

LECTURE NOTES OF INTERNAL MEDICINE

Nephrology

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Symptoms of Urinary System

1. Dysuria, frequency & urgency: (lower urinary tract symptoms)

- **Dysuria** means pain on passing urine rather than difficulty in doing so
- **Frequency** means that the urine is passed more often than normal without an increase in the total volume.
- **Urgency** is a strong desire to pass urine, which may be followed by incontinence if the circumstances are not suitable.

- Dysuria, frequency and urgency are associated with irritation of the bladder and urethra by infections, tumor or stone.
- Dysuria alone may be due to urethritis.
- Urgency alone may be due to anatomical change as in gynecological disorder or neurological disease.
- Frequency alone may be due to anxiety or abnormal bladder muscle tone (Detrusor instability).

2. Polyuria

This means an increase in urinary output $> 3\text{L/d}$ regardless the frequency of micturition. Causes (see endocrine).

- D.M
- Diuretic therapy
- C.R.F (early)
- D.I
- Psychogenic (polydipsia)
- Polyuric phase of acute tubular necrosis

- Severe polyuria will cause thirst, which may be the presenting symptom.
- Normal urine volume = 600 ml - 1800 ml/d.

3. Oliguria and anuria

- **Oliguria:** Urine output $< 400\text{ ml/d}$ (which is the minimal volume of urine which is necessary to excrete the waste products), this varies with diet, physical activity and metabolic rate as well as renal function.

Causes: See Acute renal failure.

- **Anuria** means that urine volume is $< 100\text{ ml} / 24\text{hrs}$, it raises the possibility of urinary tract obstruction.

- 200 ml - 300 ml urine output / day might be sufficient for a healthy man on a protein free diet, whereas 2L might be insufficient when chronic renal failure is present.
- Non oliguric renal failure is relatively common, (20% of cases) and frequently unrecognized.



4. Haematuria: Presence of blood in urine attributed to bleeding from the urinary tract

Painless

- Glomerulonephritis.
- Urinary tract infection, tuberculosis and bilharziasis.
- Cancer bladder or papilloma.
- Hypernephroma.
- Malignant hypertension.
- Renal cystic disease or renal vascular disease.

Painful

- Renal stones.
- Urinary tract infections.
- Renal papillary necrosis.

- *When there is also frequency or dysuria the bleeding mostly from bladder.*
- *Hematuria that clears during micturation arises from the urethra.*
- *Hematuria all through usually arises from the kidney.*
- *Terminal hematuria is also of bladder origin as in cases of bilharziasis*

5 Pneumaturia:

- It means sensation of passing bubbles in the urine, this is usually caused by vesicocolic fistula (malignancy).

6 Alteration of the force of micturation:

- A poor urinary stream is common in old males due to senile prostate.
- The force of the stream can be determined by asking the patient to demonstrate how near he has to stand to an imaginary toilet. This also can occur with a urethral stricture (less common).

- Other features of prostatic neck obstruction (often termed prostatism) include hesitancy, urinary spray, post micturation dribbling and frequency. Nocturia also occurs due to incomplete emptying of the bladder.

7. Nocturia:

- The need to pass urine at night or during the sleeping hours may be a life long habit. As a newly developing habit it may be due to:
 - Prostatic obstruction
 - Heart failure, the diuresis resulting from the improvement in renal blood flow which occurs with recumbency.



8. Incontinence (Types and causes)

- It is defined as inability of the urinary bladder to retain urine.
- Many ♀ suffer from urinary incontinence provoked by the stress of laughing, sneezing or coughing, this is due to gynecological disorders.
- Retention with overflow leads to incontinence (see neurogenic bladder).
- Urgency may also lead to incontinence (urge incontinence).

- **NB:** Some patients have urge and stress incontinence at the same time.

Causes of urinary incontinence:

- Incoordination of bladder sphincter function in old age.
- Spinal cord trauma or compression.
- Multiple sclerosis.
- Pelvic floor damage during childbirth in females.
- Benign prostatic hypertrophy, prostatic carcinoma in males.

9. Urogenital pain:

- The renal parenchyma is pain free and renal pain is associated with conditions causing stretching of the renal capsule and renal pelvis.
- Renal colic (ureteric colic) is usually due to ureteric obstruction by calculus or blood clot.

Renal pain:

- As in hydronephrosis and staghorn stone, it is intermittent in polycystic kidney due to spontaneous bleeding into a cyst. Also renal pain occurs with acute pyelonephritis.
- It is described as dull aching pain in the loin.

Ureteric colic:

- It is a more severe pain due to obstruction of the ureter by stone or blood clot. The pain radiates downward to the groin and genitalia. Once a stone reaches the bladder, it becomes usually asymptomatic unless it enters the urethra to cause dysuria. The ureteric colic is usually severe and sustained associated with nausea and vomiting.

10. Other urinary symptoms

Strangury: It is severe suprapubic pain associated with inability to pass urine, dysuria and urgency. It is usually due to acute bladder neck obstruction by a stone or blood clot.'

Urgency: It is a sudden need to pass urine.

Hesitancy: It is a delay in initiating urine flow.



INVESTIGATIONS OF URINARY SYSTEM

Kidney Function Tests

1- Blood urea (N= 20 -40 mg/dl)

- The level of urea depends both on the G.F.R & its production rate. Also it is heavily influenced by protein intake, increased tissue catabolism and GIT bleeding ($\uparrow$ production). So it $\uparrow\uparrow$ with protein diet, tissue breakdown (provided that there is renal insufficiency).
- Also it $\downarrow\downarrow$ with chronic advanced liver disease (as it is produced in the liver) and with reduced catabolism in old age ($\downarrow$ production).
- **Example:-** (in patient with the serum creatinine 10 mg/dl $\oplus$ mild $\uparrow\uparrow$ urea associated liver disease must be considered).

2- BUN (blood urea nitrogen) (N= 10-20 mg/dl)

- It is similar to blood urea as regard the influencing factors affecting its blood level.

$$\therefore \text{Urea} = \text{BUN} \times 2$$

3- S. creatinine (N= 0.7-1.4 mg/dl)

- The level of the serum creatinine is much less dependent on the diet but is more related to the age, sex & muscular mass.
- So S. creatinine is a better guide to (GFR) than urea.
- It starts elevation when kidney Function (GFR) is reduced $> 70\%$

4- BUN : Creatinine Ratio: (normally it is 10 : 1)

Causes of $\uparrow$ ratio	Causes of $\downarrow$ ratio
Example: (urea 400 mg/dl, S.cr. 4 mg/dl) $\therefore$ BUN 200 $\therefore$ ratio 50 : 1 1. High protein diet. 2. GIT bleeding. 3. Hypercatabolic patient e.g. trauma, tissue breakdown 4. Corticosteroid therapy. 5. Pre renal failure? 6. Sepsis	Example: (urea 120 mg/dl, S.cr. 10 mg/dl) $\therefore$ BUN = 60 $\therefore$ ratio 6 : 1 1. Associated liver disease. 2. Acute tubular Necrosis. 3. Haemodialysis patients (urea more dialyzable). 4. Low protein diet



5- Creatinine Clearance:

- It is a method to measure GFR approximately.
- It is the volume of plasma cleared from creatinine/min. = $\frac{U \times V}{P}$

U = urine creatinine mg/dl.

V = volume of urine/min = $\frac{\text{Urine volume in 24hrs}}{1440}$

P = plasma creatinine mg/dl.

- **Normal Value(90-140 ml/min for males, 80-125 ml/min for females)**
- Serum creatinine starts elevation when creatinine clearance < 25%-30%.
- The glomerular filtration rate (GFR) varies with age and sex but is approximately 120-130 ml/min/1.73 m² surface area. It can be measured by renal scan using Diethylene triamine penta-acetic acid labeled with technetium (^{99m}Tc-DTPA), it is more accurate than creatinine clearance. GFR 35-50% of normal is sufficient to maintain the patient symptom free, at GFR 20-35% azotemia occurs with initial manifestations of renal insufficiency, at GFR < 20-25% the patient develops overt renal failure.

6- Cystatin-C level correlates better with radioisotope estimation of GFR than creatinine and more sensitive. It is not secreted by tubules and is unaffected by gender.

Calculation of creatinine clearance (Cockcroft & Gault equation)

$$\text{Creatinine clearance} = \frac{(140 - \text{age}) \times \text{B.W in Kg}}{72 \times \text{Plasma creatinine}}$$

- The calculated clearance should be reduced by 15% for women.

kidney function tests are classified as follows:

A-Glomerular function Assessment:

- Blood urea.
- Serum creatinine, cystatin –C Level.
- GFR measurement by renal scan or by creatinine clearance.

B-Tubular function assessment:

- Proximal tubular function is assessed by serum potassium and phosphorus, also by detection of Glycosuria in absence of hyperglycemia, amino aciduria and B₂ microglobulin in urine.
- Distal tubular function assessed by measurement of urinary acidification by ammonium chloride test and concentrating capacity by water deprivation test.



Urine analysis

Physical Examination:

A. Color

- Normally it is amber yellow due to urochrome pigment which is a break down product of Hb related to bile pigments found in the urine.

Abnormal colors:

1. **Colorless = polyurea**

- D.M.
- Compulsive H₂O intake.
- D.I.

2. **Reddish**

- Haematuria.
- Myoglobinuria.
- Drugs e.g. Rifampicin (orange-red).
- Haemoglobinuria.
- Beetroot, Rhubarb.

3. **Brownish**

- Bilirubin.
- Flagyl.
- Nitrofurantoin.

4. **Bluish:** Amitriptyline (Tryptizole).

5. **Greenish?!** Pseudomonas.

6. **Blackish:** Alkaptonuria.

B- Aspect

- Cloudy or turbid urine provides a warning of possible abnormality as presence of pyuria, hematuria, excessive epithelial cells, excessive amorphous urate or mucus.

C- Odour

- Fruity or sweet odour may be present in cases of ketonuria.

D- PH (Normally acidic, pH= 5-7)

<u>Causes of alkaline Urine</u>	<u>Causes of Acidic urine</u>
- Renal tubular acidosis (kidney tubules unable to excrete H⁺). - Na HCO₃ or Na citrate intake. - High vegetable diet. - Urinary tract infection with urea splitting organism e.g proteus	- Normal urine. - Ascorbic acid (Vit C).

- Urine pH is unnecessary except in the diagnosis and treatment of renal tubular acidosis. It is also helpful in the treatment of renal stones.



E- Specific gravity

- Measurement of urine osmolality is more accurate.
- **1003 - 1025 (or more)**
- After H₂O deprivation for 12 hours it reaches 1025 or more.
- After plenty fluid intake it reaches 1003 or less.

<u>Causes of ↓ specific gravity</u>	<u>Causes of ↑ specific gravity</u>
- Diabetes insipidus - Tubulointerstitial disease - Compulsive H₂O intake	- D.M - Increased proteins - Volume depletion

- **NB:** Urine specific gravity is a measure of the weight of dissolved particles in urine but osmolality reflects the number of such particles.

Chemical examination:

It includes:

- Proteins (see below)
- Glucose and ketones (see D.M.)
- Bilirubin and urobilinogen (see hepatology)

Urinary proteins

- Normally, there is a trace of protein.
- It is a glycoprotein secreted by the cells of the ascending limb of the loop of Henle called (Tamm Horsfall) + trace of albumin, (normal urine protein) = **150-200 mg/24 hr.**
- Slightly higher values up to 300 mg daily may be excreted by adolescents.

Causes of proteinuria (albuminuria)

1. Heavy proteinuria > 3.5gm/24 hr urine

= Nephrotic \$ (glomerular Disease).

2. Mild proteinuria < 3.5gm

- Nephritic \$.
- Tubulointerstitial disease.
- Orthostatic.
- Exercise.
- Febrile albuminuria.
- Excessive RBCs or pus cells may give False albuminuria.
- Congestive heart failure → Congested kidney → escape of protein through the glomerulus.



Methods of measurement of proteinuria:

- 1- Timed 24 hour urinary excretion.
- 2- Random urine samples in which albumin concentration is related to urinary creatinine concentration i.e. albumin/cr ratio.
- 3- Dipsticks are available (Cannot detect Bence-Jones/ proteins)

- Normal urine contains albumin **< 20 mg/L**, micro albuminuria = albumin between **20-150 mg/L** this is an indicator of early diabetic nephropathy.
- Proteinuria can be classified into:
 - **Glomerular** e.g. glomerulopathies.
 - **Tubular** e.g. Interstitial nephritis.
 - **Over flow** e.g. multiple myeloma (Bence-Jones proteinuria), myoglobinuria.
 - **Hemodynamic** e.g congestive heart failure, fever and exercise.

Microscopic examination of urine sediment

A- Pus cells = dead WBC (Normally up to 4 / H.P.F.)

- If **> 4 / H.P.F** = pyuria, it is significant if **> 10/ H.P.F**.
- Pyuria indicates an inflammatory reaction within the urinary tract.
- So if pyuria + ve, Culture of mid stream urine sample is indicated.

→ +ve culture!? (Bacterial growth)

According to the Bacterial Count

- **≥ 100.000 /mm** = Infection.
- **10.000 - 100.000** = suspicion of infection, to be reported
- **< 10.000** = may be due to contamination !?

→ - ve culture = Sterile pyuria

Causes

- 1- Urinary tract infection in patient under antibiotic.
- 2- T.B.
- 3- Renal stones.
- 4- Graft rejection.
- 5- Glomerulonephritis.
- 6- Drug induced interstitial nephritis.
- 7- Non gonococcal urethritis caused by mycoplasma and Chlamydia.

- **Drug induced interstitial nephritis** e.g. methicillin, penicillins, cephalosporins, sulfonamides, rifampicin → (Hypersensitivity) → eosinophiluria.
- It is important to use the morning mid stream urine samples for microscopic examination.
- Recently the bacterial count is modified according to certain situations e.g. in diabetics, pregnant females, presence of urinary catheter or immunocompromized patient.



B- R.B.Cs Normally up to 5/ H.P.F.

If > 5 = Haematuria

Prerenal	Renal	Post-renal
- Anticoagulant therapy - Bleeding tendency	- G.N. - Pyelonephritis - Tumors, stone	- Stone - Tumors

Glomerular haematuria (dysmorphic RBCs) i.e. RBCs deformed (crenated).

C- Casts

- Microscopic cylindrical structures due to coagulation of tubular protein (Tamm-Horsfall proteins) + albumin ± cellular element formed within kidney tubules.
- Because they are formed inside the tubules, they indicate upper urinary tract lesion (inside the kidneys.) i.e. within the nephrons.
- Any excessive cells or ↑ albumin in urine → coagulation of tubular Protein → cast formation.
- The name of the cast may refer to its cellular element.
- The presence of red or white blood cells in the casts gives evidence of inflammatory parenchymal renal diseases.
- Casts may contain cellular material (RBCs, WBCs, tubular cells), lipids, fibrin, bile and crystals.

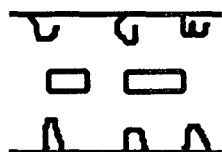
I-RBC- casts (Indicates acute glomerulonephritis)

Inflammation of glomeruli leads to → (↑ RBCs + ↑ albumin + coagulation of tubular protein) → RBCs cast.

II-WBC - casts (Indicates pyelonephritis in a patient with urinary tract infection), also present in interstitial nephritis.

Inflammation → tubular protein coagulation + WBCs → WBCs cast.

III- Tubular cell cast and granular casts



- Both casts consist of (Coagulation of tubular protein+ degenerated or necrosed tubular cells).
- If casts remain in the kidney for a short period they appear as tubular cell casts, if the casts remain in the kidney for long time the cells are partly degraded to form coarse granular casts.
- Tubular casts or coarse granular cast in a patient with acute renal failure help to make the diagnosis of acute tubular necrosis.
- Coarse granular casts may present in chronic parenchymal diseases as chronic glomerulonephritis or chronic Interstitial nephritis.



IV-Hyaline casts: (nephrotic \$)

- (Hyaline cast is sometimes normal in urine)
- Tubular protein + albumin → Hyaline cast (no cellular element).

V-Fatty casts: = (lipid cast), (Nephrotic \$)

- Tubular protein + albumin + lipiduria.
- Common in nephrotic \$.

VI-Broad casts:

- Cast formed in dilated kidney tubules in C.R.F.

VII- Crystal casts

- In patients who are taking triametrene and also cases of hypercalcemia or hyperuricosuria.

NB:

- Hyaline and fine granular casts may present in individuals without renal disease.
- More coarsely granular casts occur with pathological glomerular and tubular diseases.

D- Urine Crystals

- (In the absence of specific symptoms crystals of calcium oxalate and uric acid are of little clinical significance)
 - 1- Uric acid present in acidic urine, acute uric acid nephropathy and hyperuricosuria.
 - 2- Calcium phosphate, in alkaline urine.
 - 3- Calcium oxalate, in acidic urine and hyperoxaluria.
 - 4- Cystine, in cystinuria.



Radiology

1- **Plain X-ray urinary tract:** (KUB) i.e kidneys, ureters, bladder.

- Stone.
- Nephrocalcinosis.
- Calcification of urinary bladder (Bilharziasis).
- Changes of renal osteodystrophy.
- Air within the kidneys in severe infections in diabetics.

2- **Intravenous pyelography(IVP):-**

Dye → I.V uptake → concentration → excretion. The contrast medium concentrates in the renal tubules and produces a nephrogram image, As the medium passes into the collecting system, the calyces, renal pelvis, ureters and bladder are visualized.

- Few minutes after the injection of the contrast → visualization of the soft tissue shadow of the kidney (**nephrogram**).
- After 5-10 minutes, the films obtained are used for evaluation of the collecting structures, ureter and bladder which are best demonstrated within the first 20 minutes.
- Abdominal compression is used to produce greater visualization of the calyceal system and to allow better visualization of the entire ureter after compression is released.

Value:

- 1- It is considered to be an anatomical description of the urinary system.
- 2- Stones, tumors (filling defect).
- 3- Details of ureters.
- 4- Rapid sequence I.V.P. may be helpful to diagnose renal Artery Stenosis (see later).

Complications:

- 1- Anaphylactic shock.
- 2- Acute renal failure as the dye is nephrotoxic → ATN = contrast nephropathy.

Patients liable to contrast nephropathy:-

- | | | |
|---------------------------------|---------------------|---------------------|
| - D.M. | - Old age. | - Multiple myeloma. |
| - Patient under ACE inhibitors. | - Renal impairment. | - Volume depletion |



I.V.P. (infusion method):

- Its advantage is to decrease incidence of contrast nephropathy as we give the dye with saline by infusion.
- You can give mannitol after the procedure → diuresis & rapid excretion of the dye

Ascending pyelography: (Retrograde pyelography)

- Cystoscopy → ureteric catheter → flushing of dye → visualization of ureter, bladder, pelvis.
- It is mainly used to investigate lesions of the ureters.
- It is invasive and may introduce infection.
- It can be used if there is contraindication of IVP as previous allergy to contrast media or impaired kidney function.

Antegrade pyelography:

- It involves percutaneous puncture of a renal calyx with insertion of a fine catheter and injection of the contrast.
- It is used in patients with upper urinary tract obstruction.
- The catheter can be left in situ to allow urine drainage in oliguric patients.

3. Sonar:-

Value:

1- Size of kidney (12 × 6 × 3) cm

- Bipolar length (12-14cm)

→ Shrunk

- Symmetrical → Chronic G.N.
- Asymmetrical → Chronic Pyelonephritis

→ Enlarged

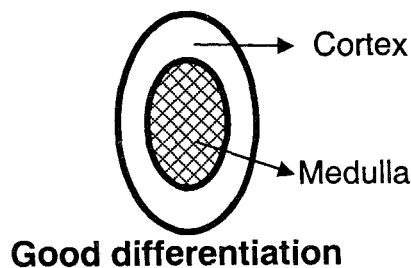
- Hydronephrosis
- Amyloidosis
- Polycystic kidney
- Diabetic nephropathy

2- Stones, tumours, cyst.

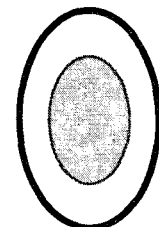
3- Dilated pelvicalyceal system

4- Echogenicity

- Normally, there is a good differentiation between cortex & medulla. If there is poor differentiation = parenchymal disease, e.g. glomerulonephritis or pyelonephritis.



Good differentiation



Poor differentiation



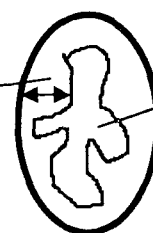
5- Parenchymal thickness

- Normally it is around **2 cm**

6- Biopsy guided by sonar

7- Visualiation of bladder

- Especially bladder emptying, to assess the residual urine after micturation e.g. in cases of bladder neck obstruction, lower part ureters and prostate.



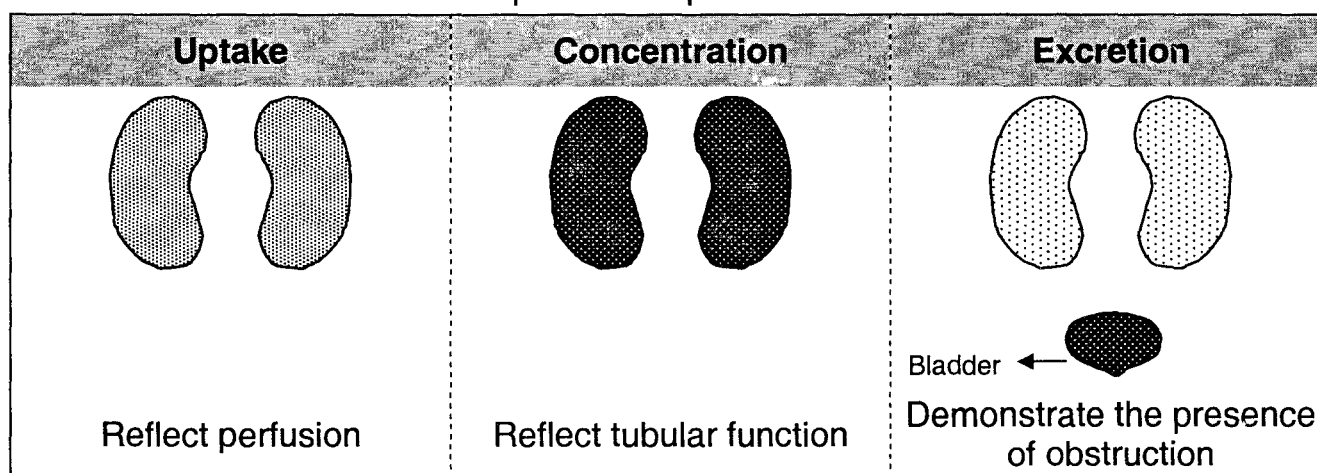
Dilated
pelvicalyceal
system

Q: Value of abdominal sonar:

1. Liver.
2. Kidney.
3. Gall bladder.
4. Spleen.
5. Ascites.

4- Renal scan

- Radioisotope I.V. → uptake → concentration → excretion



Value of renal scan (scintigraphy)

1. Dynamic scintigraphy (by Technetium labeled diethylene triamine penta acetic acid (Tc-DTPA) or hippuran

- Renal blood flow, to diagnose cases of renal artery stenosis.
- Urinary tract obstruction.
- Bladder emptying (residual urine).
- Measurement of GFR.

2. Static scintigraphy (DMSA scan) i.e dimercaptosuccinic acid

- Relative split kidney function, the function is divided between both kidneys with a range of 45-55%.
- Kidney visualization e.g. in identifying ectopic kidney.
- Localization of infection using gallium or isotopically labeled leucocytes may be of value to localize an infection e.g. renal abscess.



5- Renal biopsy (For diagnosis, prognosis and follow up)

Indications

- 1- Nephrotic syndrome in adults.
- 2- Nephritic syndrome in adults.
- 3- Asymptomatic haematuria or proteinuria.
- 4- Focal lesion.
- 5- Unexplained acute renal failure.
- 6- Unexplained chronic renal failure with normal or near normal kidney size.
- 7- Diagnosis of systemic disease with renal involvement e.g. amyloidosis.

Chronic renal failure with normal sized kidney or enlarged kidney can be met with diabetic nephropathy or amyloidosis kidney.

Contraindications:

- 1- Obstructive uropathy.
- 2- Shrunken kidneys (less than 60% of the expected bipolar length).
- 3- Solitary kidney (except in renal graft).
- 4- Uncontrolled hypertension or bleeding tendency.

Complications: (Mortality 0.1%)

- Injury → hematuria.
- Rupture kidney.
- Infection.
- Perirenal hematoma may cause hypertension.

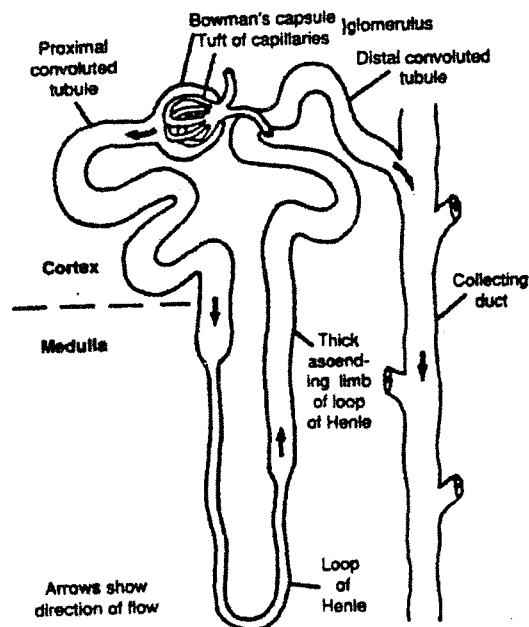
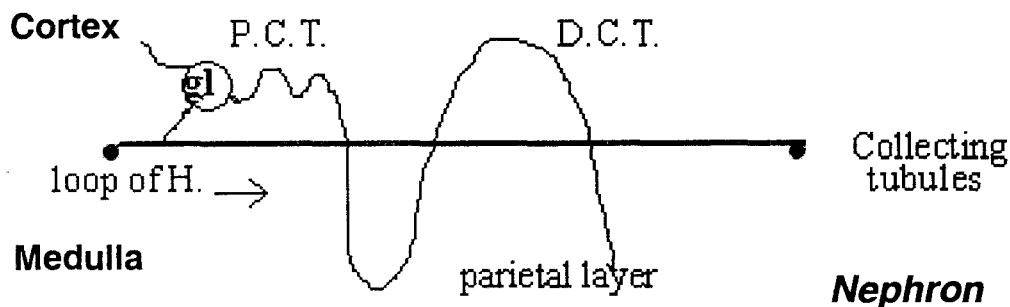
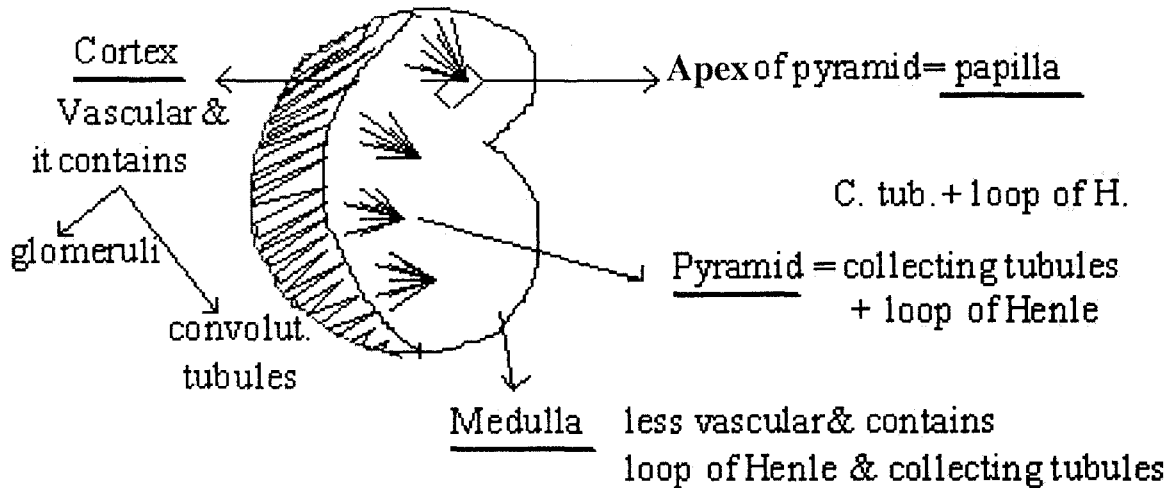
Q. Other investigations of the kidney (see later).

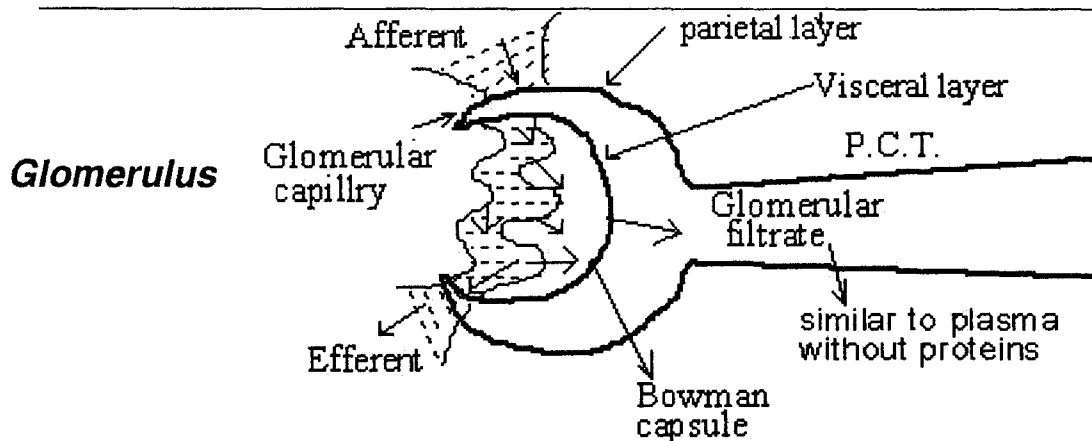


RENAL ANATOMY

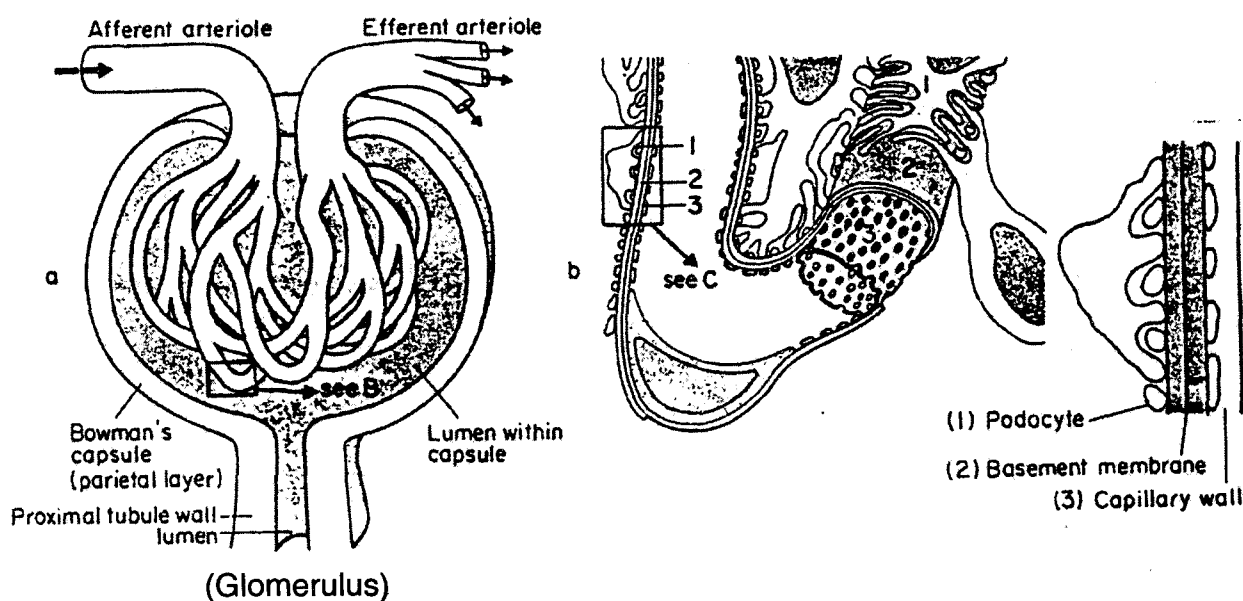
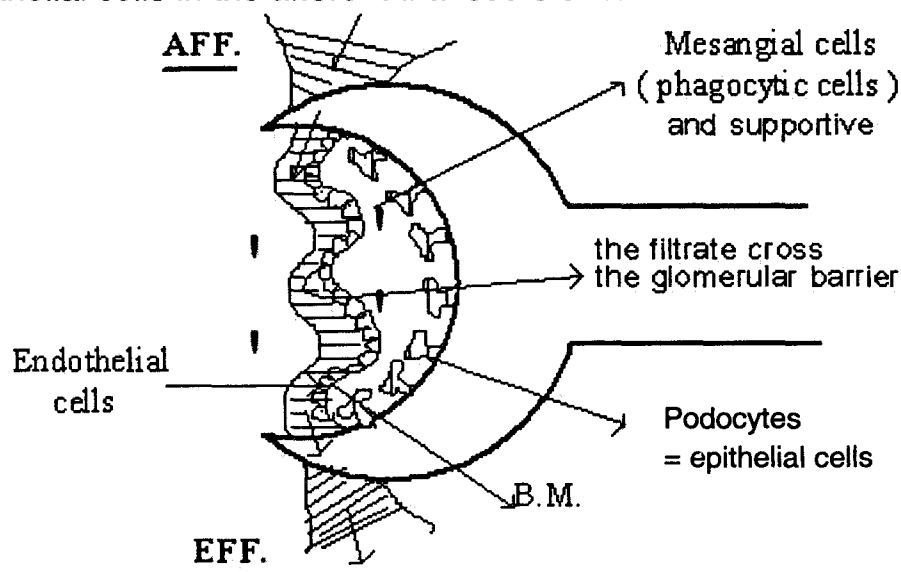
- Kidneys are retroperitoneal structures
- Each adult kidney weighs about 120-170 gm

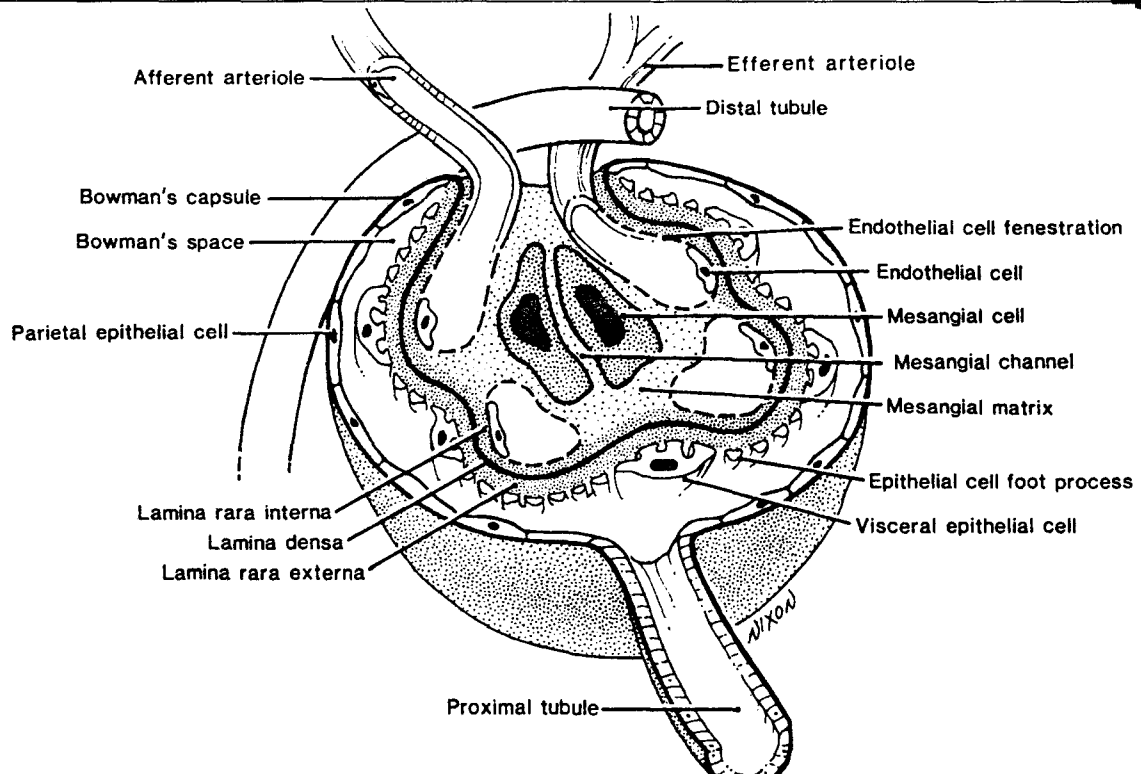
Cross Section



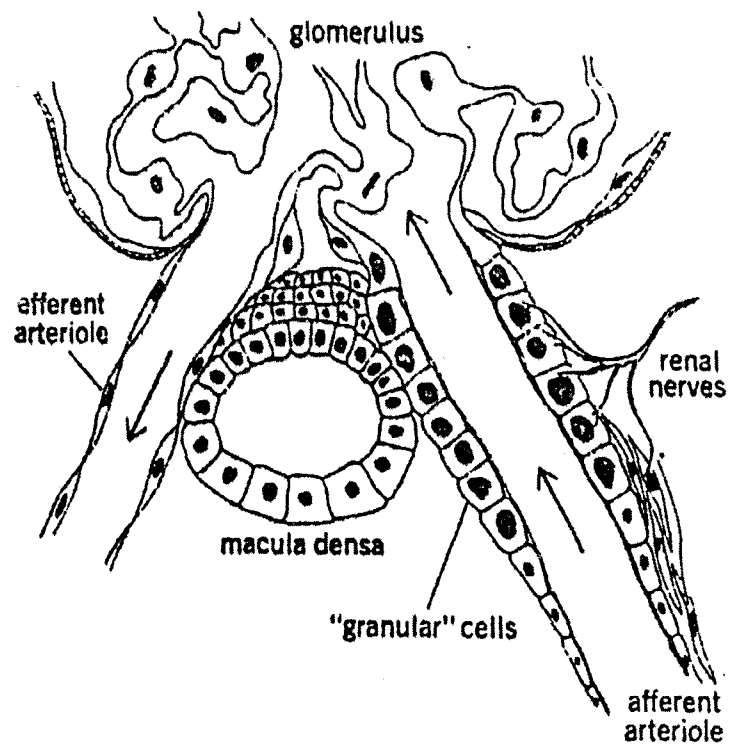


- Each kidney composed of one million nephrons.
- The blood supply of the kidneys about 1300 ml/min.
- At the junction between afferent arteriole and distal tubule there is the juxtaglomerular apparatus which is composed of macula densa and myoepithelial cells in the afferent that secretes rennin.



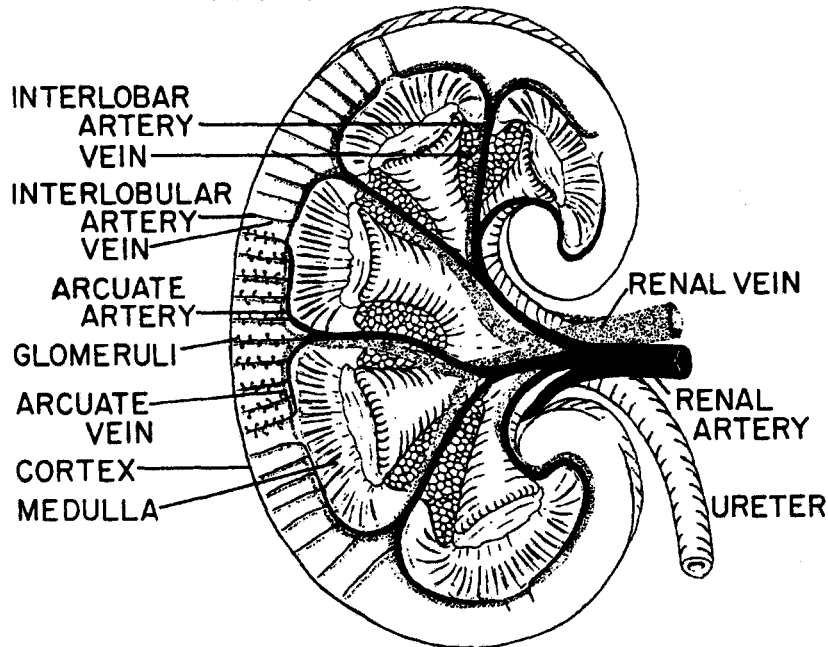
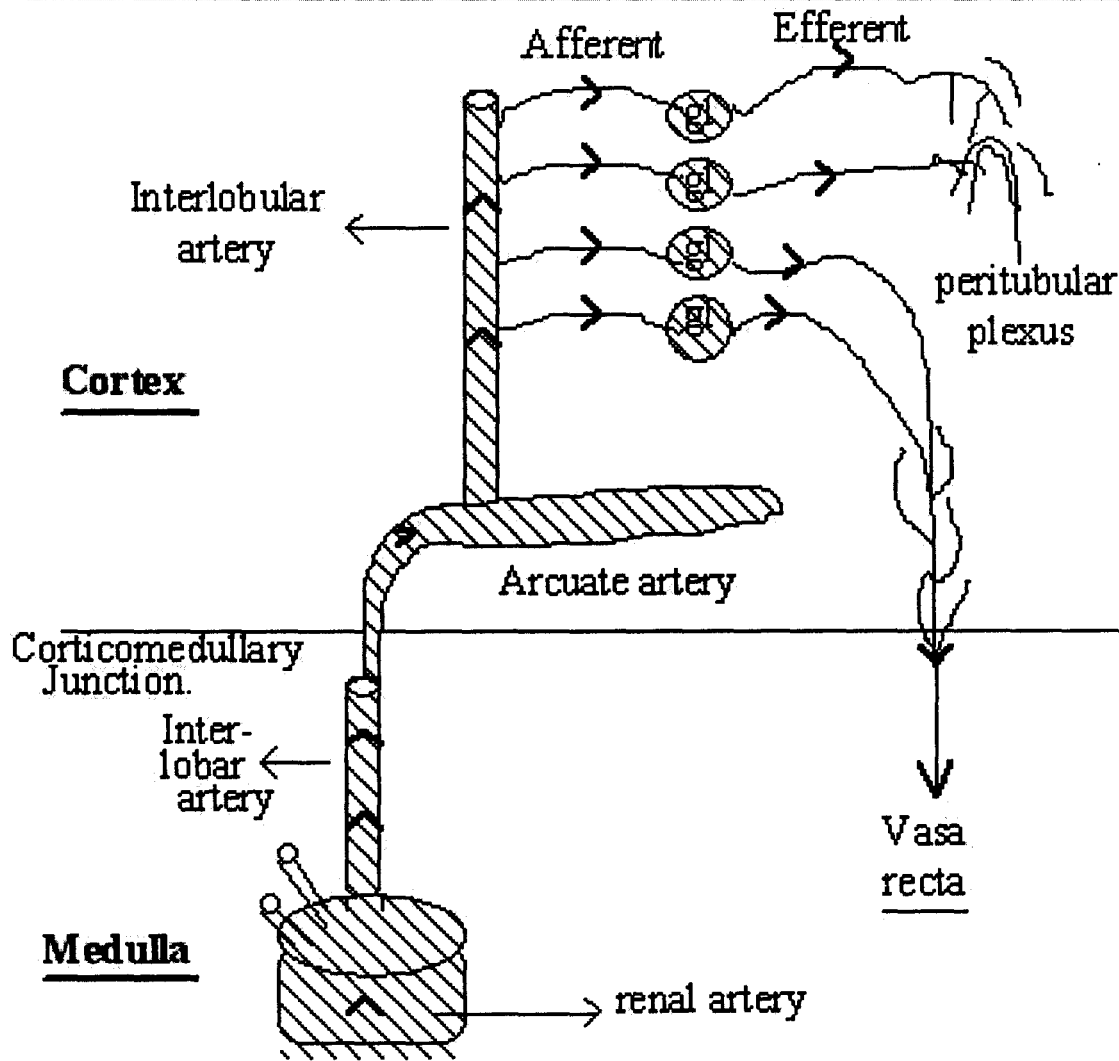


(Glomerulus)



(Juxta-glomerular apparatus)

Intra renal Circulation





RENAL Physiology

Function of the kidney:

- 1- **Excretory:** excretion of waste products & drugs.
- 2- **Regulatory:** control of body fluids volume & composition.
- 3- **Endocrinal:** production of erythropoietin, renin & P.G.
- 4- **Metabolic:** metabolism of vitamin D.

Endocrine function of the kidney:

- Renin angiotensin system.
- Production of PG & erythropoietin.
- It is a site of action of ANP and parathormone.
- Vitamin D metabolism.

Function of the kidney tubules:

1- P.C.T.

- Reabsorption of 65% of Na and most K and Ca.
- Reabsorption of all HCO_3^- .
- Reabsorption of 65% of water (obligatory water reabsorption).
- Reabsorption of all A.A and glucose.

2- Loop of Henle

- Reabsorption of Na, Cl, Ca, K in ascending limb and reabsorption of H_2O in descending limb.
- It increases the medullary tonicity which is important in the process of urine concentration in collecting tubule as follows:
 - Na outflow from ascending limb $\rightarrow \uparrow$ Na in medulla $\rightarrow \uparrow$ medullary tonicity.
 - ADH $\rightarrow$ open H_2O channels of collecting tubules through cAMP $\rightarrow$ This will subject the fluid in the collecting tubules to the high medullary tonicity $\rightarrow \text{H}_2\text{O}$ reabsorption $\rightarrow$ urine concentration.

3- Distal tubules

- Na reabsorption & K excretion through aldosterone.
- Also there is reabsorption of H_2O and Ca.
- Secretion of H^+ and ammonia.

4- Collecting tubules

- Concentration of urine as above.
- The amount of reabsorbed water is variable (facultative water reabsorption) depending on the blood level of ADH.



CHRONIC RENAL FAILURE (CHRONIC kidney disease)

Definition:

It is a gradual slowly progressive (within years) irreversible deterioration of kidney function with development of the clinical syndrome of uremia (Progressive course of ongoing loss of kidney function).
Finally it progresses to end stage renal failure.

End stage renal disease (ESRD) = GFR < 10-15 ml/m

It is a stage of C.R.F. at which kidney function cannot sustain life.
So replacement therapy is indicated (dialysis or transplantation).

Stages of chronic Kidney disease :-

- Stage 1 : Kidney damage (pathologic abnormalities or abnormalities in blood or urine tests or imaging studies) with normal GFR ($GFR \geq 90 \text{ ml/m/1.73}^2$)
- Stage 2 : Kidney damage with mild ↓ GFR (GFR 60-89)
- Stage 3 : Moderate ↓ GFR (GFR 30-59)
- Stage 4 : Severe ↓ GFR (GFR 15-29)
- Stage 5 : Kidney failure (GFR < 15)

Causes:

- 1- Diabetic nephropathy (longstanding history of D.M).
- 2- Systemic hypertension (long duration).
- 3- Chronic GN (history of puffiness).
- 4- Chronic interstitial nephritis e.g chronic pyelonephritis (history of recurrent UTI), drug abuse.
- 5- Obstructive uropathy → stones, bilharziasis
- 6- Analgesic nephropathy (abuse of paracetamol + aspirin).
- 7- Lupus nephritis (young ♀ + arthropathy).
- 8- Congenital polycystic Kidney (+ve F.H).
- 9- Gout (History of arthropathy).
- 10- Undetermined etiology.

The uraemic \$ is due to accumulation of products e.g. urea, phosphate, parathyroid hormone, guanidine, phenols, indols, beta 2 microglobulin and deficiency of Ca, Vitamin D, erythropoietin, testosterone and estrogen.



Clinical Picture

i.e. (Complications of C.R.F)

1- G.I.T.

1. Nausea & Vomiting → persistent & not responding to usual treatment.
2. Diarrhea.
3. Hepatitis (due to blood transfusion) (hepatitis C, B).
4. Hiccough (central effect).
5. Gastritis as uremic toxins are irritant to gastric mucosa with increased gastrin level.
6. GIT bleeding.
7. Decreased gastric emptying with increased risk of reflux oesophagitis.
8. Ammoniacal odour of mouth (urea excreted in saliva with splitting by bacteria → NH_3). i.e uremic fetor.

2- Blood:

A) Anemia

1. Erythropoietin deficiency.
2. Decrease intake with haematinic deficiency e.g. Iron, Vit. B₁₂, Folate.
3. Bleeding tendency.
4. Decreased life span of RBCs and toxic B.M depression.
5. Blood loss during hemodialysis or through GIT.
6. B.M fibrosis due to hyperparathyroidism !?
7. ACE inhibitors may decrease erythropoietin release → anemia.

B) Bleeding tendency

1. Capillary fragility.
2. Thromboasthenia due to the uraemic toxins.

3- C.V.S

1. **Pericarditis** → uremic toxins are very irritant to pericardium. It is a feature of severe preterminal uraemia or inadequate dialysis. It usually resolves with intensive dialysis.
 - **Haemorrhagic pericardial** effusion with the danger of pericardial tamponade may occur so, anticoagulants should be used with caution.
2. **Systolic and diastolic dysfunctions** are also common.
 - **Diastolic dysfunction** is due to left ventricular hypertrophy and contributes to hypotension during fluid removal and hemodialysis.
 - **Systolic dysfunction** is due to myocardial fibrosis, abnormal myocyte function, myocardial calcification, carnitine and selenium deficiency.
3. **Arrhythmias** due to electrolyte disturbances.
4. **Hypertension** due to salt and H₂O retention and hyperreninism.



Patient with C.R.F, with normal or decreased blood pressure

- Salt losing nephropathy e.g. tubulointerstitial disease.
- Hyporeninism e.g. Diabetic nephropathy, obstructive uropathy and interstitial nephropathy.

Patient with C.R.F with no or mild anemia

Polycystic kidney, hypernephroma with chronic renal disease
hydronephrosis, (These diseases → ↑↑ erythropoietin production).

4- Endocrine & metabolism:

1. Insulin Resistance

- Impaired glucose tolerance and not D.M (uremic pseudodiabetes).
- Also insulin resistance may contribute to hypertension & lipid abnormalities.

2. Insulin is catabolized by and to some extent excreted by the kidney so insulin requirements in diabetic patient with renal impairment will be decreased.

3. Thyroid dysfunction with sluggish TSH release !?

- ↑ TRH → release of prolactin (also there is decrease in prolactin clearance) → Amenorrhea, galactorrhea & Impotence

4. Ca ↓ → 2ry hyperparathyroidism.

5. Impaired clearance of triglycerides and hypercholesterolaemia may occur in advanced renal failure.

6. **Decreased serum testosterone** level with impotence and decreased spermatogenesis.

7. Disturbance of the cyclical changes in female sex hormones → oligomenorrhea or amenorrhea.

5- Bone disease (renal osteodystrophy)

1. Decreased renal production of 1-hydroxylase enzyme → ↓ production of active vitamin D. this leads to increased parathyroid hormone release (**2ry hyperparathyroidism**).

2. Active vitamin D deficiency also results in calcium malabsorption → 2ry hyperparathyroidism.

3. Phosphorus retention occurs due to reduced excretion by the kidneys. This results in 2ry hyperparathyroidism.

4. Secondary hyperparathyroidism leads to increased osteoclastic activity with cyst formation and bone marrow fibrosis (**osteitis fibrosa cystica**).

5. Active vitamin D deficiency and ↓ Ca will result in impaired bone mineralization (**Osteomalacia**).

6. Long standing parathyroid hormone excess may cause increased bone density (**osteosclerosis**) particularly in the spine where alternating bands of sclerotic and porotic give rise to **rugger Jersey** appearance.



7. Impaired mineralization also occurs with aluminium toxicity due to phosphorus binders containing aluminium or as a result of exposure to aluminium in water source used to make up dialysate fluids for hemodialysis.

- Aluminium accumulation also impairs bone mineralization → osteomalacia.
- Phosphorus retention → ↓ S. Ca.
- Adynamic bone disease means that both bone formation and resorption are decreased.
- Gout and pseudogout also occur in CRF.

6- Chest

1. Pneumonia (↓ immunity).
2. Acidotic breathing.
3. Non cardiogenic pulmonary edema.

7- Neurological

1. *Neuropathy*

- Motor → Weakness.
- Sensory → Glove & Stock hypoesthesia.
- Autonomic neuropathy
 - Impotence.
 - Diarrhea & Constipation.
 - Gastroparesis.
 - Orthostatic hypotension.

2. *Uraemic myopathy.*

3. *Uraemic myoclonic jerk.* (myoclonus).

4. *Convulsions.*

5. *Dysequilibrium* \$: due to rapid ↓↓ of blood urea by intensive dialysis → (Brain edema).

6. *Uraemic encephalopathy.*

7. *Strokes* e.g. cerebral hge, due to hypertension and bleeding tendency.

8. *Carpal tunnel* \$ due to amyloidosis (B₂ microglobulin).

9. *Restless legs syndrome* (irresistible need to move legs, often interfering with sleep).

10. *Dialysis Dementia* (AI related), it may be associated with aluminum bone disease and microcytic anemia.

In CRF retention of beta 2 microglobulins leads to neuropathy, carpal tunnel syndrome and amyloid infiltration of the joints.



8- Skin

1. **Itching** due to:
 - Hyperparathyroidism.
 - Hyperphosphatemia.
 - Hypercalcemia (due to Ca containing P binders + vit D).
 - Elevated calcium and phosphate product.
2. **Color (earthy look)**, it is a mixture of 3 colors !?.
 - Yellow → due to urochrome pigment retention.
 - Pallor → due to anemia.
 - Increased melatonin.
3. **Recurrent pyogenic infections.**
4. **Urea frost**: whitish powder on the skin surface (another cause of itching)
5. **Bronze color** due to haemosiderosis.

9- Acid base & electrolytes

1. $\text{Ca} \downarrow$, $\text{P} \uparrow$ and $\text{Al} \uparrow$ (excreted through the kidney).
2. $\text{K} \uparrow$ (excreted through the kidney).
3. $\text{PH} \downarrow$ (metabolic acidosis due to H^+ retention).
4. Na and water retention with normal sodium level, hyponatremia may occur due to excessive ingestion of water, hypernatremia is infrequent in chronic renal failure.

10- Urinary manifestations

1. Manifestations of the cause as UTI, renal stones.
2. Early polyurea and nocturia due to impaired concentrating ability.

Aggravating factors for progression of renal disease (reversible factors in uremia)

- 1) **Vascular volume depletion**:
 - a- Absolute: aggressive use of diuretics, GIT fluid losses.
 - b- Effective: low COP, renal hypoperfusion with nephrotic \$ or liver disease with ascites.
- 2) **Nephrotoxic drugs** e.g. NSAIDs or aminoglycosides.
- 3) **Urinary tract obstruction** e.g. stone or prostatic hypertrophy.
- 4) **Infections**: sepsis with hypotension or urinary tract infection.
- 5) **Radiographic contrast materials** which are used in IVP, angiography e.g. (coronary or renal angiography) and CT scan with contrast.
- 6) **Hypertensive crisis**.
- 7) **Metabolic**: e.g. hypercalcemia, hyperphosphatemia, hyperlipidemia, DM and obesity.
- 8) **High protein diet**
- 9) **Smoking**



Investigations

I. To prove renal failure:

Blood Urea ↑, serum creatinine ↑, PH ↓, K ↑.

II. To prove chronicity

1. (↓ Ca, ↑ P, ↓ Hb) these changes are usually present in CRF but may also occur with acute renal failure.
2. Broad casts in urine.
3. Low fixed specific gravity (**1010**) = Isothenuria.
4. Sonar (most important)
 - Shrunken kidney.
 - Advanced hydronephrosis
 - Polycystic kidney.
 - Poor differentiation between cortex & medulla (parenchymal disease).
 - Remember that in Diabetic nephropathy & amyloidosis the kidney size is usually normal or enlarged.

III. Causes (to control any reversible factors if possible)

1. **Urine:** for pus cells usually indicate active bacterial infection, RBCs casts in cases of glomerulonephritis.
2. **Plain X-ray** for stones.
3. **Sonar:** for stones or hydronephrosis.
4. **Markers for S.L.E.**
5. **Eosinophilia** suggests vasculitis or allergic tubulointerstitial nephritis.



Treatment of C.R.F.:

A- Conservative (medical ttt)

Indications:

1. Fair general condition (= Minimal symptoms = Stable C.R.F.).
2. S. Cr. < **8mg/dl**.
3. Blood urea < **200 mg/dl**.

The above 3 indications must be fulfilled together.

Lines of medical ttt:

1. Diet:

- Low protein diet, about **40 gm** (small piece of meat) i.e. **0.6gm/kg** of which 60% contains proteins rich in essential amino acids e.g. eggs, lean meat and milk. Low protein diet decreases glomerular hyperfiltration so reduces glomerulosclerosis. Also protein restriction reduces phosphate load.
- Carbohydrate (source of energy **250 gm/d**).
- Low potassium diet (fruits & citrus fruits).
- Sodium
 - If there is salt losing nephropathy e.g tubulointerstitial disease give Na supplements.
 - If there is salt retention (in most patients), restrict Na.
- Fluid chart, (the fluid intake = **500 cc** + volume of urine in the previous day). Dilutional hyponatremia may occur if water intake exceeds the capacity to excrete the water load.
- Prolonged dietary protein restriction should be avoided. Also it is preferable to start dialysis therapy a little earlier than to cause malnutrition. For dialysis patients the recommended protein intake must be increased.

2. GIT manifestations:

- Vomiting, give domperidone.
- Hiccough, give domperidone.
- Gastritis, we can use H₂ blockers or proton pump inhibitor.



3. Phosphate chelators:

- Oral Ca carbonate acts as a Calcium supplement & also reduces absorption of Dietary Phosphorus, 500mg tab tds before meals.
- Also Ca acetate can be used.
- Al hydroxide must be avoided as a phosphate chelator.
- H₂ blockers decrease the effectiveness of phosphate binders.
- Newer non calcium non aluminum containing resins (e.g. Sevelamer) can be used as phosphate binders, 800mg tablet tds before meals.

4. Endocrinal disturbances:

- Ca supplements → Calcium carbonate oral.
→ Vitamin D (one alpha). It is a synthetic analogue of vit D (alfacalcidol) tablet 0.25 µg - 1 µg/Day.
- Anabolic steroids improve bone disease & decrease protein catabolism.
- Hyperprolactinemia is treated by bromocriptine (Parlodel).

5. Anaemia:

- Iron therapy is helpful especially iron infusion.
 - Erythropoietin (Eprex, Recormon) is genetically made, the starting dose is 50 u/Kg three time/wk then the dose is adjusted to maintain a target hemoglobin of 10-12 gm/dl.
 - Avoidance of blood transfusion lessens the chance of infection or sensitization to HLA antigens, which becomes a barrier to successful renal transplantation in the future.
- Failure to respond to adequate dose of erythropoietin may be due to iron deficiency, bleeding, malignancy or infection.

6. CVS manifestations:

1. Hypertension:
 - B Blockers.
 - ACE inhibitors.
 - Ca channel blockers.
2. Pericarditis: It is an indication of dialysis.
3. Heart failure → (see CVS).
4. Arrhythmia → (see CVS).

- Combination of antihypertensive drugs with large dose of diuretics is useful to correct sodium and water retention.

7. Impotence: It can be treated by Sildenafil (Viagra).



8. Acid base and electrolyte disturbance:

Hyperkalemia

- Dietary restriction of potassium intake.
- Cation exchange resins to remove potassium in GIT. E.g polystyrene sulphonate resins (sorbisterit) 15gm oral/8hrs with Laxative e.g Lactulose.
- Glucose insulin infusion.
- If there is no response → dialysis.

Acidosis (correction of acidosis helps to correct hyperkalemia).

- Sodium bicarbonate, but it may cause fluid retention.
- Calcium carbonate used as calcium supplement and phosphate binder. Also it has a beneficial effect on acidosis.
- If there no response → dialysis.

9. Pruritis is improved by controlling Ca/P balance and hyperparathyroidism. Antihistaminics, oral charcoal and ultraviolet photo therapy are helpful.

10. Lastly treat any reversible factors

- Stone → surgery.
- D.M → control.
- UTI → antibiotics.
- Hypertension → control.
- Avoid nephrotoxic drugs.

⊕ follow up monthly with periodic investigations for creatinine, urea, Na, K, Hb, Ca and P.

Q Slowing progression of renal disease ? (renoprotection protocol)

- 1- Dietary protein restriction → ↓ glomerulosclerosis.
- 2- Control serum lipids (LDL) to decrease mesangial proliferation and sclerosis.
- 3- ACE inhibitors or angiotensin receptor blockers may exert beneficial effects due to their effects on intrarenal hemodynamics especially in patients with diabetic nephropathy.
- 4- Control blood pressure, add diuretics to prevent hyperkalemia and help to control blood pressure, glycemic control in diabetics.
- 5- Avoid nephrotoxic drugs.

B- Dialysis:

Indications:

1. Bad general condition.
2. S. Cr. > 8 mg/dL and > 6 mg/dL in D.M or GFR < 10 ml/min for non diabetics and GFR ≥ 15 ml/min for diabetics.
3. Blood urea > 200 mg/dL.

One indication is enough to start dialysis.



	<u>Haemodialysis</u>	<u>Peritoneal dialysis</u>
Advantages	- Less invasive than peritoneal Dialysis. - Rapid action.	- It is a natural membrane and able to remove the middle molecule substances. - No need for heparin use. - No hemodynamic changes (no need for extracorporeal circulation of blood).
Disadvantages or complications	- See later.	- Infection (peritonitis). - Delayed response, also it is time consuming. - Injury of viscous organ.
Indications	- It is the usual dialysis modality (see later).	- Bleeding tendency. - Diabetic nephropathy (some prefer Peritoneal Dialysis in diabetic nephropathy) - Hypotension (usually it does not lead to hemodynamic disturbances)
Contraindications	- Bleeding tendency !? - Hypotension.	- Urgent case (Hemodialysis is preferred). - Ascites. - Peritoneal adhesions. - Abdominal hernia or intraabdominal sepsis.

Nutrition & medications for patients under regular H.D:

- 1) The protein intake must be increased, 1.2 gm/Kg.
- 2) Antihypertensives and hypolipidemic drugs.
- 3) Phosphate binders.
- 4) Active vitamin D (alfacalcidol).
- 5) Vitamin B, iron and erythropoietin therapy.

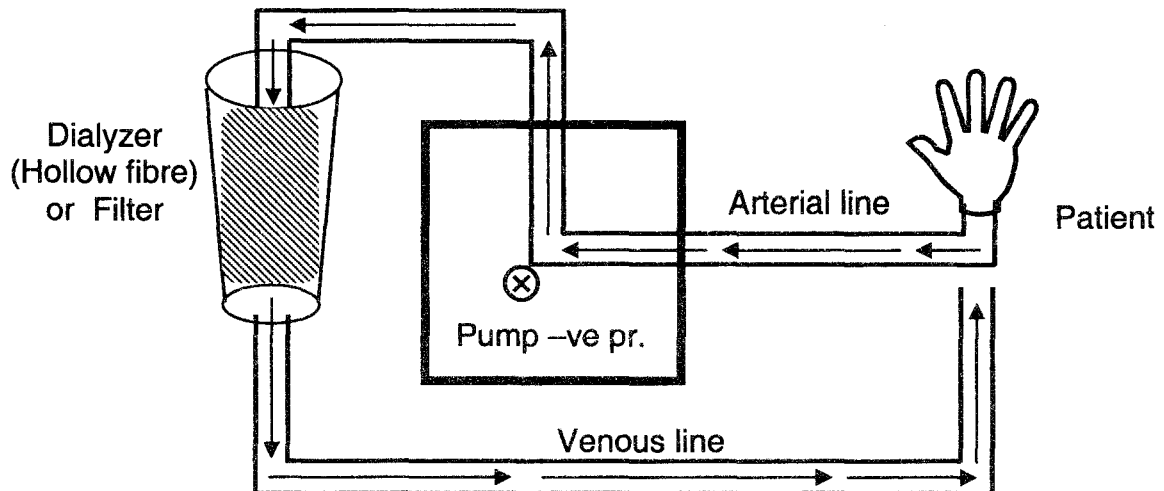
C- Transplantation (see later).



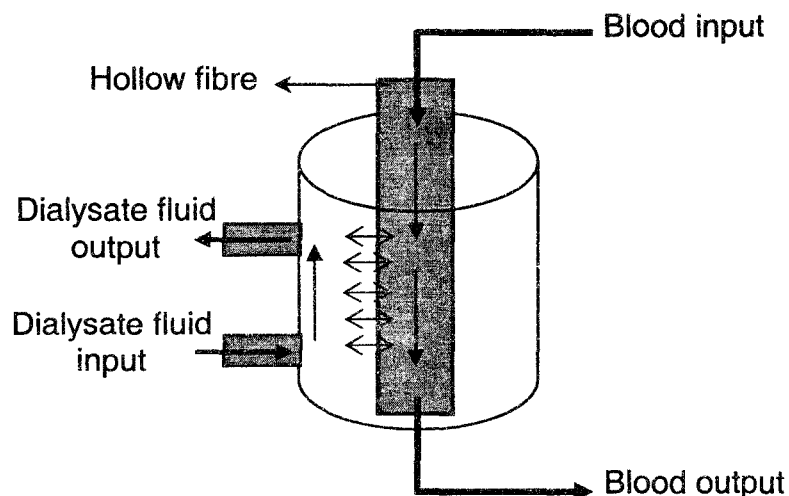
Techniques of Dialysis

Haemodialysis:

- Three sessions /wk.
- Session (4 hrs).



Dialysate & blood become in contact with each other through a semipermeable membrane with exchange according to concentration gradient through the membrane of hollow fibres.



Connection of patients to haemodialysis machine (vascular access)

A-V fistula:

- It is done between Radial or brachial artery & cephalic vein.
- Its value is to avoid collapse of the veins when they are subjected to the -ve pressure of the machine.
- After few weeks the veins of U.L become distended with thickening of their wall due to increased venous pressure (arterialization of vein) which becomes ready for connection after about 4 wks.

**Acute cases:**

- Connect the patient from a big vein to withstand the -ve pressure of the machine. We can use femoral vein by femoral vein catheter. Also internal Jugular or subclavian veins can be used (They are preferred).
- This is a transient measure until the fistula becomes ready for connection.

Q: Indications of haemodialysis:

- 2- Acute & chronic renal failure.
- 3- Hyperkalemia or hypercalcemia.
- 4- Drug toxicity (Salicylates, Barbiturate & Alcohol toxicity)!?
- 5- Ultra filtration & reinfusion (used in treatment of Ascites)
- 6- Ultrafiltration to treat pulmonary edema.

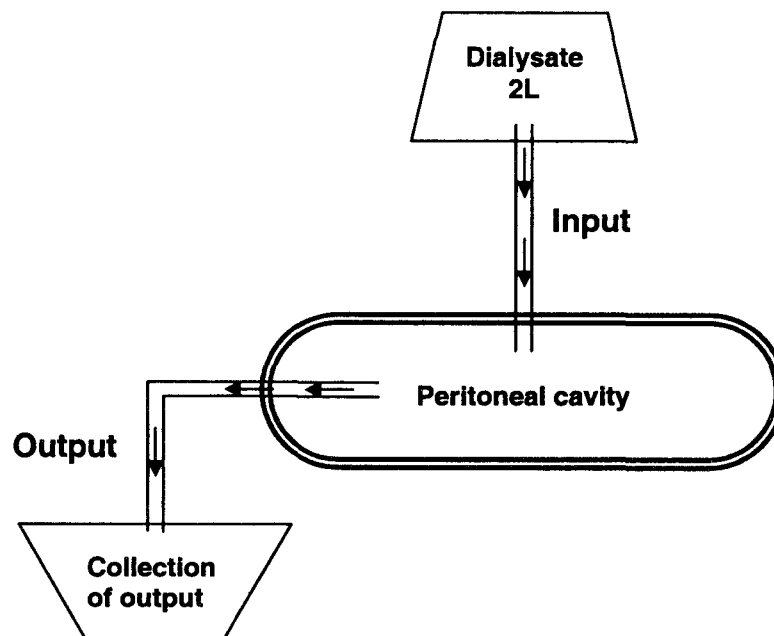
Complications of Hemodialysis:

- | | |
|---------------------------|---------------------------|
| - Infection (hepatitis). | - Bleeding (heparin). |
| - Brain edema. | - Hypotension. |
| - Air embolism. | - Dialysis Dementia. |
| - Atherosclerosis. | - Infective endocarditis. |
| - Pseudogout. | - Serositis. |
| - Depression. | - Pruritis.. |
| - Dialysis amyloidosis. | |



Peritoneal dialysis

Intermittent peritoneal dialysis



- **The run (45 minutes):**
 - Input (15 minutes).
 - Exchange (15 minutes).
 - Output (15 minutes).
- Patients with CRF need *(exchanging 20-60 L of dialysis fluid three times a week)*.
- To guard against infection give
 - Systemic antibiotic.
 - Intraperitoneal antibiotic.
- **Tenckoff catheter:** Self retained catheter in the peritoneum.

Complications of peritoneal dialysis

- Injury (perforation of viscus)
- Peritonitis
- Hypokalemia
- Hyperglycemia with solutions containing high dextrose concentration.

2) C.A.P.D: (Continuous ambulatory peritoneal dialysis)

Isotonic fluid introduced to the peritoneum 2L / 6 hrs, each exchange needs about 20-40 minutes.



ACUTE RENAL FAILURE

Def: Sudden onset of deterioration of kidney functions within a period of, days or weeks and results in uremia, it is reversible with treatment of the cause.

Causes:

I. Prerenal: (correctable, i.e. normal kidney with ↓ perfusion)

- - **Hypovolemia**
 - Blood → hemorrhage
 - Plasma → burns
 - Fluids → Gastroenteritis
- **Shock with normal intravascular volume**
 - Cardiogenic shock
 - Massive pulmonary embolism
- **Others:** third spacing e.g. pancreatitis, hepatorenal syndrome.

Drugs which impair renal autoregulation, such as ACE inhibitors and NSAIDs increase Liability to prerenal failure

Pathogenesis of prerenal failure:

- The kidneys receive about 25% of the cardiac output at rest.
- If cardiac output is reduced or if there is hypovolemia, regional vasoconstriction occurs limiting the blood flow to organs other than the heart and brain.
- Initially the blood flow is diminished to the skin then GIT and muscles.
- Usually the kidney is able to maintain glomerular filtration close to normal despite wide variations in renal perfusion (autoregulation).
- Further decrease of COP or intravascular volume leads to further depression of renal perfusion with drop of glomerular filtration due to selective cortical vasoconstriction → oliguria.

C/P of prerenal failure

- Manifestations of the cause e.g. marked reduction of blood pressure with oliguria, decreased skin turgor, reduced jugular venous pressure and dry mucous membranes.



Investigations of prerenal failure

- Increased BUN and creatinine in blood.
- BUN : Cr ratio tends to be high > 20:1.
- Urine Na < 20 mmol/L.
- Urine osmolarity > 500 m.osmol/L.
- Urine analysis showing no cells or cellular casts, but few hyaline or granular casts may be present.
- Sonar is usually normal.

Treatment of prerenal failure

- Treatment of the cause e.g. blood transfusion, I.V fluid therapy or treatment of heart failure.
- Central venous pressure (CVP) must be monitored to determine the rate of administration of fluids.
- Small dose dopamine may be of value to increase the renal blood flow!?

2. Renal causes = (Intrinsic parenchymal renal disease):

- Acute tubular necrosis (ATN).
- Acute interstitial nephritis.
- Acute severe pyelonephritis → with papillary necrosis e.g. in D.M.
- Rapidly progressive glomerulonephritis.
- Malignant hypertension.
- Atheroembolic renal disease.

C/P of acute renal failure due to intrinsic renal disease:

1- Manifestations of renal failure e.g.

- Oliguria and hypertension.
- Nausea and vomiting.
- Acidotic breathing.
- Weakness and arrhythmia due to hyperkalemia.
- Hypervolemia with development of pulmonary edema.
- Uraemic encephalopathy.

2- Manifestations of the cause

- Allergic manifestations or rash in acute hypersensitivity interstitial nephritis.
- Puffiness in acute G.N.
- Vascular purpura in vasculitis.
- Malignant hypertension.
- Prerenal factors in ATN.



Investigations:

- High urea and creatinine, BUN : Cr ratio is not high.
- Urine sediment is helpful e.g. RBCs, WBCs.
- Eosinophilia and eosinophiluria in hypersensitivity nephritis.
- ANCA and high ESR in vasculitis

Treatment:

I- General measures

- Good fluid chart.
- Control blood pressure. NaCHO₃ for acidosis.
- Low protein diet.
- Glucose/insulin for hyperkalemia.
- Domperidone for vomiting.

II- Treatment of the cause e.g.:

- Pulse steroid therapy in rapidly progressive G.N or vasculitis.
- Stop drugs causing nephrotoxicity.
- Antibiotics for sepsis or pyelonephritis.

III- Dialysis: the indications (see later).

B. Post-renal = (obstruction):

- Bilateral ureteric obstruction.
- Unilateral ureteric obstruction with non functioning or absence of the other kidney.

C/P of post acute renal failure:

- Patients are usually less severely ill than patients with prerenal or intrinsic renal disease.
- Manifestations of the cause as renal colic, hematuria or anuria (in contrast to oliguria associated with ATN).
- Uremic manifestations may be delayed until BUN > 150 mg/dL and S. Cr > 10 mg/dL.

Patient with acute onset of: Loin pain, Anuria, Deterioration of kidney function

- Suspect urinary tract obstruction.
- Investigated by sonar (for stones & signs of back pressure)
- Treatment by urological interference e.g. ureteric catheter, ureteric stents and/or nephrostomy tube.



Acute Tubular Necrosis (ATN)

Causes:

1- **Ischemic causes (Prerenal factors)** if not corrected rapidly).

2- **Toxic causes**

→ Endogenous

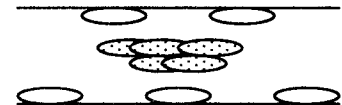
- Hemoglobin (Hemolytic anemia).
- Myoglobin (Rhabdomyolysis).
- Bilirubin Nephropathy in obstructive jaundice.

→ Exogenous:

- The dye of I.V.P, CT scan or angiography (contrast nephropathy).
- Drugs: aminoglycosides.
- Toxins of gram - ve septicemia.

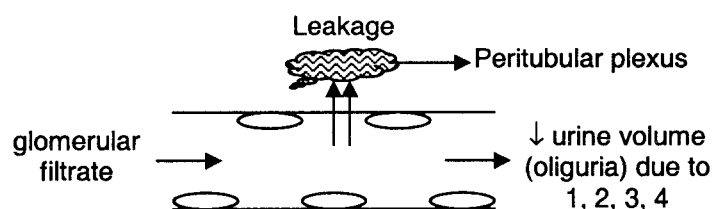
Pathology of tubular necrosis:

1- The **necrosed epithelial Cells** fall to the lumen of tubules → **granular casts** will formed → tubular obstruction will occur



2- **Glomerular contraction** → ↓ surface area available for filtration, due to reflex afferent arteriolar vasospasm.

3- **Peritubular leakage (back leak):** loss of function of the tubular cells leading to leakage of the glomerular filtrate to the peritubular plexus



Recovery will occur due to

- Relief of tubular obstruction.
- Regeneration of tubules, but the kidney tubules remain unable to concentrate urine for a time.

- **Ischemia** → diffuse affection of all kidney tubules.
- **Toxins** → mainly affect P.C.T.



Mechanism of ATN:

- 1- Entry of calcium into cells due to disruption of the cell membrane with an increase in cytosolic cell calcium concentration, this disturbs mitochondrial respiration leading to anaerobic glycolysis and intracellular acidosis.
- 2- Cortical blood flow may be further reduced by local and systemic vasoconstriction induced by thromboxane, vasopressin, angiotensin and endothelins.
- 3- Increased production of intracellular proteases.
- 4- Cell injury resulting from reperfusion with blood after initial ischemia.
- 5- Reduced prostaglandin production.

Clinical Picture (3 stages)

I. Oliguric phase: (2-4 wks)

Causes: (see before).

C/P: (do not forget manifestation of the cause).

- 1- **Urine volume** → Oliguria < 400 cc/D.
→ Anuria < 50 or < 100 cc/D.
- 2- **GIT** → Vomiting, nausea.
- 3- **CVS** → Hypertension.
→ Hypervolemia → pulmonary edema.
- 4- **Metabolic errors** → K ↑ → weakness, arrhythmia.
→ Acidosis → acidotic breathing.
- 5- Drowsiness, fits and coma.

Investigations:

1. Creatinine ↑, urea ↑.
2. pH ↓, K ↑.
3. Ca ↓, P ↑ or may be normal.
4. Hb ↓ or may be normal.
5. Urine → Granular casts or tubular casts.
6. Sonar almost normal kidney.



Management:

- The aim of management is to keep the patient alive until spontaneous recovery of renal function occurs.
- **General measures:**
 - Good nursing.
 - Daily body weight to assess fluid balance changes.
- **Hyperkalemia** by Ca gluconate (10 ml of 10% solution) to reduce the risk of arrhythmia. Reduction in serum potassium is achieved by I.V administration of 100 ml of 50% glucose plus 10 units of rapid acting insulin. Ion exchange resins, e.g polystyrene sulphonate resins (Sorbisterit) orally to prevent subsequent hyperkalemia.
- **Acidosis** treated with I.V sodium bicarbonate.
- **Fluid balance** i.e. daily fluid intake should equal urine output plus losses from fistulae and from vomiting plus an allowance of 500 ml daily for insensible loss.
- **-Diet**
 - Sodium and potassium restriction with rare exception.
 - Protein restriction to 40 gm/day if it is hoped to avoid dialysis.
 - Patients treated by dialysis must receive 70 gm/day protein.
 - Hypercatabolic patients will require an even higher nitrogen intake to prevent negative nitrogen balance.
- **Control blood pressure.**
- **Vitamin supplements** are usually needed.

Q : Indications of hemodialysis in acute renal failure

- Bad general condition (severe symptoms).
- Serum K > 7 mEq/L which is not controlled by conservative measures.
- Marked acidosis ($\text{HCO}_3^- < 15$)/Normal (22-26).
- Volume over load with or without pulmonary edema → ultrafiltration.
- Pericarditis.

2. Polyuric phase : (for 3 - 4 Ds)

Causes:

- 1- Relief of tubular obstruction.
- 2- Regeneration of kidney tubule but they are still unable to concentrate urine.
- 3- Urea retention (osmotic diuresis)



Clinical Picture:

- Improvement of general condition.
- $\downarrow$ Na, $\downarrow$ K due to diuresis.
- Urine output 3-5 L /d.

Treatment

- Fluid, replacement is sometimes required with Na and K supplements.

3. Post diuretic phase:

- Clinical improvement.
 - Kidney functions become normal.
 - Urine output becomes normal volume, concentrated.
- If the oliguria is not reversible, the diagnosis is cortical necrosis and not ATN and CRF will develop.
 - No need for renal biopsy to diagnose ATN.

How can you differentiate prerenal, renal & post renal uraemia?

1. At first bladder outflow obstruction is ruled out by insertion of a urethral catheter or flushing of an existing catheter for the possibility of obstruction.
2. Absence of upper tract dilatation on renal ultrasonography can rule out urinary tract obstruction in most cases.
3. If there is no diuresis after fluid intake $\pm$ frusemide or low dose dopamine, acute intrinsic renal failure is present. The following table is to differentiate prerenal failure from failure due to intrinsic renal disease.

	<u>Prerenal</u>	<u>Intrinsic</u>
Urine Na	< 20 mmol/L	> 40 mmol/L
urine osmolarity	> 500 mOsmol/L	< 350 mOsmol/L
BUN:creatinine ratio	high ratio	low ratio

How to differentiate Acute from chronic renal failure?

1. A rapid rate of change of serum urea & creatinine suggesting an acute process.
2. Small kidneys with increased echogenicity diagnostic of chronic process.
3. Evidence of renal osteodystrophy is indicative of chronic disease.
4. Measurement of carbamylated Hb (a product of non enzymatic reaction between urea & Hb) if high suggesting a chronic disease.
5. $\downarrow$ Hb, $\downarrow$ Ca, $\uparrow$ P may suggest a chronic disease.
6. Low fixed specific gravity of urine (1010) and presence of broad casts in urine analysis indicates chronic renal failure.



Glomerulonephritis or Glomerulonephritides

Definition: Glomerulonephritis is an immune mediated glomerular injury with symmetrical simultaneous involvement of both kidneys at the same time.

Mechanism of glomerular injury:

- Circulating immune complex.
- In situ formation of immune complex.
- Antiglomerular basement membrane antibody (anti-GBM) e.g. Good pasture syndrome.

The above mechanisms activate secondary mechanisms that produce glomerular damage.

Secondary mechanisms of glomerular injury:

- Complement activation.
- Fibrin deposition.
- Platelet aggregation.
- Activation of kinin system.
- Inflammation with neutrophil dependent mechanisms.

Immune complex or anti GBM antibody deposition trigger the above secondary mechanisms resulting in an increase in capillary permeability and glomerular damage.

Glomerular syndromes (Presentations of G.N)

i) Acute nephritic syndrome:

Nephronal hematuria (RBC casts and/or dysmorphic RBCs) temporarily associated with renal impairment or acute renal failure.

ii) Nephrotic syndrome:

- Heavy proteinuria ($> 3.5 \text{ gm/D/1.73m}^2$).
- It may be pure nephrotic syndrome with bland sediment or mixed nephrotic / nephritic syndrome with active sediment.

iii) Rapidly progressive glomerulonephritis:

Nephronal hematuria (RBCs cast and / or dysmorphic RBCs) with renal failure developing over weeks to months and diffuse glomerular crescents.

iv) Asumptomatic urinary abnormalities:

- Isolated proteinuria ($< 2 \text{ gm/D/1.73m}^2$).
- Hematuria (with or without proteinuria) e.g. in IgA nephropathy and Alport's syndrome.

v) Chronic G.N (see later).



Glomerulonephritis or Glomerulopathies Presented with Nephrotic \$

1- Minimal lesion (Nil \$):

This is not a true glomerulonephritis due to absence of inflammation & inflammatory cells.

- Common in children (> 85% to 90% of nephrotic \$ in children).
- 20 % of adult nephrotic \$.
- It is steroid sensitive.
- There is selective proteinuria.
- Spontaneous remission in 40-50% of cases may occur.
- Renal failure usually does not occur!? (see glomerulosclerosis).

Causes:

1. Primary: Idiopathic.
2. Secondary: NSAID - lymphoma.

Clinical Picture: Nephrotic \$ (see later).

N.B.: A suggested explanation for the proteinuria is the production of a factor that increases glomerular permeability to protein; this factor is mostly produced by T lymphocytes.

Microscopic examination:

- **Light**: Almost normal (nil)
- **E/ M**: Fusion of foot process of epithelial cells or effacement.
- **Immunofluorescence**: -ve (nil) - (no antibodies or complement).

Treatment:

- Prednisolone **60 mg/m²** orally for **4 wks** or until proteinuria disappears (the average body surface area is 1.73 m²).
- When the urine has been free from proteins continue the drug for **2 wks** then prednisolone should be gradually reduced over **4 wks**.
- For those who have frequent relapses and require repeated courses of corticosteroids, the use of alternate day prednisolone therapy may reduce the incidence of steroid toxicity.

Cyclophosphamide may be used 2 mg/kg/d & continued for 2 wks after remission or withdrawn after 6 wks if no response.

Indications:

- Steroid resistant cases.
- Steroid dependent cases.
- Frequent relapses

Recently cyclosporine can also be used.



Prognosis:

- There is remission and exacerbation.
- Relapses occurring many years later are recognized but even in the long term there does not seem to be any deterioration of renal function !? (see glomerulosclerosis).

2- Membranous G.N

- It accounts for about 45% of nephrotic \$ in adults.
- If occurs in old age search for malignancy.
- CRF can occur within 5-10 yrs.
- Characterized by heavy proteinuria + ↑↑ incidence of renal vein thrombosis.

Causes: (pathogenesis most likely in situ immune complex)

1. 1ry.
2. 2ry: SLE – hepatitis B - malaria (*Plasmodium malariae*) - gold - penicillamine – captopril - Neoplasm of lung, stomach or breast.

Clinical Picture: Nephrotic \$ (see later).

Microscopic examination:

- Thick basement membrane due to deposition of immune complex)
- **Light:** Thick basement membrane.
- **E/M:** More details (Thick basement membrane & subepithelial spikes).
- **Immunofluorescence:** Ig G - C3



Treatment:

- In patients with mild proteinuria (< 4 gm/d) or with moderate proteinuria (4-8 gm/day) with normal GFR we can give just conservative treatment i.e. diuretics, ACE inhibitors to reduce proteinuria and to control blood pressure with observation for either spontaneous remission or progression.
- Patients with moderate proteinuria as above with no response to the above therapy or patients with proteinuria ≥ 8 gm/d with or without diminished GFR may be treated with combination of corticosteroids and chlorambucil for 6 months period or with cyclosporine. This treatment may cause remission and decrease the incidence of chronic renal failure.

Prognosis:

- 50 % of patients develop chronic renal failure, 25 % have complete remission, while another 25% experience a partial remission (proteinuria < 2gm but > 200 mg/D). These patients may maintain a stable GFR for decades.



3- Focal & Segmental glomerulosclerosis (FSGS)

- Accounts for 10-15% of nephrotic syndrome in children.
- Adult can also be affected (15-20% of adult nephrotic syndrome).
- It is steroid resistant.
- It can lead to CRF within about 10 years.

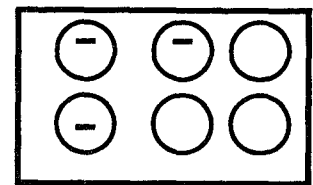
Causes:

- Primary → idiopathic.
- Secondary:
 - AIDS associated nephropathy.
 - Heroin nephropathy.
 - Reflux nephropathy.
 - Bilharziasis.
 - Obesity.
 - Sickle cell disease.
 - Solitary kidney.

Clinical Picture: Nephrotic \$ (see later).

Microscopic examination:

- **Light:** Almost normal.
- **E/M:**
 - Focal = some glomeruli are affected.
 - Segmental i.e part of each glomerulus is affected.
 - Glomerulosclerosis (partial or total replacement of glomerulus by hyaline material).
- **Immunofluorescence:** IgM - C₃.



Treatment:

☆ Immunosuppressive therapy for idiopathic FSGS:

- First line, steroids (daily or every other day), prolonged therapy with taper for 6 months.
- Second line, for those with increased risks of steroids (DM, obesity), cyclosporine or cyclophosphamide.
- Third line therapy: mycophenolate.

☆ Treatment of the cause in secondary FSGS.

☆ For both idiopathic or secondary forms: control blood pressure, ACE inhibitors, lipid control.

- Recurrence of FSGS in transplants occurs in 40% of patients.
- Heroin abusers and patients with HIV usually follow a much more rapid deterioration (progression to ESRD within < 1 year).



4- Amyloidosis Kidney

- It is not a glomerulonephritis, but it is considered to be glomerulopathy.
- It presents with nephrotic \$, then deterioration of kidney function, eventually leading to chronic renal failure.

Causes:

1. Rheumatoid disease.
2. Suppurative lung \$.
3. Familial Mediterranean Fever (FMF):
 - Polyserositis with recurrent abdominal pain + rebound tenderness.
 - Fever (recurrent).
 - Nephrotic \$ usually develops late.
4. Multiple myeloma – non Hodgkin's lymphoma..

- Amyloid deposition in kidney may be consisting of immunoglobulin light chains (AL-amyloid) which occurs in cases of multiple myeloma, Waldenstrom's disease, non Hodgkin's lymphoma or in primary amyloidosis.
- Amyloid A is found in long standing inflammatory conditions e.g. suppurative lung diseases, rheumatoid arthritis and FMF.

Clinical Picture:

- Cause + nephrotic \$
- Amyloidosis kidney also leads to renal tubular acidosis and nephrogenic diabetes insipidus.

Diagnosis:

- Biopsy and staining by Congo red, this gives pink color & shows green birefringence by polarized microscope.

Treatment:

- Treatment of the cause to prevent further amyloid deposition.
- Steroids and melphalan may be helpful in primary amyloidosis.
- Colchicine in F.M.F. ↓↓ the incidence of amyloidosis ?!
- Treatment of nephrotic \$ and chronic renal failure.



5- Diabetic Nephropathy

- It is not a glomerulonephritis but is considered to be a glomerulopathy.
- It is related to control of Diabetes and also to duration.
- It may be a part of **Diabetic triopathy** :
 - Retinopathy
 - Nephropathy
 - Neuropathy
- Diabetic nephropathy is the commonest cause of end stage renal disease (ESRD).
- It occurs in 30-50% of IDDM (due to long natural history) and in 10-15% of NIDDM.
- It is rare during the first 5 years of D.M, after which the incidence increases until it reaches a peak after 15 years of D.M.
- Diabetic nephropathy is characterized by persistent albuminuria (> 300 mg/24 hours), decline in GFR and hypertension.
- Renal biopsy had shown that a good percent of patients with NIDDM have nephropathy that is related to their diabetes. Presence of RBCs casts or low levels of complement should lead to a search for other causes of renal disease in diabetics.
- Diabetic retinopathy is found in 90% of IDDM, nearly one third of type 2 diabetes with proven diabetic nephropathy have no evidence of retinopathy.

Pathophysiology:

- Early there is renal hypertrophy associated with glomerular hyperfiltration (GFR >150ml/min this is related to glycaemic control).
- The afferent arteriole becomes vasodilated leading to increase of the intraglomerular filtration pressure → damage of glomerular capillaries → glomerular sclerosis.

Pathology:

- Early, there is basement membrane thickening with mesangial expansion
- Later there is diffuse or nodular glomerulosclerosis, the latter is sometimes known as the Kimmelstiel-Wilson syndrome.

The presence of linear deposition of IgG along the capillary walls and deposition of IgM and C₃ is a non specific passive trapping.



Stages of diabetic nephropathy:

- Hyperfiltration (raised GFR above normal by 20-30%). This is related to glycemic control.
- Stage of microalbuminuria. (> 30 mg/d and < 300 mg/d)
- Gross proteinuria $\pm$ nephrotic $\$$ (1-5 years after onset of proteinuria).
- Renal impairment, then renal failure (GFR declines 1ml/min/month after the onset of gross proteinuria).
- End stage renal disease (ESRD).

Clinical Picture and diagnosis

- D.M. + nephrotic $\$$ then CRF develops.
- Hypertension is common.
- Early diagnosis by appearance of **micro albuminuria** which is tested by radioimmunoassay or by using special dipsticks.
- **Microscopic examination:** There is thickening of basement membrane; also there is hyaline arteriosclerosis of both afferent and efferent arterioles.
- **Ultrasound examination:** normal or large kidney size. No active urinary sediments.

Treatment

- Restriction of dietary proteins.
- Control of blood sugar prevents the early hyperfiltration.
- Control of blood pressure.
- ACE inhibitors (must be used early e.g stage of micro-albuminuria)

Actions:

- Vasodilatation of efferent arteriole.
- $\downarrow$ Intra glomerular pressure (antiproteinuric effect).
- $\downarrow$ Process of glomerulosclerosis $\rightarrow$ $\downarrow$ the progression of renal disease.

Diagnosis of diabetic nephropathy is usually not dependent on renal biopsy!?

Problems

- 1- Patient with biharziasis $\rightarrow$ nephrotic $\$$ = Bilharzial nephropathy (FSGS – membranoproliferative).
- 2- Generalized lymphadenopathy then nephrotic $\$$?
AIDS $\rightarrow$ FSGS
lymphoma $\rightarrow$ minimal lesion
- 3- Fever then nephrotic $\$$?
FMF $\rightarrow$ (Amyloidosis kidney)
Malaria $\rightarrow$ (malarial nephropathy)
- 4- Arthropathy then nephrotic $\$$?
SLE $\rightarrow$ Nephrotic $\$$
Rheumatoid $\rightarrow$ Amyloidosis kidney.
 $\rightarrow$ Drugs: NSAID, penicillamine, gold $\rightarrow$ nephrotic syndrome.
- 5- Patient with long durated D.M plus nephrotic $\$$ the diagnosis is mostly diabetic nephropathy.



Glomerulonephritis presented with Nephritic \$

Diffuse Proliferative G.N

It is the commonest cause of nephritic \$.

Causes:

1- Post infectious

- Streptococcal.
- Non streptococcal
 - Staphylococcal.
 - Pneumococcal.
 - Viral → Mumps, hepatitis.

Diffuse proliferative G.N associated with visceral abscess has been reported more frequently in patients with pulmonary abscess.

2- SLE.

3- Henoch-Schonlein purpura.

It is common in children, there is:

- Purpuric eruption.
- Abdominal pain.
- Arthritis.
- Haematuria.

4- Shunt nephritis (Infected ventriculoatrial shunts).

Clinical Picture: of diffuse proliferative G.N (nephritic \$).

Microscopic examination

- **Light:** cells ↑ (endothelial - and - mesangial) + PNL, macrophage infiltrate.
- **E/M:** details with subepithelial complex deposits (humps).
- **Immunofluorescence:** IgG-C₃.

Treatment

- Cause e.g
 - Infection: give antibiotic.
 - SLE: give steroids.
- Treatment of nephritic \$ e.g fluid chart, antihypertensives diuretics (see later).

Prognosis: *poor prognostic criteria in post infectious GN are:*

- Old age.
- Nephrotic range proteinuria.
- Hypertension.
- Sclerosis in glomeruli.



Rapidly progressive G.N i.e. RPGN (Crescentic G.N):

It is a severe form of G.N. Rapidly progressive G.N means nephronal hematuria (RBCs casts and/or dysmorphic RBCs), proteinuria with renal failure, developing within weeks to months with diffuse glomerular crescent formation in more than 70% of glomeruli.

Classification and causes of rapidly progressive G.N:

1- Infectious diseases

- Poststreptococcal G.N.
- Infective endocarditis.

2- Multisystem diseases

- SLE.
- Henoch-Schonlein purpura.
- Wegener's granulomatosis and microscopic polyarteritis.
- Good pasture's syndrome.

3- Drugs

- Hydralazine, penicillamine.
- Allopurinol, rifampicin.

4- Primary glomerular disease i.e. Idiopathic or primary crescentic G.N

- **Type I** with linear deposits of Ig (anti-GBM antibody mediated).
- **Type II** with granular deposits of Ig (immune complex mediated).
- **Type III** with few or no immune deposits of Ig (Pauci immune).

a) ANCA mediated.

b) ANCA –ve.

ANCA i.e. anti neutrophil cytoplasmic antibodies are detected in cases of wegener's granulomatosis and microscopic polyarteritis.

Clinical presentation of RPGN

- Picture of acute renal failure which may be oliguric or anuric.
- Manifestations of the cause e.g. SLE, previous upper respiratory tract infection or vasculitis.
- Rapidly rising serum creatinine.
- Urine analysis showing RBCs, RBCs casts and proteinuria.
- Renal biopsy shows the crescents.



Treatment of RPGN

- **Pulse corticosteroid therapy.**
 - Methylprednisolone 1000 mg I.V over 30-60 minutes for 3-5 days.
 - It must be started early before the development of irreversible renal failure. Pulse steroid therapy is effective particularly in immune complex or ANCA mediated cases. Pulse steroid therapy must be followed by oral prednisone 1 mg/kg/d. then gradual withdrawal with improvement, then low dose maintenance with follow up.
 - Cyclophosphamide can be used with or without steroid as a pulse therapy 0.5-1 gm/m² monthly. Once remission has been achieved, azathioprine should be substituted for cyclophosphamide.
 - In cases of intolerance to azathioprine or cyclophosphamide mycophenolate can be tried.
- **Plasmapheresis** is also effective.

Good pasture \$

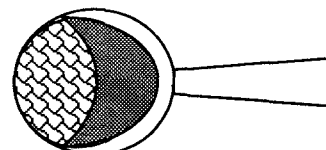
It is an autoimmune disease due to circulating antiglomerular basement membrane antibody.

Clinical Picture

- As above (see RPGN).
- Hemoptysis as there is similarity between glomerular B.M. & alveolar membrane.

Investigations

- **Ab against GBM.**
- **Biopsy**
 - Light: crescents
 - E/M: details → The crescent formed of epithelial cells + macrophages.
 - Immunofluorescent: no immune complex but there is linear deposits of IgG.



Treatment of good pasture \$:

- Steroids + cytotoxic drugs (pulse therapy as above).
- Plasmapheresis

NB: Steroid therapy is not effective in RPGN with anti-GBM antibody.

Problems

- Infection then nephritic = post infectious G.N.
- Arthropathy with nephritic = Lupus nephritis.
- Haemoptysis + renal impairment = Good Pasture \$, T.B or Wegener's granulomatosis.



Group of G.N Presented with Nephrotic \$ or Nephritic \$ or Mixed Nephrotic/Nephritic

i.e (Nephrotic range proteinuria with active urine sediment)

1. Membranoproliferative (MPGN) or Mesangiocapillary

Causes:

- Primary: Idiopathic MPGN.
- Secondary: Infectious diseases e.g hepatitis C with cryoglobulinemia, IE, B.
- SLE and neoplasms (leukemia, lymphoma).

Clinical Picture:

- Some cases presented with
 - Nephritic \$ (15-20%).
 - Asymptomatic proteinuria (25-30%).
- Mixed picture is common (active urine sediments + nephrotic range proteinuria).
- 30% of patients develop CRF at the end of 10 years.

Investigations:

- Serum $C_3 \downarrow$ (hypocomplementemia) with normal C_4 .
- Biopsy:
 - **Light:** → The basement membrane is thickened.
→ Proliferation of mesangial cells.
 - **E/M:** details

<u>Type I</u>	Subendothelial seposits.
<u>Type II</u>	Dense deposits (intra membranous).
<u>Type III</u>	Morphologic variants with features similar to both type I and type II.
 - **Immunofluorescence:** (C_3 – IgG).

- In type II there is a nephritic factor (IgG which activates C).
- **Prognosis:** Bad prognosis, type II recurs in transplanted kidney.
- G.N. with $\downarrow C$. → Membranoproliferative - poststreptococcal – SLE

Treatment:

- The role of steroids or cytotoxic drugs is controversial.
- The use of these drugs is not recommended.
- Antiplatelet drugs (aspirin 375 mg/d $\pm$ dipyridamole 75-100mg/d) may have a beneficial effect.
- In children, a trial of steroids may be of values.
- As in all proteinuric diseases ACE inhibitors should be used to decrease proteinuria.

Prognosis:

- Poor prognostic criteria include the presence of nephrotic syndrome or azotemia at the time of diagnosis. Spontaneous remission of proteinuria occasionally occurs.



2. Mesangioproliferative GN.

Causes:

- Idiopathic
- IgA nephropathy (Berger's disease)
- Biharziasis
- SLE

Clinical Picture:

- It may be presented with nephrotic \$, nephritic \$ or haematuria.

IgA Nephropathy (Berger's disease)

- Common in young adults.
- Commonly presented with recurrent haematuria with upper respiratory tract infection (synpharyngeal).
- 20 % of cases develop nephrotic \$.
- G.N in Henoch-Schonlein purpura has similar pathological features and is sometimes regarded as the same condition.
- Many diseases may be associated with IgA deposits e.g chronic Liver disease, celiac disease and spondyloarthropathies

Microscopic examination

- **Light:** Proliferation of mesangial cells.
- **E/M:** Mesangial proliferation.
- **Immunofluorescence:** IgA + C₃ in the mesangium.

Treatment:

- Patients with proteinuria > 3 gm/d should receive prednisone for 4-6 months.
- Fish oil (omega 3) may be useful in some patients with slowly progressive disease.
- Long term Ab advocated as the episodes of macroscopic haematuria associated with upper respiratory tract infection!?

Prognosis

- Progressive renal insufficiency develops in 20 to 30% of patients after 20 years.
- Some have a more rapid progression with renal failure within 4 years.
- Poor prognostic criteria include nephrotic range proteinuria, hypertension and higher grade renal biopsy changes. These criteria can be considered as indications of therapy.
- Surprisingly, recurrent macroscopic haematuria is a good prognostic sign!?

Q Proliferative G.N

Proliferative G.N means an increase in cell number due to hyperplasia of one or more of the resident glomerular cells with or without inflammatory cell infiltration. It has the following subtypes:

- Diffuse proliferative G.N.
- Focal Proliferative G.N
- Crescentic G.N.
- Membranoproliferative G.N.
- Mesangioproliferative G.N.



Nephrotic \$

- It is a syndrome characterized by heavy proteinuria $> 3.5 \text{ gm /24 hrs / } 1.73\text{m}^2$ with hypoproteinemia, edema and hyperlipidemia.
- Usually hypercholesterolemia & lipiduria are present due to increased lipoprotein production by hepatocytes.
- Edema is due to hypoalbuminemia and secondary hyperaldosteronism.

Causes

Primary G.N

- Minimal Lesion.
- Membranous G.N.
- FSGS.
- Membranoproliferative.
- Mesangioproliferative.

Secondary G.N

a) Systemic disease

- Diabetic nephropathy.
- SLE - Rheumatoid disease.
- Amyloidosis - sarcoidosis.

b) Infections: Bilharziasis – malaria – hepatitis B – HIV.

c) Drugs: Penicillamine – Captopril.

d) Malignancy: e.g. lymphomas – carcinomas.

e) Hereditary: e.g. Alport's syndrome .

f) Miscellaneous:

- Myxedema – Thyroiditis.
- Renovascular disease.

Glomerulopathies presented with nephrotic \$

* Nephrotic \$ with bland urine sediments

- * Minimal lesion
- * Membranous
- * FSGS
- * Diabetic nephropathy
- * Amyloidosis

* Nephrotic \$ with active urine sediments (mixed nephrotic / nephritic)

- * Membranoproliferative
- * Mesangioproliferative
- * Secondary GN to SLE, Henoch Schonlein disease or cryoglobulinaemia

Clinical Picture

1. **Edema** (hypoalbuminemia + 2ry hyperaldosteronism).
 - Starts as puffiness then LL edema.
 - Serous membranous trasudation e.g. pleural effusion, ascites, pericardial effusion.
 - Gradual onset.
2. **No hypertension or oliguria or azotemia** except late in some types.
3. **Manifestations of the cause** as SLE, DM.



Problems

- Patient with nephrotic \$ + dyspnea, D.D:
 - Pleural effusion → Stony dull
 - Pericardial effusion → Inspiratory filling of neck veins
 - Pulmonary embolism → Chest pain
 - Pneumonia → Fever chest pain dyspnea
- Patients with nephrotic \$ are liable to pneumonia due to loss of Ig in urine & cytotoxic drugs or steroids therapy → immunodeficiency.
- Proteins lost in urine

a) Albumin.	d) Protein C, S.
b) Immunoglobulin.	e) Anti thrombin.
c) Thyroglobulin.	f) Transferrin.
- Protein C & S are natural circulating anticoagulants → So loss of them in urine → DVT → Pulmonary embolism.

D.D of nephrotic \$

- Other causes of generalized edema
- G.N presented by nephrotic \$.

Investigations

1. Serum creatinine, blood urea, BUN → normal.
2. Late in some G.N → ↑ serum creatinine and blood urea or BUN.
3. S. albumin ↓↓.
4. Urine → ↑↑ protein > **3.5gm/24h urine**.
→ Cast (hyaline or fatty cast).
5. Biopsy (**diagnosis - prognosis - response to ttt**) → Light - E/M - immunofluorescence (see before in different types of G.N).

Treatment

1) Diet

- Normal protein intake is advisable with proteins of high biologic values.
- Excessive protein intake → increase urinary protein excretion which may lead to glomerulosclerosis. With the development of renal impairment modest protein restriction is advised.

2) Salt poor albumin should not be used except in cases of severe hypoalbuminemia with refractory anasarca as the albumin will be lost in urine within 24-48 hours.

3) Diuretics e.g loop diuretics can be used, also spironolactone can be added to correct hyperaldosteronism. Excessive diuresis should be avoided to prevent the occurrence of prerenal failure.

4) ACE inhibitor to decrease proteinuria

5) Hypolipidemic drugs e.g. Atorvastatin 10-20 mg/D to decrease plasma cholesterol.

6) Specific therapy according to the type of glomerulopathy (see before).

7) Treatment of the cause.



Acute G.N. (Nephritic \$)

- *It is a clinical syndrome characterized by sudden onset (days) of haematuria, proteinuria, oligurea & hypertension and azotemia with RBCs casts, dysmorphic RBCs in urine, the proteinuria is a non nephrotic range proteinuria.*

Causes

1. Post infectious

- Usually, it develops **7-20 days** after streptococcal infection with group A beta hemolytic streptococcus of a nephritogenic type (1, 2, 4, 12, 18, 25, 49, 55, 57, 60).
- Staphylococci- pneumococci – viral.

2. SLE.

5. Infective endocarditis.

3. Vasculitis.

6. Shunt nephritis.

4. Henoch-Schonlein purpura.

7. Cryoglobulinemia.

Clinical Picture

1. **Oligurea** as cell proliferation of glomeruli → ↓GFR.
2. **Hypertension**
 - Hypertensive encephalopathy.
 - Hypertensive heart failure.
3. **Edema** → mainly due to salt & H₂O retention.

Investigations

1. Urea ↑, Cr↑, RBCs and RBCs casts in urine.
2. Proteins < 3 gm/day, sometimes > 3 gm/day.
3. Markers for SLE, ASOT, ANCA.
4. C₃, C₄ levels may be reduced.
5. Cryoglobulins are increased in cryoglobulinemia.
6. Renal image is usually normal.
7. Biopsy, specially if there is rapidly progressive renal failure suggesting crescentic G.N (RPGN).



Treatment

1. Fluid chart

- Control blood pressure
- Salt restriction
- Protein restriction is required only if severe uremia occurs.
- Regular measurement of blood pressure and daily weighing.

2. Mild to moderate hypertension and edema may respond to salt restriction and diuretics e.g. frusemide, but other hypotensive agents may be required.

3. Treatment of the cause e.g. antibiotics for post infectious G.N and steroids in SLE.

4. Treatment of complications.

- Hypertensive encephalopathy is treated by parenteral agents e.g. hydralazine, nitrates or Na nitroprusside by slow I.V infusion. Fits can be controlled with I.V diazepam.
- Pulmonary edema is treated as usual (see CVS). High doses of frusemide may be required. If this fails to produce diuresis, fluids can be removed by ultrafiltration using the hemodialysis machine.

Prognosis

- 1. Poststreptococcal G.N:** The prognosis in children is excellent. A small number of adults develop hypertension and / or renal impairment later in life.
- 2. Acute G.N of unknown cause:** The prognosis is less good.
- 3. Systemic vasculitides and crescentic G.N:** are usually of poor prognosis is poor.

Chronic G.N

- It is the end result of many glomerular disease associated with progressive loss of functioning nephrons.
- Early there is mild proteinuria with a slight decrease in GFR and minimal hypertension.
- These patients generally progress to ESRD.
- The differentiation of chronic G.N from other hypertensive nephrosclerosis is usually difficult but the presence of heavy proteinuria and / or glomerular bleeding suggests G.N.
- The presentation of these patients is unfortunately late and the correct diagnosis is never ascertained.



Tubulo INTERSTITIAL DISEASES

- Group of diseases characterized by infiltration with inflammatory cells and edema in interstitial tissues with tubular damage but the glomeruli are spared in acute cases. In chronic cases there is increased interstitial fibrosis with hyalinized glomeruli.

Acute interstitial nephritis: (drug induced hypersensitivity nephritis)

Causes:

- Acute hypersensitivity nephritis caused by *Penicillins, sulpha, cephalosporins, rifampicin, thiazides, frusemide, allopurinol & NSAID.*

Acute infectious interstitial nephritis i.e acute pyelonephritis see Later

Diagnosis:

- 1- Acute renal failure (oliguric or non oliguric).
- 2- Manifestations of allergy (fever - rash), arthralgia.
- 3- Urine showing eosinophiluria wBcs casts & also there is eosinophilia.
- 4- Urinary protein < 1 gm /d
- 5- PCT defects e.g. Glucosuria, Phosphaturia and aminoaciduria
- 6- Distal tubular defects e.g hyperkalemia, RTA
- 7- Medullary defects→ urine concentrating defects.

Treatment

- Stop drugs ± short term steroid ?!.
- Dialysis for ARF.
- **Prognosis:** Most patients have good recovery of kidney function but may be left with significant interstitial fibrosis.



Chronic interstitial nephritis

Causes:

- NSAID.
- Lead.
- Gouty nephropathy.
- Sickle cell anaemia.
- Irradiation.
- Chronic pyelonephritis. (infection)

Diagnosis:

- 1- Manifestations of the cause.
- 2- Usually there is polyuria due to defects in urine concentration.
- 3- Proteinuria usually < 1 gm.
- 4- Salt wasting may occur, tubular defects as above.
- 5- Papillary necrosis may occur in cases of analgesic abuse or sickle cell anemia, the sloughed papilla may cause ureteral colic or produce acute ureteric obstruction
- 6- Chronic renal failure occurs late.

Treatment

- Cause.
- Treated as CRF.



URINARY TRACT INFECTION (U.T.I)

Acute Pyelonephritis

Causes

Organisms

- E. coli.
- Klebsiella - pseudomonas.
- Proteus.
- Staph – enterococcus fecalis.

Routes of infection:

- Ascending from urethra & bladder (Peri urethral colonization).
- Hematogenous.
- Lymphatic (periurethral & periureteric lymphatics).

Pathology:

Infiltration of tubules and interstitium with PNL. The Bacterial inflammation is also present in calyceal and relvic mucosa, more advanced changes occur in diabetics e.g necrotizing papillitis

Predisposing factors:

1. **Sex:** ♀ > ♂
 - Short urethra.
 - Absence of bactericidal prostatic fluid.
2. **Obstruction:**
 - Young age → stone.
 - Old age → prostatic enlargement.
3. **Pregnancy:**
 - Hormones → relaxation of ureters → stasis.
 - Pressure of uterus → stasis.
4. **Neurogenic bladber** e.g. paraplegia.
5. **Catheter:** it is a nosocomial infection.
6. **Vesico ureteric reflux:**
 - During micturation, urine may pass upward to ureters up to renal pelvis.
 - Reflux → infection and vice versa.
 - Reflux → reflux nephropathy (FSGS) → nephrotic \$.
7. **Renal diseases** oliguria ↓ washout of urine → ↑ liability to infection.
8. **Systemic disease** e.g. D.M.



Clinical Picture

1. **Classic**

- FAHM.
- Loin pain.
- $\pm$ Turbid urine.
- Rigors
- $\pm$ Dysuria, frequency.
- Tender renal angle.

2. **Children:** fever without localization,
Sometimes fever $\rightarrow$ reflex vomiting $\rightarrow$ misdiagnosed as gastroenteritis.

3. **Pregnancy:** UTI may occur without symptoms (asymptomatic bacteriuria)
i.e organism $> 100,000$ ml + no symptoms.
40 % of cases develop pyelonephritis So asymptomatic bacteriuria must be treated.

4. **D.M.** - Severe pyelonephritis with necrosis of the papilla
- Acute necrotizing papillitis (= acute papillary necrosis $\rightarrow$ acute renal failure).

D.D.

- * Appendicitis.
- * Prenephric abscess:
 - * No urinary symptoms or findings.
 - * Pain & tenderness in loin.

Investigations:

1. Urine

- Culture +ve
- WBCs casts as it is an upper U.T.I
- Pus cells $\uparrow$
- $\uparrow$ Nitrites in urine

2. Blood: ESR $\uparrow$, CRP, leucocytosis.

3. Investigations of the cause:

- Plain X-ray $\rightarrow$ stone.
- IVP $\rightarrow$ stone, stricture.
- Micturating cystogram (for reflux).
- Pelvi-abdominal ultrasound

Most gram negative organisms reduce nitrates to nitrites. Dipsticks that detect significant pyuria depend on the release of esterases from leucocytes. Positive dipstick tests for both nitrite and leucocytic esterases are highly predictive of acute infection.

Prophylactic measures in females with recurrent UTI

- Fluids **2 L/D**
- Regular emptying of bladder / **3 hrs.**
- Double micturation if reflux present.
- Emptying bladder before and after intercourse.



Treatment:

1. Start with co-trimoxazole tab. **2 tab twice daily or Amoxicillin cap. 500 mg / 6 hrs** or ciprofloxacin 500 mg/12 hr.
2. Then give Ab according to culture for **7-10 days**.
3. Repeat the culture during the course of treatment & then **7 & 21 days** after ttt → the cultures must be -ve.
4. If culture is +ve during follow up:
 - Same organism within **7 d** means Relapse.
 - Other organism or the same after 2 wks with -ve culture means Reinfection.

Search for the cause & treat, if there is no apparent cause with resistant organism you can give Ab for 2-6 wks according to culture with follow up.

5. **Alteration of pH :**

- Alkaline urine (Na HCO_3) → potentiate sulpha & aminoglycosides.
- Acidic urine (vit C) → potentiate tetracycline.

6. **Fluid intake :**

- ↑ urine output → ↑ washout of urine.
- But it may dilute the urinary concentration of Ab ?!

Drugs used in urinary tract infection:

- | | |
|---|--|
| 1- Co-trimoxazole. | 2 tab / 12 hrs. |
| 2- Ampicillin | 500 mg / 6 hrs. |
| 3- Amoxicillin | 500 mg / 6 hrs (better than Ampicillin). |
| 4- Nitrofurantoin | 100 mg / 8 hrs orally. |
| 5- Nalidixic acid | 500 mg / 6 hrs. |
| 6- Garamycin(Nephrotoxic) | 3 mg / kg / d in divided dose (Amp 80 mg / hrs). |
| 7- 3 rd G. Cephalosporines e.g. Cefotaxime | 2 gm / d I.M. & I.V. (minimal nephrotoxicity). |
| 8- Ofloxacin | 400 mg / 12 hrs. |
| 9- Ciprofloxacin | 500 mg / 12 hrs. |



Chronic pyelonephritis

It results from vesicoureteric reflux or obstructive uropathy leading to recurrent pyelonephritis with papillary damage, chronic interstitial nephritis and cortical scarring. There is interstitial fibrous tissues with hyalinized glomeruli.

Clinical Picture:

- 1- History of recurrent UTI.
- 2- Polyuria as the kidney tubules are unable to concentrate the urine, late oliguria occurs.
- 3- Chronic renal failure.

Investigations:

- 1- Urine → + ve culture, few pus (cells) + few WBCs casts.
- 2- Sonar → shrunken kidneys, renal stones
- 3- IVP → clubbed calyces.
- 4- Micturating cystogram for reflux.

Treatment

- 1- Antibiotic according to culture for **7-10 days**.
- 2- Then suppressive therapy for 3-6 ms with low dose antibiotic (urinary antiseptic), the therapy is better to be guided by urine culture and sensitivity).

e.g. **Amoxicillin 250 mg/d.**
Nitrofurantoin 50 mg/d.
Trimethoprim 100 mg/d.

} Urinary antiseptic dose
- 3- Intravaginal estrogen therapy has been shown to produce reduction in the number of episodes of U.T.I. in postmenopausal women.
- 4- Reflux in children ceases around puberty with growth of the bladder base. Generally, early detection and treatment of infection with or without ureteral reimplantation to create a competent valve can prevent further scarring.

Adjustment of the dose of aminoglycosides according to S.Cr.

- Gentamycin (garamycin) full dose is 80 mg / 8 hrs.
- Example, In patient with S. Cr. 4 mg / dl

The required dose:

$$1. = \frac{\text{Full dose}}{\text{S.Cr.}} = \frac{240}{4} = 60 \text{ mg / d.}$$

$$2. \text{ Or give } 80 \text{ mg/8 X S. creatinine} = 80 \text{ mg/32 hrs.}$$



Cystitis & Urethritis

Clinical Picture

- 1- Dysuria, frequency.
- 2- Good general condition.

Investigations:

Pus, + ve culture, no WBCs casts.

Treatment

- 1- Sutrim 2 tabs / 12 hrs for 3-5 days.
- 2- Ciprofloxacin 500 mg / 12 hrs for one week.
- 3- Amoxicillin 3 gm / 24 hrs (once).
- 4- For pregnant females or diabetics, give antibiotic for 7 days.

Urethral \$

Female with symptoms suggestive of urethritis & cystitis & no bacterial growth in urine culture.

Causes

- Chlamydia, give tetracycline.
- Toilet preparation.
- Urethral congestion with intercourse.
- Post - menopausal.

Viral Renal Infections

- Secondary immune complex G.N may result from chronic viral infection e.g. Hepatitis B → membranous G.N, Hepatitis C → membranoproliferative G.N, HIV → focal glomerulosclerosis.
- Infections associated with acute interstitial nephritis e.g CMV, HIV and Epstein-Barr virus.



Tuberculosis of Urinary Tract

- It is usually 2ry to T.B else where & occurs as blood borne infection.
- The initial lesion occurs in cortex then pelvis and ureters → bladder & epididymis.

Clinical Picture:

1- General features of T.B e.g night fever, night sweating, loss of weight, loss of appetite.

2- Dysuria, haematuria.

Investigations:

- Sterile pyuria + specific culture. IVP and sonar should be done after (2-3 ms) as ureteric strictures may develop in the healing phase.

Treatment:

- Anti - T.B (INH and rifampicin)

Upper UTI = pyelonephritis	Lower UTI = prostatitis, cystitis, urethritis
<u>Clinical Picture</u> – Loin pain – Toxaemia (fever, rigors) – ± dysuria	– -ve – Dysuria, frequency
<u>Blood Picture</u> – TLC ↑ – ESR ↑ – CRP +ve	– -ve
<u>Urine</u> – Pyuria – +ve culture – WBC casts – Organism coated with antibodies	– Pyuria – Positive culture – No WBC casts. – -ve



RENAL STONES

Most of renal stones are composed of Ca oxalate and phosphate, these are more common in males.

Types of renal stones:

- 1- Ca oxalate (65%).
- 2- Ca phosphate (15%).
- 3- Magnesium - ammonium phosphate stones (10-15%).
- 4- Uric acid stones (3-5%).
- 5- Cystine stones (1-2%).

Predisposing factors:

1- Metabolic causes

A- Ca stones: mainly Ca oxalate & Ca phosphate associated with:

- i- Hypercalcuria, it may be idiopathic or due to renal tubular acidosis. Also it occurs with high Na diet and with loop diuretics.
- ii- Hypercalcemia
 - Sarcoidosis.
 - Vit D intoxication.
 - Hyperparathyroidism.
- iii- Hyperoxaluria
 - Type I (hereditary) or primary hyperoxaluria. It is autosomal recessive.
 - Type II is due to excessive absorption of oxalate from intestine (intestinal oxaluria). It may be seen in malabsorption \$ e.g IBD and chronic pancreatitis due to binding of intestinal Ca by fatty acids within the bowel allowing free oxalate to be absorbed.

B- Uric acid stones: in hyperuricemia & hyperuricosuria.

C- Cystine stones: Cystinuria.

2- Obstruction & infection

Urinary tract infection → (epithelial debris + pus debris) → act as nidus → deposition of crystals → stones.

3- Dietary factors: Excessive intake of milk & its products → Ca stones.

4- Climate: Hot weather with excessive sweating.

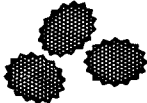
5- Primary renal disease

- Polycystic kidney disease.
- Medullary sponge kidneys.



- Renal tubular acidosis.

Pathology:

1. Oxalate stone		Usually brownish, mamillated, single, or multiple → haematuria.
2. Uric acid stone		Whitish, smooth, single or multiple, radiolucent.
3. Phosphate		Whitish, single or multiple, present in alkaline urine. Radioopaque → laminated.
4. Cystine		Single or multiple, radioopaque.

- **Deposition of Ca in the renal parenchyma (nephrocalcinosis)**
This may occur in hyperparathyroidism, renal T.B, vit D intoxication & renal tubular acidosis.
- **Stag horn calculi:** Stone filling the renal pelvis & branching into the calyces.

Presentation of renal stones

O Obstruction ↓ Hydronephrosis	M Migration ↓ Colic	U Ulceration ↓ Haematuria	M Metaplasia ↓ Malignancy	I Infection ↓ Pyelonephritis
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Clinical Picture

1- **Asymptomatic**

2- **Renal colic**

- Loin.
- Radiates to groin and scrotum or labium.
- For few hrs or days.

3- **Loin dull aching pain** occurs with hydronephrosis or pyonephrosis.

4- **Recurrent UTI** e.g. pyelonephritis.

5- **Haematuria.**

6- **Bladder obstruction** due to stone at the bladder neck resulting in anuria.

7- **Post renal acute renal failure.**

8- **Chronic renal failure.**

O/E

- Tender loin.
- Palpable kidney with hydro or pyonephrosis.
- Signs of renal failure.



Investigations

1. X-ray

- All stones are radioopaque.
- Pure Uric acid → radiolucent but with Ca deposition → radioopaque).

2. Urine

- RBCs (painful haematuria).
- Pyuria with 2 ry infection.
- Crystals e.g oxalate, phosphate, urate.

3. S. Ca, uric acid

4. 24h urinary Ca, urate, oxalate.

5. **IVP** → back pressure e.g hydroureter, hydronephrosis. It also shows stones or strictures.

6. **Sonar** → back pressure, stones, hydronephrosis.

7. **Renal scan** → reveals pattern of obstruction.

Treatment

I- Medical ttt:

1. Renal colic

- Bed rest - warmth to loin.
- Analgesics: morphia 15-30 mg or pethidine 100 mg I.M.
- Antispasmodic: atropine sulfate.
- NSAID → (nephrotoxic).
- Infusion method by I.V drip (Saline + atropine + papaverine).

2. Treatment of stable cases

- Fluids + antispasmodics when needed $\pm$ diuretics + specific therapy (see later).
- Stones may pass spontaneously if small < 0.5 cm diameter, but stones larger than 1 cm usually require intervention.

3. **Treatment of complications** e.g. UTI, acute or chronic renal failure (see before).



Specific therapy according to type and aetiology of stone

Idiopathic Hypercalcuria:	- Thiazides → ↓ Ca in urine.
Primary hyperparathyroidism	- Surgery
Renal tubular acidosis	- Na citrate → alkaline urine.
Oxalate stones	- Cholestyramine can bind oxalate especially in malabsorption syndrome. - Magnesium citrate.
Uric acid stones	- Na citrate → alkaline urine. - Allopurinol.
Cystine stones	- Excessive fluids. Alkali therapy (Na citrate). - Penicillamine: it forms more soluble penicillamine–cystine complex.

Prophylaxis of renal stones

- 1- Ample of fluids
- 2- Milk ↓ & cheese in Ca stones.
- 3- ↓ Spinach rhubarb in oxalate stones.
- 4- ↓ Liver, ↓ kidney, ↓ sardines in cases of uric acid stones.
- 5- Treatment of the cause with the previous specific therapy.

II- Surgery and other interventional maneuvers:

Indications

- 1- Big stone.
- 2- Multiple stones.
- 3- Stag horn stone.
- 4- Stone in renal pelvis.
- 5- Complicated stones with obstruction e.g. hydronephrosis.



A- Surgery:

1. Nephrolithotomy for renal calculi.
2. Pyelolithotomy for pelvic stones.
3. Ureterolithotomy for ureteric stones.

Recently percutaneous nephrolithotomy can be done by creating a percutaneous track to remove stones in the calyces and renal pelvis by endoscopy.

B- Endoscopy:

1. Ureteric stones can be removed by endoscopy with ureteric catheter.
2. Bladder stones can be removed by endoscopy, the stones can be gripped in a lithotrite and crushed then the stone fragments are washed out.

C- Extra corporeal shock wave lithotripsy (ESWL):

For renal calculi. Most fragments can pass spontaneously through urethra. Fragments that do not pass can be removed percutaneously. ESWL can also be used for stones in upper ureter !?

- Stag horn stones are best removed by open surgery.
- Large bladder stones can be removed by open cystotomy.
- Ureteric stones can be pushed into the upper urinary tract by endoscopy to allow percutaneous nephrolithotomy or ESWL.



AUTOSOMAL dominant Polycystic Kidney disease (ADPKD)

- ADPKD is characterized by the development of multiple renal cysts. It is usually associated with extrarenal manifestations e.g. hepatic and cardiovascular.
- It is considered to be the commonest inherited nephropathy.

Pathology:

- Both kidneys are enlarged with multiple cysts compressing renal parenchyma.
- Cysts are not communicating with each other.



Clinical Picture

(Clinical manifestations rarely occur before the age of 20 to 25 years)

- 1) Dull aching loin pain due to increasing renal size.
- 2) Acute loin pain and / or haematuria due to haemorrhage into a cyst or cyst infection.
- 3) Renal stones (uric acid).
- 4) Hypertension due to activation of rennin angiotensin system.
- 5) Chronic renal failure.
- 6) Hepatic cyst, mitral valve prolapse.
- 7) Subarachnoid haemorrhage associated with rupture of berry aneurysm.
- 8) **O/E:** Large irregular kidneys. Sometimes there is hepatomegally.

Differential Diagnosis

- Hydronephrosis.
- Tumours.
- Other cystic renal diseases.



Diagnosis:

- IVP: spider leg appearance (calyces are elongated & attenuated). It is better avoided for fear of nephrotoxicity.
- Sonar
- CT scan.

- There is a gene for ADPKD located on the short arm of chromosome 16 in 85% of cases.
- ADPKD accounts for 3-10% of all patients under regular dialysis in the west.
- Anemia does not usually occur with ADPKD.

Treatment

The aim is prevention of complications and preserving renal functions

- 1- Hypertension treated by ACE inhibitors, infection treated by quinolones or cotrimoxazole as they penetrate into the cysts, treatment of renal failure.
- 2- Screening by U/S after the age of 20 years as before the age of 20 the renal imaging may give false results.
- 3- Counseling for those > 20 yrs.

Other cystic diseases of the kidney

- 1- **Simple cysts:** they are mostly asymptomatic and are usually discovered accidentally during imaging studies.
- 2- **Acquired cystic kidney disease** in patients with ESRD undergoing dialysis. Occasionally carcinomas complicate this disorder.
- 3- **Medullary cystic disease** (autosomal recessive disease): it is associated with retinitis pigmentosa, nocturnal enuresis due to urinary concentrating defect.
- 4- **Medullary sponge kidney:** it is presented by renal stones, nephrocalcinosis occurs in 50% of cases.



TUBULAR DEFECTS OF THE KIDNEY

1- Renal Tubular Acidosis Type I (Distal tubular acidosis)

Pathology:

- Kidneys are unable to lower the pH of urine due to inability to secrete H^+ → acidosis.
- Acidosis → ↓ tubular reabsorption of Ca → hypercalcuria → stones.
- Stunted growth, rickets.
- Tubules are unable to concentrate the urine → polyurea & ↓ K.

Diagnosis:

Ammonium chloride loading test:

NH_4 CL is given & urine & blood are examined:-

- Acidosis ↑
- Urine pH does not fall below 5.5

Treatment

- 1- Sodium bicarbonate.
- 2- K supplement.

2- Type 2 renal tubular acidosis (proximal)

It may be isolated or part of Fanconi syndrome.

Pathology:

- HCO_3 reabsorption in P.C.T is defective → acidosis.
- ↓ K as HCO_3 is excreted in urine as potassium salts.
- NH_4 CL test → urine pH falls below 5.5.

Treatment

- Na HCO_3 with severe acidosis.
- K supplement.

3- Renal glycosuria

It is a benign defect, inherited as an autosomal recessive trait. Glucose appears in the urine in presence of normal blood glucose. It is proximal tubular defect.

4- Cystinuria

↓ reabsorption of filtered cystine → Cystine in urine → cystine stones.

5- Other tubular defects

- D.I. (nephrogenic).
- Fanconi syndrome (Glycosuria, Aminoaciduria, Phosphaturia).

Alport's S (hereditary nephritis)

- ♂ > ♀.
- G.N with haematuria & proteinuria.
- Nerve deafness.
- Late ESRD occurs.



PREGNANCY & kidney

1- Effect of renal disease on pregnancy :

- I.U.F.D.
- Pre eclampsia.
- SLE may progress !?

2- Effect of pregnancy on kidney :

- Toxemia → proteinuria.
- Pyelonephritis.
- Acute renal failure
 - Abortion.
 - Postpartum haemorrhage.
 - Hemolytic Uremic \$.

RENAL VASCULAR disorders

1) Arteries: Thrombosis or embolization leading to renal infarction.

2) Arterioles and microvasculature:

- Hypertensive nephrosclerosis leading to chronic renal failure.
- Malignant hypertension leading to acute or rapidly progressive renal failure.
- Scleroderma leads to malignant crises with hypertension and rapidly progressive renal failure.
- HUS / TTP → renal failure, thrombocytopenia and hemolytic anaemia.
- Atheroembolic renal disease: It is due to showers of cholesterol rich atheromatous material from ulcerated atheromatous plaques which may reach the kidney from aorta and / or renal arteries after catheterization of abdominal aorta or at renal artery angioplasty. Anticoagulants and thrombolytic agents may also precipitate cholesterol embolization. It is presented as rapidly progressive renal failure with systemic embolization (poor prognosis).

3) Renal vein thrombosis:

- It occurs in nephrotic \$, renal cell carcinoma and with thrombophilia.
- It leads to acute renal failure, proteinuria and pulmonary embolism.



Renal Artery Stenosis (R.A.S)

R.A.S. accounts for 1-2 % of all cases of hypertension.

Types:

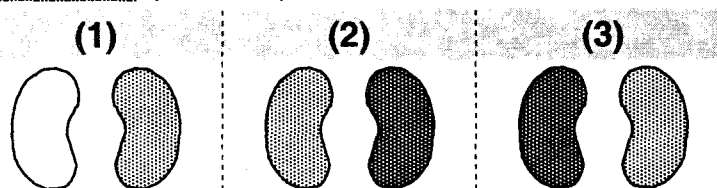
- Fibromuscular dysplasia, a third of cases, usually women < 45 yrs.
- Atherosclerotic type, two thirds of cases, in old age (males > 60 yrs).

Clinical picture:

- 1- Hypertension. It may be malignant.
- 2- Abdominal bruit.
- 3- Fundus examination showing hypersensitive retinopathy.

Investigations:

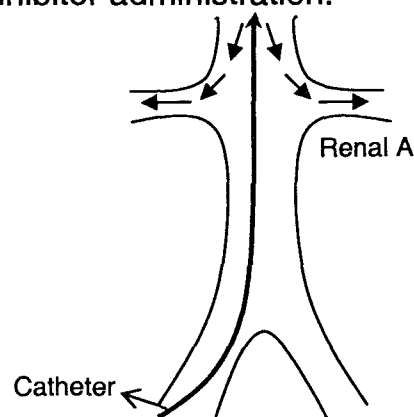
- 1- Rapid sequence IVP (Old test)



Nephrogram = soft tissue shadow of the Kidney

Dye is given & 3-4 films are taken in the 1st few minutes.

- 2- Sonar: the ischemic kidney may be smaller.
- 3- Renal scan: showing defect in perfusion, in unilateral cases there is fall in uptake on the affected side following ACE inhibitor administration.
- 4- Renal angiography (diagnostic).
 - A- Flush aortography.
 - B- Selective renal angiography
→ catheter into renal artery.
 - C- Digital subtraction angiography.
- 5- Duplex scan.
- 6- Renal vein renin:
It is ↑ in the ischaemic side.
- 7- Magnetic resonance angiography (MRA)



Is used in patients with renal impairment to avoid contrast nephropathy.

Treatment:

- 1- **Medical treatment**: antihypertensive (see CVS).
- 2- **Angioplasty** with or without stenting.
- 3- **Surgical revascularization.**

- ACE inhibitors and ARBs are contraindicated in bilateral renal artery stenosis.
- Renal artery stenosis leads to hypokalemic hypertension.



DRUG INDUCED NEPHROPATHY

I. Acute renal Failure:

Prerenal:

- Diuretics → hypovolemia (loop diuretics).
- Decreased renal blood flow e.g ACE inhibitors.

Renal

- A.T.N → aminoglycosides.
- Acute interstitial nephritis → methicillin, sulphonamides and NSAID.

Postrenal:

- Anticoagulants (clots of blood),
- Crystalluria with sulfa.
- Retroperitoneal fibrosis due to methysergide.

2. Chronic renal failure: Analgesic nephropathy (chronic interstitial nephritis).

3. Nephrotic \$: Gold, tridione, NSAID, ACE inhibitors, penicillamine.

4. Acute G.N: Rifampicin, albumin infusion.

5. Tubular defects

- Outdated tetracycline (Fanconi \$).
- Lithium → D.I.

6. Acute interstitial nephritis: see above.

7. Chronic interstitial nephritis: see above.

Analgesic nephropathy (occurs after cumulative ingestion of 2-3 kg of the drug)

1- *Aspirin.*

2- *Phenacetine or paracetamol.*

3- *NSAID.*

- Analgesic nephropathy is more common in women. Patients are often neurotic or depressed usually with headache (analgesic abuse).

Pathology:

- There is a chronic interstitial nephritis, papillary necrosis
- 1, 2, 3 are transformed into toxic metabolites → cellular toxicity due to:
 - Glutathione depletion with paracetamol
 - Anti P.G effect (Aspirin & NSAID) → ↓↓ blood supply of the kidney.
 - Uncoupling of O*P

Clinical Picture:

* CRF.

* Anemia.

* UTI.

- * Haematuria or urinary tract obstruction due to sloughing of a renal papilla (papillary necrosis).

Treatment: as CRF.



RENAL NEOPLASMS

Renal Carcinoma (Hypernephroma)

- It is an adenocarcinoma, composed of large cells, spread by lymphatics & blood or by direct spread. It may be bilateral.
- It arises from proximal tubules.

Clinical Picture

It rarely presents before the age of 40 years, the average age is around 55 years.

1- **Haematuria, loin pain.**

2- **Palpable mass.**

3- **Paramalignant \$:**

- Hypertension due to excessive renin secretion.
- ↑ Ca (parathormone like).
- Polycythaemia (erythropoietin).
- Neuromyopathy.

4- **Fever, left sided varicocele** may be associated with left sided tumors due to invasion of renal vein with obstruction of the left testicular vein.

Investigations:

- 1- ESR is usually high.
- 2- Sonar.
- 3- IVP – CT scan - MRI.
- 4- Renal angiography.

Treatment

- Nephrectomy for unilateral tumors.
- Partial nephrectomy in bilateral tumors or in unilateral tumors with contralateral diseased kidney.
- Nephrectomy may lead to regression of metastases !?.
- Radiotherapy is of no value.
- Medroxyprogesterone may control metastases.
- Interferon can be tried.

Nephroblastoma (Wilm's Tumor)

- Presented in the 1st three years of life. It may be bilateral.
- It presents as an abdominal mass, rarely with haematuria.
- It is diagnosed by sonar, CT, excretion urography and angiography.
- A combination of nephrectomy, radiotherapy and chemotherapy gives good results and the majority of children can be cured even with metastases.



HEPATORENAL Link

1- Bilharziasis:

- Bilharzial nephropathy (FSGS - Membranoproliferative)
- Obstructive uropathy.

2- Viral hepatitis: Immune Complex G.N (virus B, C).

3- Obstructive jaundice: Direct bilirubin → Bilirubin nephropathy.

4- Hepatorenal syndrome: severe LCF → Acute renal failure.

5- Renal failure → dialysis → viral hepatitis (virus B, C).

HEPATORENAL SYNDROME

- Hepatorenal syndrome is a renal failure which occurs in cases with severely compromised liver function in absence of clinical, laboratory or anatomic evidence of other known causes or renal failure.
- It is a functional renal failure i.e. No organic lesion in the kidneys.
- It closely resembles prerenal failure except that it does not respond to conventional volume replacement.
- Hepatorenal syndrome may occur insidiously over a period of weeks to months or appear suddenly within few days.
- The common precipitating factors are deterioration of liver function, the use of NSAIDs, excessive diuresis or GIT bleeding.
- Hepatorenal syndrome is marked by intense renal vasoconstriction even in the presence of systemic vasodilatation. The renal blood flow is diverted away from the renal cortex with decline of GFR. Thromboxane A₂ is increased (vasoconstrictor), prostaglandin E₂ is decreased (vasodilator) & endothelins are increased (vasoconstrictors). Also there is activation of rennin-angiotensin and sympathetic nervous systems.
- It is diagnosed by absence of proteinuria or abnormal urinary sediment with urine sodium < 10 mmol/L.
- Also there is oliguria with no response to volume expanders to be differentiated from reversible prerenal azotemia.
- There is no specific treatment. We can give dopamine (1-2 µg /Kg/m) to increase renal blood flow!?. Recovery depends on improvement of liver function. The prognosis is very poor unless liver transplantation can be done.



Kidney Transplantation

Indications → ESRD

- Chronic G.N.
- Obstructive Uropathy.
- Lupus nephritis.
- APDKD.
- Chronic interstitial nephritis.
- Hypertensive nephrosclerosis.

Recurrence of the disease may occur after transplantation in the following

- e.g.
- 1- Membranoproliferative G.N (type II).
 - 2- Good pasture's \$.
 - 3- FSGS.
 - 4- Type I oxaluria (primary oxalosis).

Preoperative

- 1- ABO & HLA for Donor & Recipient.
- 2- **Donor**
 - All routine investigations.
 - Angio – renal scan - I.V.P.
- 3- **Recipient** → Micturating cystogram to exclude reflux and other routine investigations.

Operative

- 1- Nephrectomy.
- 2- Kidney perfusion to wash blood capillaries to Θ microthrombi.
- 3- We try to shorten
 - Cold ischaemia (the time after nephrectomy till transplantation).
 - Hot ischaemia (the time between clamping of renal vessels till nephrectomy)
- 4- The kidney is transplanted in the pelvic cavity with vascular anastomosis with the iliac vessels & uretero vesical anastomosis.

Postoperative: (to inhibit rejection)

- 1- Steroids.
- 2- Azathioprine.
- 3- Cyclosporine.
- 4- Mycophenolate.
- 5- Antilymphocyte & antithymocyte globulin.
- 6- Tacrolimus.



Episodes of acute rejection treated by methyl prednisolone infusion.

Common complications:

- A.T.N.
- Rejection
- Renal vein thrombosis.
- Renal artery thrombosis.
- Urine leakage at uretrovesical anastomosis.
- Complications of immunosuppression.
- Recurrence of the primary renal disease.

Type I oxaluria (primary oxalosis) treated by liver and kidney transplantation.

Cyclosporine= Sandimmun

- It is a potent immunosuppressive agent which prolongs survival of transplants involving skin, kidney, liver, heart, pancreas & B.M.

Mechanism

- It $\ominus$ release of interleukin 2 so $\rightarrow$ inhibits release of cytokines without affection or the rapidly dividing cells of B.M.

Contraindication

- Known hypersensitivity.

Side effects

- Hypertrichosis.
- Hepatotoxicity.
- Nephrotoxicity.
- G I T upset.

Preparation

- Sandimmun oral solution.
- Sandimmun tablets.



RENAL INVOLVEMENT in SYSTEMIC DISEASES

I. Systemic Lupus :-

WHO classification of lupus nephritis

- * **Type I** : Mesangial deposits (normal glomeruli on Light microscopy).
- * **Type II** : Mesangial immune deposits with mesangial cell hypercellularity and matrix expansion, clinically there is mild renal disease.
- * **Type III** : Focal proliferative GN. There is haematuria and proteinuria.
- * **Type IV** : Diffuse proliferative GN. There is haematuria, proteinuria and hypertension.
- * **Type V** : Membranous GN. There is heavy proteinuria, haematuria, hypertension with nephritic \$.
- * **Type VI** : Glomerulosclerosis with progressive renal failure.

Management of Lupus nephritis

- Oedema and hypertension should be treated.
- Type I requires no steroids nor immunosuppressives.
- Type II is benign, but steroids are usually required.
- Type III, IV and V usually need steroid and cyclophosphamide for induction then maintenance therapy with steroids, azathioprine or mycophenolate.

2. Vasculitis :-

- PAN may lead to renal infarction and hypertension.
- Wegener's granuloma leads to ANCA associated GN.
- Churg- Strauss \$ Leads to ANCA associated GN.
- Henoch Schonlein purpura is associated with IgA nephropathy.



3. Rheumatoid disease and ankylosing spondylitis :-

Lead to amyloidosis kidney.

4. Scheroderma Leads to hypertensive renal crisis :-

5. DM → Diabetic nephropathy (See before)

6. Amyloidosis :- (See before)

7. Hepatic renal disease :-

- IgA nephropathy is more common in patients with chronic liver disease.
- Hepatorenal \$ (See before).
- Acute renal failure (in cases of bleeding).

8. Good pasture \$:- (See before)

9. Hemolytic uraemic \$ with acute renal failure due to thrombosis in small arteries and arterioles. :-

10. Multiple myeloma :-

The disease may lead to :

- Light chain cast nephropathy (intratubular deposition of light chains).
- Al amyloidosis.
- Hypercalcaemic or hyperuricaemic nephropathy,
- Contrast nephropathy (interaction between light chains and radiocontrast).

11. Leukaemias and Lymphomas Lead to tumour Lysis \$ (acute uric acid nephropathy). Lymphomas also may lead to minimal lesion glomerulopathy.

12. Sickle cell nephropathy, papillary necrosis, nephrogenic DI. Membranous or mesangioproliferative GN (rare)

Cryoglobulinaemic renal disease, see rheumatology

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