Kidney in systemic disease

**Introduction**
A variety of systemic conditions can affect the function of the kidneys, from acute illnesses to more insidious illnesses.

<table>
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<th>To identify kidney involvement</th>
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<tr>
<td>1. Creatinine/GFR levels</td>
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<td>2. Albuminuria/Proteinuria/Haematuria.</td>
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<td>3. Structural damage (Diagnostic imaging)</td>
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<td>4. Hydronephrosis/Polycystic kidney disease</td>
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<table>
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<th>Renal involvement in systemic diseases</th>
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<td>Immunologically mediated diseases</td>
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<td>1. SLE</td>
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<td>2. Vasculitis</td>
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<td>3. Rheumatoid arthritis</td>
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<td>4. Goodpasture syndrome</td>
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<td>5. Henoch-Schönlein purpura</td>
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<td>6. Scleroderma</td>
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<td>Hypertensive nephropathy</td>
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<td>1. Multiple myeloma</td>
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<td>2. Amyloidosis</td>
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<td>3. Cryoglobulinemia</td>
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<td>Diseases associated with paraproteinaemia and neoplasia</td>
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<tr>
<td>1. Hepatorenal syndrome</td>
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<td>2. Cardiorenal syndrome</td>
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<th>SLE &amp; kidney lupus nephritis</th>
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<tr>
<td>Renal histopathological in SLE (types = stages)</td>
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<tr>
<td>I. Normal (minimal mesangial LN)</td>
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<tr>
<td>II. Mesangial proliferative GN</td>
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<tr>
<td>III. Focal Proliferative GN.</td>
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<td>IV. Diffuse Proliferative GN.</td>
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<td>V. Membranous GN.</td>
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<td>VI. Advancing sclerosing L.N.</td>
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<th>Vasculitis</th>
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<tbody>
<tr>
<td>Giant cell and Takayasu rarely cause significant renal disease</td>
</tr>
<tr>
<td>Medium sized polyarteritis nodosa main renal artery and cause infarction</td>
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<tr>
<td>Small vessel vasculitis as HSP, SLE and Wegeners glomerulonephritis</td>
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<table>
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<tr>
<th>Wegeners Granulomatosis</th>
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<tr>
<td>Small vessel vasculitis</td>
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<tr>
<td>Granulomatous inflammation with necrosis</td>
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<tr>
<td>Typical men, middle age</td>
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<tr>
<td>Affection</td>
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<tr>
<td>a. Granulomes</td>
</tr>
<tr>
<td>b. 92% ear nose throat</td>
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<tr>
<td>c. 85-90% pulmonary involvement</td>
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<tr>
<td>d. 90% kidney involvement</td>
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<td>e. Skin</td>
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<td>f. Joints, heart etc etc</td>
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<th>Hennoch Schönlein purpura</th>
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<td>Vascular purpura, abdominal pain, arthralgias, hematuria, proteinuria</td>
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<tr>
<td>The renal disease usually mild , but nephrotic syndrome and acute kidney injury can occur</td>
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<tr>
<td>Immunoglobulin deposition is mainly Ig A in glomerular mesangium distribution ( similar to Ig A nephropthy)</td>
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<tr>
<td>Prognois is usually good. There no treatment of proven benefit</td>
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<tr>
<td>Steroid therapy is ineffective</td>
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<tr>
<td>Treatment is usually supportive</td>
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<tr>
<td>But with crescent GN aggressive immunosuppression has been tried</td>
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### Goodpasture Syndrome

- Antibody against glomerular basement membrane
- Affects young men
- Pulmonary hemorrhage, iron deficiency anemia, progressive renal failure
- Anti-GBM AB 90% positive; histology: linear capillary loop staining with IgG, C3, extensive crescent formation.

**Treatment**
- 1. Plasma exchange
- 2. Steroids
- 3. Cyclophosphamide

**Prognosis**
- Depend on extent of glomerular damage at initiation of treatment
- Follow remitting relapsing course
- If left untreated autoantibodies diminish spontaneously within 3y.

### Rheumatoid Arthritis and Gout

- There is no specific renal lesion in gout and RA
- In RA the renal lesion is usually secondary to:
  1. Therapy (penicillamin, gold therapy and analgesics)
  2. Amyloidosis
  3. Vasculitis

### Systemic Sclerosis (Scleroderma)

- Chronic multisystem disease characterized by fibrosis, vasculopathy of skin and visceral organs
- 10% of patients develop scleroderma renal crisis (accelerated hypertension – rapidly progressive kidney failure, proteinuria)
- The treatment of choice is ACE inhibitors.

### Antiphospholipid Syndrome

- Central feature of APS is recurrent thrombosis (both venous, arterial) and fetal loss in presence of antiphospholipid AB
- Such AB primary or secondary to infections (HIV, HCV), autoimmune dis. (SLE)
- 50% of patients have renal involvement with proteinuria.
- Thrombotic microangiopathy is a rare but well recognized present.
- Lupus nephritis – like lesion is seen in some cases.
- The only proven treatment warfarin with INR of 3-4
- Use of steroids or plasmapharesis (life threatening renal involvement with thrombotic microangiopathy)

### Other Immune-mediated Kidney Diseases

1. Sjögren sy → nephrosis sy
2. Sarcoidosis → membranous GN
3. Chr active hepatitis(hepatitis B) → membranous, mesangiocap.GN
4. Biliary cirrhosis → tubular dysfunction.

### Metabolic Diseases and the Kidney (Diabetes mellitus) → diabetic nephropathy

#### Introduction
- Common problem - 30 - 40% of dialysis patients are diabetics
- Risk factors
  1. Long standing diabetes.
  2. Genetic predisposition.
  3. Hypertension.
  4. Poor glycemic control
- Strongly associated with retinopathy

#### Stages

1. Increased GFR and hyperfiltration
2. Normal GFR and mild mesangial expansion
3. Microalbuminuria
4. Overt proteinuria
5. CRF

#### Diagnosis

- Clinical diagnosis
- Long standing DM particularly in type 1
- Proteinuria or microalbuminuria

- Retinopathy
- Inactive urinary sediment
- Normal sized kidneys

#### Management

1. **Tight glycaemic control**, ideally achieved through combination of dietary modification, pharmacotherapy (including insulin regimen) and regular physical activity.
2. **Tight BP control** of at least 140/80 through the use of ACE inhibitors/Angiotensin-2 receptor antagonists ± diuretics/beta-blockers.
3. ACE inhibitors are of benefit in normotensive diabetics with microalbuminuria.
4. Optimisation of **other vascular risk factors** through use of aspirin and statins (vastly increased cardiovascular risk caused by diabetic nephropathy).
5. Renal replacement therapy (including transplantation) in those with established kidney disease.
**Paraproteinemia and kidney**

**Introduction**
Paraproteinaemia represents a group of related diseases characterised by an unbalanced or disproportionate proliferation of immunoglobulin-producing cells (mature B cell, most common plasma cell), usually from a single clone.

**Multiple myeloma**
- Acute kidney injury is common, 20—30% of affected individual at time of diagnosis, due to nephrotoxic effect of abnormal Igs.
- Types of renal lesions are associated with myeloma:
  - light chain cast nephropathy, AL amyloidosis, light chain deposition dis., plasma cell infiltration, Fanconi syndrome, hypercalcaemic, hyperuricaemic nephropathy, radiographic nephropathy.
- Treatment of underlying myeloma, bortezomib based chemotherapy (decrease light chain production).

**Amyloidosis (primary)**
- Amyloidosis is a clinical disorder caused by extracellular and/or intracellular deposition of insoluble abnormal amyloid fibrils that alter the normal function of tissues. These deposits stain with Congo red.
- Nephrosis sy, 5 years survival 20%
- Treatment
  1. **High-dose chemotherapy with stem cell transplant** can help remove the substance that leads to amyloid formation in those with primary AL amyloidosis who have no more than two major organs damaged. Chemotherapy medicines alone are used to treat other patients with primary AL amyloidosis.
  2. **Secondary (AA) amyloidosis** is treated by controlling the underlying disorder and with powerful anti-inflammatory medicines called steroids, which fight inflammation.
  3. **Liver transplant** may stop the disease in those with hereditary amyloidosis.
  4. A kidney or heart transplant may also be recommended.
  5. Other treatments to help with symptoms.

**Cryoglobulinaemia**
- Cryoglobulins are Igs and complement components, which precipitate reversibly in the cold, 3 types are recognised type 1 single monoclonal in myeloma, lymphop. Disorder, type 2, 3 mixed types, 30% of mixed type: essential or recognized associated cond.: viral infection (HBV, HCV, HIV, CMV, EBV), Fungal, spirochaetal, malaria, infect. Endocarditis, autoimmune rheumatic dis. (SLE, R Rheumatoid A, sjogren s.)
- Glomerular disease is more common in type 2 than type 3.
- Treatment of cryoglobulinaemia
  1. Steroid and/or immunosuppression with cyclophosphamide
  2. Intensive plasma exchange in selected cases
  3. Rituximab (anti CD 20), spontaneous remission in 1/3 of cases.

**Hypertensive nephropathy**

**Introduction**
Hypertensive nephropathy accounts for about a quarter of all patients with ESRF. Hypertension causes a pathology known as nephrosclerosis due to ischaemia affecting the glomeruli, and hyperfiltration causing intraglomerular hypertension.

**Factors suggest hypertensive nephrosclerosis**
1. Commoner in people of African-Caribbean ethnic origin
2. Clinical evidence of hypertensive retinopathy
3. Evidence of left ventricular hypertrophy on ECG
4. History of long-standing or accelerated/malignant hypertension
5. Proteinuria <0.5 g daily
6. Hypertension preceding proteinuria
7. Significant hypertension antecedent to renal failure
8. No evidence of alternative renal/systemic cause for hypertension
9. Renal biopsy histology consistent with nephrosclerosis

**Post infectious GN**
- Immune complex nephritis can follow any bacterial, viral, fungal or parasitic infections
- Can follow infected shunts and endocarditis
- May complicate deep abscesses
- Usually present 3 weeks post infection
- The patient usually a child
- Hematuria, edema
- Oliguria, hypertension
- Fever
- Prognosis is good
- Uncommonly ARF requiring dialysis
- Treatment → antiHTN, diuretics, salt restriction, dialysis if necessary, steroid -- if recovery slow
### Kidney in liver disease

#### Sodium disturbance
- There is severe Na retention to the point that the urine may be Na free
- Very low urine Na is a marker of disease severity
- Very low urine Na indicate poor response to diuretics
- There is disturbance in Na handling due increased Na reabsorption related to excess aldosterone, increased renal sympathetic activity and alteration in ANP and prostaglandin
- If Na intake continue more than loss there would be severe Na and water retention
- Na restriction is vital in the management of ascites

#### Hepatorenal syndrome
- Progressive oliguric renal failure either insidious or rapid
- Usually occur in hospitalized patients
- May be precipitated by bleeding, aggressive diuresis or abdominal paracentesis
- Functional renal failure with very low Na
- Should differentiated from ATN and pre renal states
- Reversible, functional renal failure
- Associated with acute or chronic liver disease, hepatic failure and portal hypertension
- Type 1 acute, rapid deterioration in renal function
- Type 2 insidious onset, slowly progressive course
- Hyponatraemia is predictive
- Diagnosis of exclusion
- Prognosis depends on UNDERLYING DISEASE. Very poor prognosis without transplant. Type 1 median survival 2weeks
- Management
  a. List for liver Transplantation if a candidate
  b. Bridging therapy: terlipressin, albumin 20-40g/d, TIPSS, MARS (Molecular adsorbent recirculating system)
  c. Dialysis very difficult

### Pathogenesis
1. Splanchnic vasodilatation
2. Intense systemic vasoconstriction
3. Sympathetic activation
4. High RAAS activity

#### Defining features
1. Oliguria
2. Urine sodium <10mmol/L
3. Urine Osm > Plasma Osm
4. Serum sodium <130 mmol/L
5. Normal renal tract US
6. No sustained response to ceasing diuretics, volume expansion

#### Exclude
- Sepsis/shock
- Nephrotoxic drugs
- GI fluid losses
- Haematuria/proteinuria

### Kidney and the heart

#### Cardiorenal syndrome
- Reflect interaction between heart and kidneys
- Five groups
  - Type 1 Acute HF with AKI
  - Type 2 Chronic HF with progressive CKD
  - Type 3 AKI causing acute HF
  - Type 4 Primary CKD contributing to chronic HF
  - Type 5 Acute or chronic systemic disorders causing cardiac and renal dysfunction