Medicine

Nephrology

5th year – lecture 2

الدكتور

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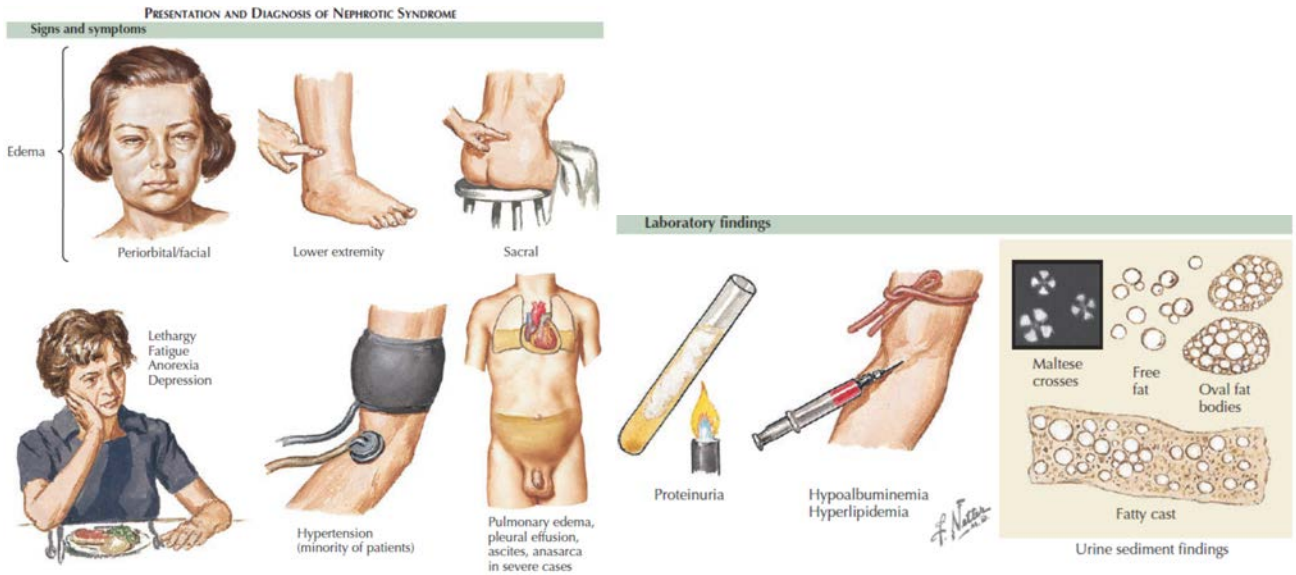
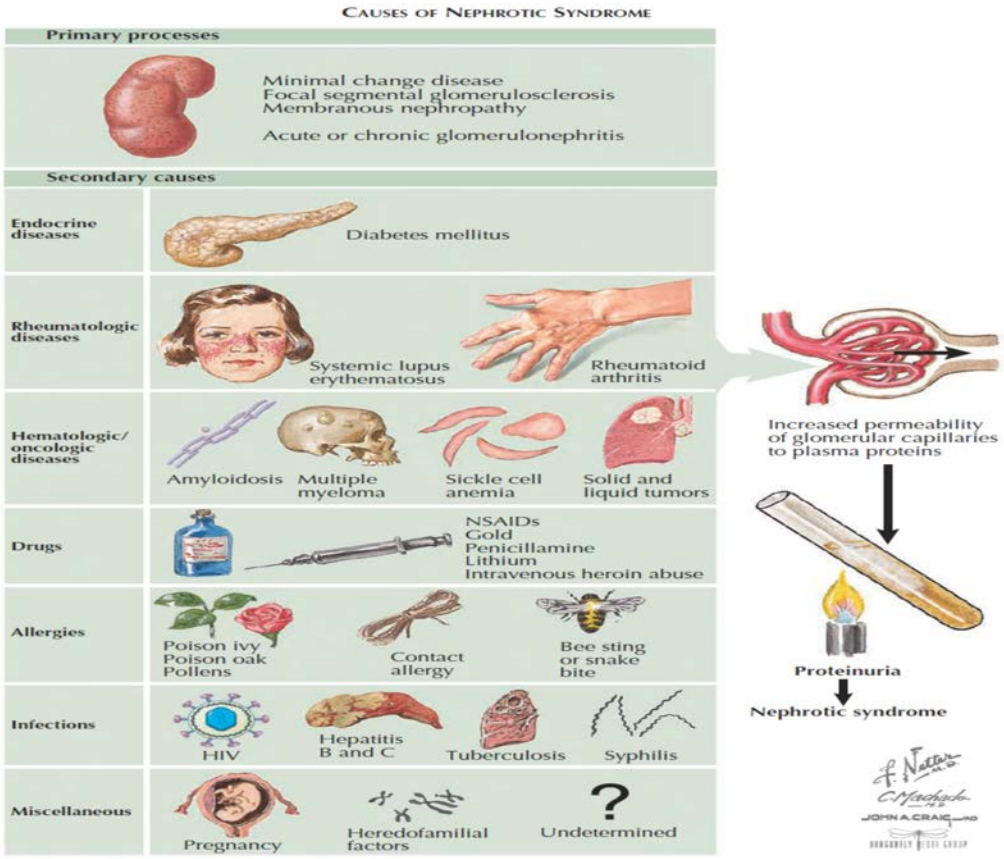
Glomerular disease

Glomerular disease is the third most common cause (after diabetes and hypertension) of chronic kidney disease (CKD) in Europe and the USA, accounting for some 10–15% of such patients. If there is predominant inflammation on kidney biopsy histology, glomerular disease may be described as a *glomerulonephritis*. If inflammation is absent, *glomerulopathy* is more correct.

Nephrotic syndrome: massive proteinuria (>3.5 g/day), hypoalbuminaemia, oedema, hyperlipidemia (elevated LDL cholesterol), lipiduria (fatty casts and oval fat bodies on microscopy).

- hypercoagulable state (due to urinary losses of antithrombin III, Protein C, and Protein S)
- patient may report frothy urine
- nephrotic syndrome is always caused by glomerular pathology on renal biopsy , Podocyte malfunction or injury is often causative.
- ***The main causes are:*** **1) minimal change disease (nil disease) e.g. glomeruli appear normal on light microscopy , 2) membranous glomerulopathy 3) focal segmental glomerulosclerosis (FSGS) 4) Nodular glomerulosclerosis (DM, amyloidosis)**
- each can be idiopathic or secondary to a systemic disease or drug .





TREATMENT

- The optimal treatment strategies depend on the underlying cause of nephrotic syndrome . Patients should adopt a low-salt diet to reduce edema and improve blood pressure control.
- Drugs: Renin-angiotensin system blockers (e.g., ACE inhibitors), to lower blood pressure and reduce the degree of proteinuria. A cholesterol-lowering medication, such as statins, Diuretics should be used as needed to treat edema; combinations of loop diuretics (e.g., furosemide), thiazides (e.g., chlorthalidone), and potassium-sparing diuretics (e.g., spironolactone) may be required.
- Steroid and immunosuppression such as azathioprine and cyclophosphamide, mycophenolate mofetil) are used in primary nephrotic syndrome.

i 15.11 Consequences of the nephrotic syndrome and their management

Feature	Mechanism	Consequence	Management
Hypoalbuminaemia	Urinary protein losses exceed synthetic capacity of liver	Reduced oncotic pressure Oedema	Treatment of underlying cause
Avid sodium retention	Secondary hyperaldosteronism Additional poorly characterised intrarenal mechanisms	Oedema	Diuretics and a low-sodium diet*
Hypercholesterolaemia	Non-specific increase in lipoprotein synthesis by liver in response to low oncotic pressure	High rate of atherosclerosis	Statins, ezetimibe
Hypercoagulability	Relative loss of inhibitors of coagulation (antithrombin III, protein C and S) and increase in liver synthesis of procoagulant factors	Venous thromboembolism	Consideration of prophylaxis in chronic or severe nephrotic syndrome
Infection	Hypogammaglobulinaemia due to urinary loss of immunoglobulins	Pneumococcal and meningococcal infection	Consideration of vaccination

*Severe nephrotic syndrome may need very large doses of combinations of diuretics acting on different parts of the nephron (e.g. loop diuretic plus thiazide plus amiloride). In occasional patients with hypovolaemia, intravenous salt-poor albumin infusions may help to establish a diuresis, although efficacy is controversial. Over-diuresis risks secondary impairment of renal function through hypovolaemia.

Glomerulonephritis (nephritic syndrome)

• **Acute glomerulonephritis**: abrupt onset of glomerular haematuria (red blood cell casts or dysmorphic red blood cells),non-nephrotic range proteinuria, oedema, hypertension and transient renal impairment.

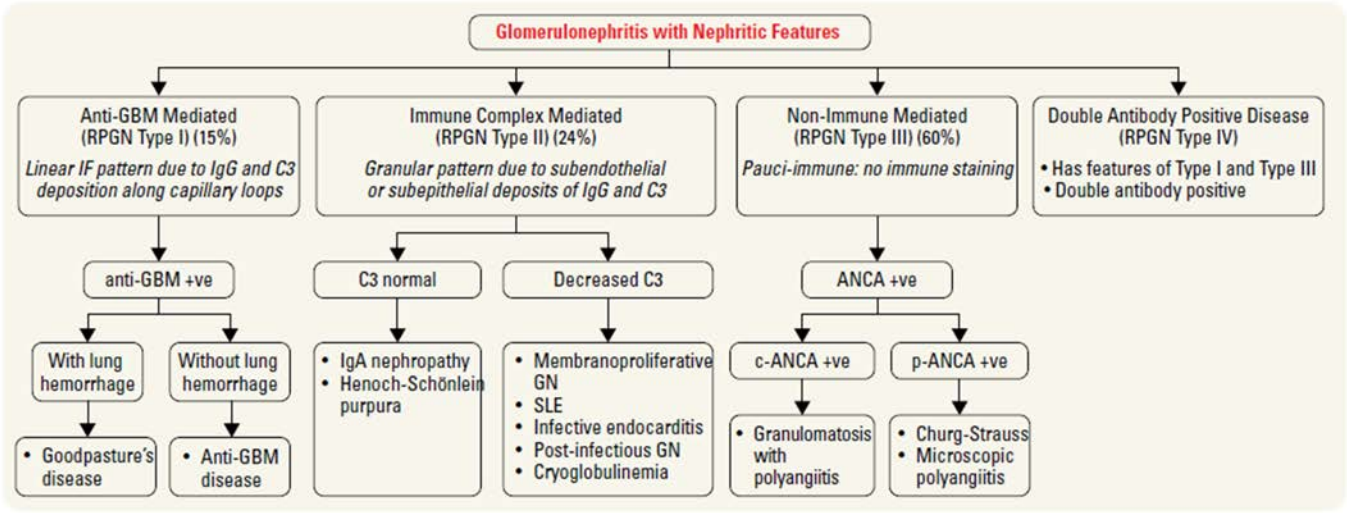
• **Rapidly progressive glomerulonephritis**: features of acute nephritis, focal necrosis with or without crescents in kidney biopsy, and rapidly progressive renal failure over weeks. It can be classified by immunofluorescence staining

• Type I: anti-GBM mediated (15% of cases)

• Type II: immune complex mediated (24% of cases)

• Type III: non-immune mediated (60% of cases)

• Type IV: double antibody positive (positive antiGBM with positive ANCA)



Clinical/Lab Features

• proteinuria (<3.5 g/d)

• hematuria (microscopic dysmorphic RBCs or macroscopic hematuria)

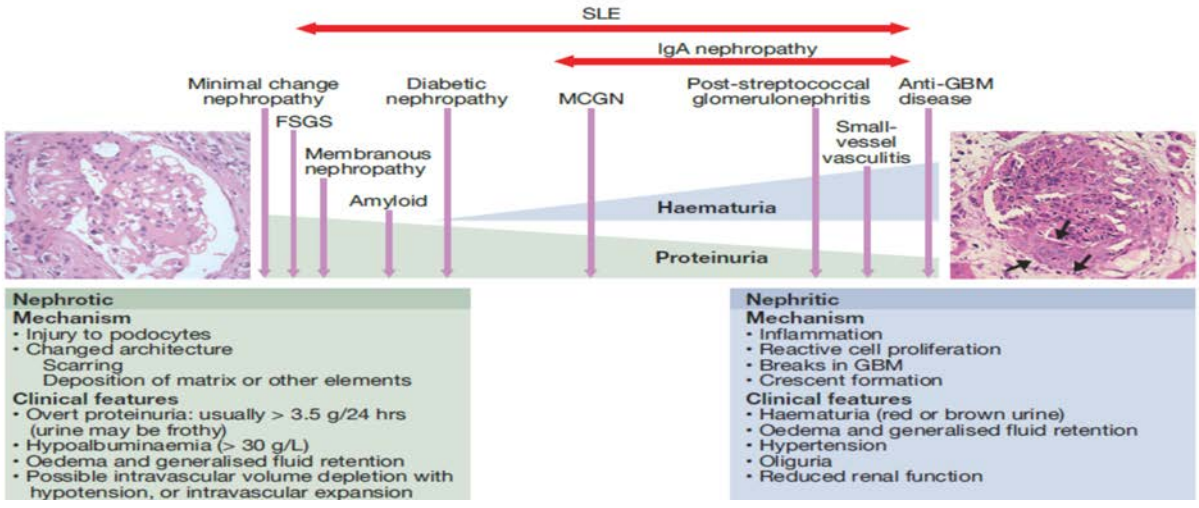
• azotemia (increased Cr and urea)

• RBC casts and/or dysmorphic RBCs in urine

• HTN (due to salt and water retention)

• Peripheral edema/puffy eyes

Mixed nephritic/nephrotic presentations: where glomerulonephritis is part of a systemic disease (e.g. lupus nephritis, cryoglobulinaemia and Henoch–Schönlein purpura), a nephritic syndrome is often associated with the nephrotic syndrome.

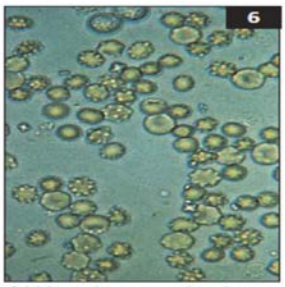


INVESTIGATIONS FOR GLOMERULAR DISEASE

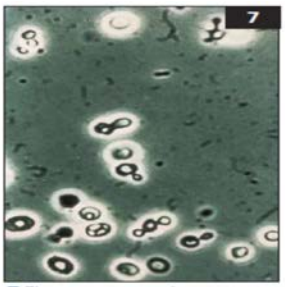
1) send for blood electrolytes, Cr, urea, albumin, fasting lipids, serum protein electrophoresis (SPEP) (for amyloidosis or multiple myeloma), C3, C4, ANA, p-ANCA, c-ANCA, cryoglobulins, HBV and HCV serology, ASOT (antistreptolysin O titers), VDRL, HIV, anti-glomerular basement membrane antibodies (anti-GBM)

2) urinalysis: Dysmorphic RBCs, RBCs casts, protein , 24 h urine for protein

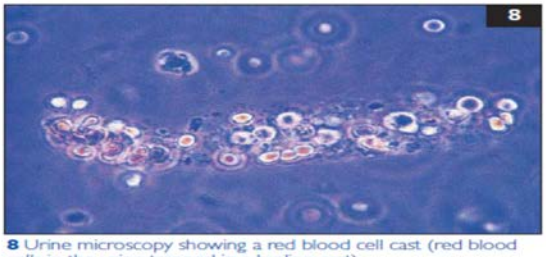
5 A pot of urine showing gross macroscopic hematuria.



6 Urine microscopy showing normal red blood cells in the urine.



7 Phase contrast urine microscopy showing cells which have irregular not smooth outlines and are 'dysmorphic'.



8 Urine microscopy showing a red blood cell cast (red blood cells in the urine trapped in a hyaline cast).

3) radiology: CXR (infiltrates, pleural effusion) , renal U/S (looking for kidney size)

4) Renal biopsy (percutaneous) should be done if heavy proteinuria or renal insufficiency and the cause is not obviously diabetic nephropathy. Renal pathology is recommended for examination in light microscopy immunofluorescence and rarely send for electron microscope.

Treatment

• depends on etiology

• Pulse steroid therapy and other immunosuppression (steroid sparing agents such as azathioprine and cyclophosphamide, mycophenolate mofetil, and biologics such as rituximab), BP control (with ACEi/ARBs agents), plasma exchange (in some case as in Goodpasture's disasese with alveolar hemorrehage), monitoring for progression to end stage renal disease.