dialysis must be considered.

Traditional indications for dialysis:
- volume overload refractory to diuretic agents
- hyperkalemia
- encephalopathy not otherwise explained
- pericarditis, pleuritis, or other inflammatory serositis
- severe metabolic acidosis
- compromising respiratory or circulatory function

Dialysis should generally be provided in advance of these complications.

Inability to provide requisite fluids for antibiotics, inotropes and other drugs, and/or nutrition should also be considered an indication for dialysis.

Dialytic options for acute renal failure:
- Intermittent hemodialysis (IHD)
- Peritoneal dialysis (PD)
- Continuous renal replacement therapy (CRRT, i.e., continuous arteriovenous or venovenous hemodiafiltration)

Chronic pyelonephritis

Causes
- Analgesic nephropathy is the most common (phenacetin and aspirin)
- Recurrent acute bacterial pyelonephritis
- Hypercalcemia, oxalosis, hyperuricemia or hyperuricosuria
- Chronic hypokalemia, proximal tubular vacuolization, interstitial nephritis, and renal cysts
- Systemic diseases: sarcoidosis, Sjögren’s syndrome
- Radiation or chemotherapy exposure (e.g., ifosfamide, cisplatin)

Symptoms
- Flank pain, recurrent subfebrility
Laboratory findings
- Gradual deterioration of renal function over time: inability to concentrate urine (max. spec. gravity↓), BUN↑, creatinine↑, acidosis/alkalosis, Na norm. or ↓, or K norm., ↑, or ↓, Cl norm. or ↓
- Proteinuria, sometimes microscopic hematuria, urinary casts
- Sterile pyuria

Imaging
Decreased cortical thickness, irregularities of the medulla (e.g., calcification, deformed papillae), deformities of the pyelon on ultrasound, CT, and MRI

Diagnosis
Is based on laboratory findings, imaging and, sometimes biopsy results

Therapy
- Elimination of toxic agents
- Treatment of underlying cause
- Large fluid intake
- Diuretics, treatment of hyper- or hypokalemia
- Treatment of infections

Chronic renal failure (CRF)

Definition
CRF is a functional diagnosis characterized by a progressive and generally irreversible decline in glomerular filtration rate.

- Azotemia: Elevated blood levels of urea nitrogen and creatinine.
- Uremia: The clinical constellation of signs and symptoms of end-stage renal failure.

Recommended equations for estimation of GFR
Estimation from the Modification of Diet in Renal Disease Study:

\[
eGFR \, (mL/min/1.73\, m^2) = 1.86 \times (PCr)^{-1.154} \times (age)^{-0.203}
\]

- Multiply by 0.742 for women
- Multiply by 1.21 for African Americans

Cockroft-Gault Equation:

\[
eClCr \, (mL/min)=((140–age) \times body\ weight\ (kg))/(72 \times PCr\ (mg/dL))
\]

- Multiply by 0.85 for women

Stages of CRF

<table>
<thead>
<tr>
<th>Stage</th>
<th>Severity</th>
<th>GFR (mL/min/1.73 m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0</td>
<td>-</td>
<td>&gt;90*</td>
</tr>
<tr>
<td>Stage 1</td>
<td>-</td>
<td>≥90**</td>
</tr>
<tr>
<td>Stage 2</td>
<td>Mild</td>
<td>60-89</td>
</tr>
<tr>
<td>Stage 3</td>
<td>Moderate</td>
<td>30-59</td>
</tr>
</tbody>
</table>
Stage 4  Severe: overt renal failure  
Stage 5  End-stage renal disease

*: with risk factors for chronic kidney disease  
**: with demonstrated kidney damage: persistent proteinuria, abnormal sediment, urine and blood chemistry, abnormal imaging studies

Causes of end-stage renal disease (%)

<table>
<thead>
<tr>
<th>Cause</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>29.9</td>
</tr>
<tr>
<td>Hypertension</td>
<td>26.0</td>
</tr>
<tr>
<td>Glomerulonephritis</td>
<td>14.4</td>
</tr>
<tr>
<td>Cystic renal disease</td>
<td>3.6</td>
</tr>
<tr>
<td>Urologic disease</td>
<td>6.0</td>
</tr>
<tr>
<td>Other</td>
<td>5.8</td>
</tr>
<tr>
<td>Unknown</td>
<td>14.3</td>
</tr>
</tbody>
</table>

Water and electrolyte metabolism in uremia

Potassium

- Adaptive processes in CRF: K excretion per nephron, K secretion by the gut
- In advanced CRF: serum K ↑, total body K stores ↓.
- Trauma, surgery, anesthesia, blood transfusion, increased dietary intake can elevate serum K levels → muscle weakness, paresthesia, peaked T waves, prolonged PR, and QRS complex, arrhythmias, cardiac arrest!

Sodium

- Increased natriuresis per nephron is the adaptive mechanism in CRF until very advanced stages.
- Sodium wasting: Destruction of the collecting ducts → salt loss → hypovolemia, extracellular volume contraction, hypotension. Occurs in pyelonephritis, medullary cystic disease, hydronephrosis, interstitial nephritis and milk-alkali syndrome.
- Sodium retention: Inability to increase Na excretion → steady state at a higher extracellular volume level → extracellular volume expansion, peripheral edema, pulmonary vascular congestion, hypertension, cardiomegaly.

Acid-base metabolism in uremia

Acid-base balance

- Renal buffering mechanisms:
  - phosphate: filtered buffer
  - ammonia: generated buffer
- In CRF: progressive reduction in net ammonia secretion, H+ retention → slowly developing METABOLIC ACIDOSIS WITH HIGH ANION GAP
- Extrarenal buffering mechanisms become involved: bone salts and intracellular buffers.
- Below GFR of 10 ml/min: progressive rise in anion gap [Na-(Cl+HCO3)] to 20-24 mEq/l, with reciprocal fall of plasma bicarbonate to 12-15 mEq/L.

Type IV renal tubular acidosis (RTA)

- Hyporeninemic hypoaldosteronism with hyperkalemia and hyperchloremic acidosis.
- Develops in relatively early stage, normal anion gap. Reciprocal fall in plasma bicarbonate levels with increase in Cl.
- Characteristic for diabetic patients or tubulointestinal disease.
Calcium, phosphate and magnesium metabolism in uremia

Calcium and phosphate
- Hypocalcemia, but tetany is uncommon.
- Hyperphosphatemia ▶ steady state at a higher PTH level = secondary hyperparathyroidism
- Prevention of hyperphosphatemia blunts the rise of PTH
- Calcium carbonate:
  o enhances Ca absorption from gut
  o provides a base equivalent for the treatment metabolic acidosis
  o effectively binds dietary phosphate
- Avoid the use of aluminum-containing phosphate binders (dementia, anemia, bone disease)

Magnesium
- Below 20 ml/min, modest elevation of serum concentration
- Accumulation due to excessive intake
- Discontinue Mg-containing antacids and cathartics

Osteodystrophy in chronic renal failure

Organ involvement in CRF

Musculoskeletal
- Osteodystrophy
- Osteitis fibrosa
- Osteomalacia - **TEETH**!
- Osteoporosis
- Osteosclerosis
- Myopathy
- Weakness, loss of muscle
- Soft tissue calcification can also occur

Cardiovascular
- Accelerated atherosclerosis
- Hypertension
• Pericarditis (hemorrhagic, indication for dialysis)
• Myocardial dysfunction

**Hematologic**
• Anemia (lack of erythropoietin, iron, RBC membrane defects, hemolysis)
• Leukocyte dysfunction
• Hemorrhagic diathesis, platelet dysfunction

**Gastrointestinal**
• Loss of appetite, anorexia nausea, vomiting → water, salt, weight loss
• Disorders of taste
• Gastroparesis
• Gastrointestinal bleeding, petechiae, peptic ulcer is common!

**Neurologic**
• CNS defects: agitation, irritability, depression, regression, rebellion
• Dialysis disequilibrium syndrome: cerebral edema
• Dialysis encephalopathy dialysis dementia: AI intoxication
• Peripheral nervous system defects: paresthesia, „restless leg” syndrome

**Carbohydrate metabolism**
• In non-diabetics: Normal fasting blood glucose, IGT, yet severe hyperglycemia is rare. Enhanced peripheral resistance to insulin → uremic pseudodiabetes.
• In diabetics: Decreased renal clearance of insulin → the requirement for exogenous insulin may decrease. Overt hypoglycemia in a small number of patients

**Other endocrine and metabolic**
• Amenorrhea, infertility in females, impotence, oligospermia in males.
• Hypothermia
• Reduced basal metabolic rate and abnormal temperature regulation due to the absent or reduced activity of the ubiquitous Na-K-ATP-ase.
• Overt hypothermia (35.5 °C) is common. Even 37.5°C may denote serious, acute infection!
• Hyperuricemia. Clinical gout is rare, „pseudogout” occurs
• Deposition of amyloid and β2-microglobulin

**Skin**
• Generalized pruritus
• Shallow, yellow discoloration ("urochromes"), bronze discoloration (hemochromatosis), uremic frost
• Extopic („metastatic”) calcification
• Urine-smelling breath

**Approach to the patient with chronic renal failure**
• Detailed clinical history - urinary tract symptoms, toxins, infections, family history) and physical examination.
• Acute reversible renal failure? Acute worsening of chronic renal failure? Chronic progressive disease?
• No symptoms and very high BUN (>100 mM/l) and creatinine (>1000 mM/l) values - acute renal disease is unlikely.
• Patients with slowly progressing CRF are often asymptomatic with much higher BUN and creatinine.


Prerenal causes: volume depletion, cardiac, liver failure, etc.


If renal parenchymal disease is present, is it treatable or not?

Consideration of the optimal diet in CRF

**Protein**

- Reducing the amount of protein lowers the BUN and reduces the symptoms, controls hyperphosphatemia and acidosis.
- 0.6 g/kg, of which at least 60% contains proteins rich in essential amino acids (eggs, lean meat, milk).
- High calorie intake improves N utilization.
- Further minimalization of N waste products: 20 g of protein /day supplemented with essential amino acids and their α-ketoanalogues.

**Vitamins**

- Supplementation with B vitamins, vitamin C, folic acid. Vitamin D only in severe renal osteodystrophy.

**Sodium**

- Patients need at least 1.5-2 g/day. No restriction unless severe edema or hypertension is present.

**Potassium**

- No restriction unless the volume of the urine is below 1 liter

**Treatment of CRF**

**Hyperkalemia**

- Treat aggravating factors: volume depletion, fever
- Discontinue potassium supplements
- Stop drugs that can cause hyperkalemia: spironolactone, amiloride, ACE inhibitors, NSAID-s, β-blockers
- K-binding resins
- Furosemide
- Dialysis (HD or PD)

**Abnormalities of Na balance**

- Since volume depletion is very deleterious, a mild volume-expanded state is desirable.
- Severe edemas - diuretics.
- Orthostatic hypotension - liberalization of Na intake (Na-carbonate).
- Hypernatremia - free water administration.
- Hyponatremia - if mild, water restriction, if severe: hypertonic NaCl, but the volume expansion may require acute dialysis.

**Hypertension**

ACE-inhibitors ARB-s (until late stages), clonidine, Ca-channel inhibitors, minoxidil
- Diuretics (furosemide, bumetadine)
- Hyperphosphatemia
- Restriction of dietary phosphorous, postprandial phosphate binders (Ca-carbonate, -acetate, sevelamer)

**Osteodystrophy**
- 1,25-OH Vitamin D3 supplementation (calcitriol, dihydrotachysterol)
- Correction of acidosis

**Anemia**
- Recombinant human erythropoietin (rHuEPO)
- Iron, folate supplementation
- Transplantation

**Carbohydrate metabolism**
- Generally, no treatment for non-diabetics
- Adjustment of the dose of insulin in patients treated with insulin

**Hyperlipidemia**
- Fat-free diet, statins

**Hyperuricemia**
- Treat only patients with tophaceous deposits or symptomatic gout. Allopurinol, in less than 100 mg/day.

**Pericarditis**
- Pericardiocentesis, indwelling catheter, intrapericardial injection of non-absorbable steroids, partial pericardiectomy
- Daily dialysis at least for a week
- Pruritus
- No specific treatment. Emulsified oils, antihistamines, phosphate restriction, dialysis

**Neuropathy**
- No specific treatment. Prolongation of the dialysis periods
- Transplantation

**Myopathy**
No specific treatment. Dialysis, aggressive nutritional supplementation, erythropoietin

**Infections**
- Early and vigorous treatment is necessary.
- The dose of the antibiotic should be determined by:
  - serum creatinine levels and creatinine clearance
  - ideally drug monitoring
- Nephrotoxic antibiotics should be avoided or used with caution!
- Hepatitis B vaccination both for patients and dialysis staff.

**Selection of treatment modality of irreversible renal failure**
Medical treatment is continued for patients with:
- extensive irremediable extrarenal disease
- severe cerebrovascular disease
- painful malignancy
- AIDS
Forms and indications for dialysis in CRF

Forms
- Hemodialysis (HD)
- Peritoneal dialysis (PD)
- Continuous ambulatory peritoneal dialysis (CAPD)
- Continuous cyclic peritoneal dialysis (CCPD)

Indications
1. When conservative therapy is inadequate, but before the development of uremic symptoms.
2. Serum K > 7 mM/l
3. Serum creatinine: 400-500 µM/l creatinine clearance: 10-15 ml/min (due to microangiopathy, dialysis is indicated somewhat earlier in diabetics)
4. Pericarditis
5. Peripheral neuropathy
6. Impaired nutritional status due to anorexia or other GI symptoms

Causes of end-stage renal disease requiring dialysis

<table>
<thead>
<tr>
<th>Cause</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetic glomerulosclerosis</td>
<td>30</td>
</tr>
<tr>
<td>Hypertensive nephrosclerosis</td>
<td>30</td>
</tr>
<tr>
<td>Chronic interstitial kidney disease</td>
<td>5</td>
</tr>
<tr>
<td>Polycystic kidney disease</td>
<td>7</td>
</tr>
<tr>
<td>Chronic glomerulonephritis</td>
<td>5</td>
</tr>
</tbody>
</table>

Renal transplantation
- Immunological background: HLA I, HLA II subclasses, co-dominant expression.
- Donor: living-related or cadaver.
- HLA typing: mandatory sharing of six-antigen (both class I and II) also for cadaver donors.
- "Crossmatch" test: donor’s leukocytes vs. recipient’s serum. If positive, the transplantation is canceled.
- Blood groups should also be compatible.

Indications to renal transplantation
Most common diseases (together almost 75%):
1. Diabetes mellitus with renal failure
2. Hypertensive renal disease
3. Glomerulonephritis
   - reversible causes of renal dysfunction excluded
   - undergo a period of chronic dialysis
   - due to prolonged overall survival and yet severe microangiopathy in diabetes, transplantation is indicated earlier than in other forms of CRF.

Contraindications to renal transplantation
Absolute
- Active glomerulonephritis
- Active bacterial or other infection
- Active or very recent malignancy
• HIV infection
• Hepatitis B surface antigenemia
• Severe degrees of comorbidity (e.g., advanced atherosclerotic vascular disease)

Relative

• Age > 70 years
• Severe psychiatric disease
• Moderately severe degrees of comorbidity
• HCV infection with chronic hepatitis or cirrhosis
• Noncompliance with dialysis or other medical therapy
• Primary renal diseases
• Primary focal sclerosis with prior recurrence in transplant
• Multiple myeloma
• Amyloid
• Oxalosis

Immunosuppressive therapy following renal transplantation

• Monoclonal antibody (OKT3)
• Anti-lymphocyte globulin (ALG)
• Cyclosporine - Inhibits IL-2 synthesis
• Azathioprine
• Prednisone
• Mycofenolate-mofetil (MMF)

Living-related transplants need less immunosuppression.