Chronic kidney disease (CKD)

Nephrology Unit

Mansoura University

Chronic renal failure or chronic renal impairment

is a progressive loss of kidney function due to progressive damage of kidney tissue by a disease involving the two kidneys.

End stage renal failure:

Is considered when renal failure is so severe that the patient can’t live without dialysis.

Recently the terms chronic renal failure and chronic renal impairment have been replaced by a new , more accurate term which is

Chronic Kidney Disease

What is the definition of CKD?

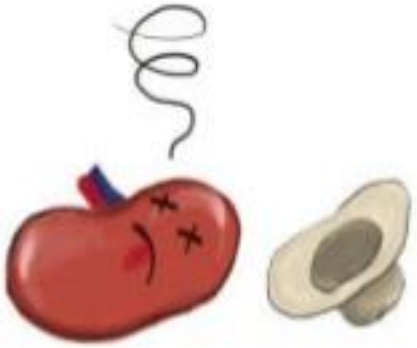
Abnormal

Kidney **structure**

or Kidney **function**

for **> 3 months**

with implications for health.



Chronic Kidney Disease (CKD)

- **Def.**

Kidney damage for more than 3 months with or without decrease in GFR.

This damage could be:

1. Structural (detected by kidney biopsy, or by radiology)
2. Functional (detected by laboratory assessment as s. creatinine, proteinuria or hematuria).

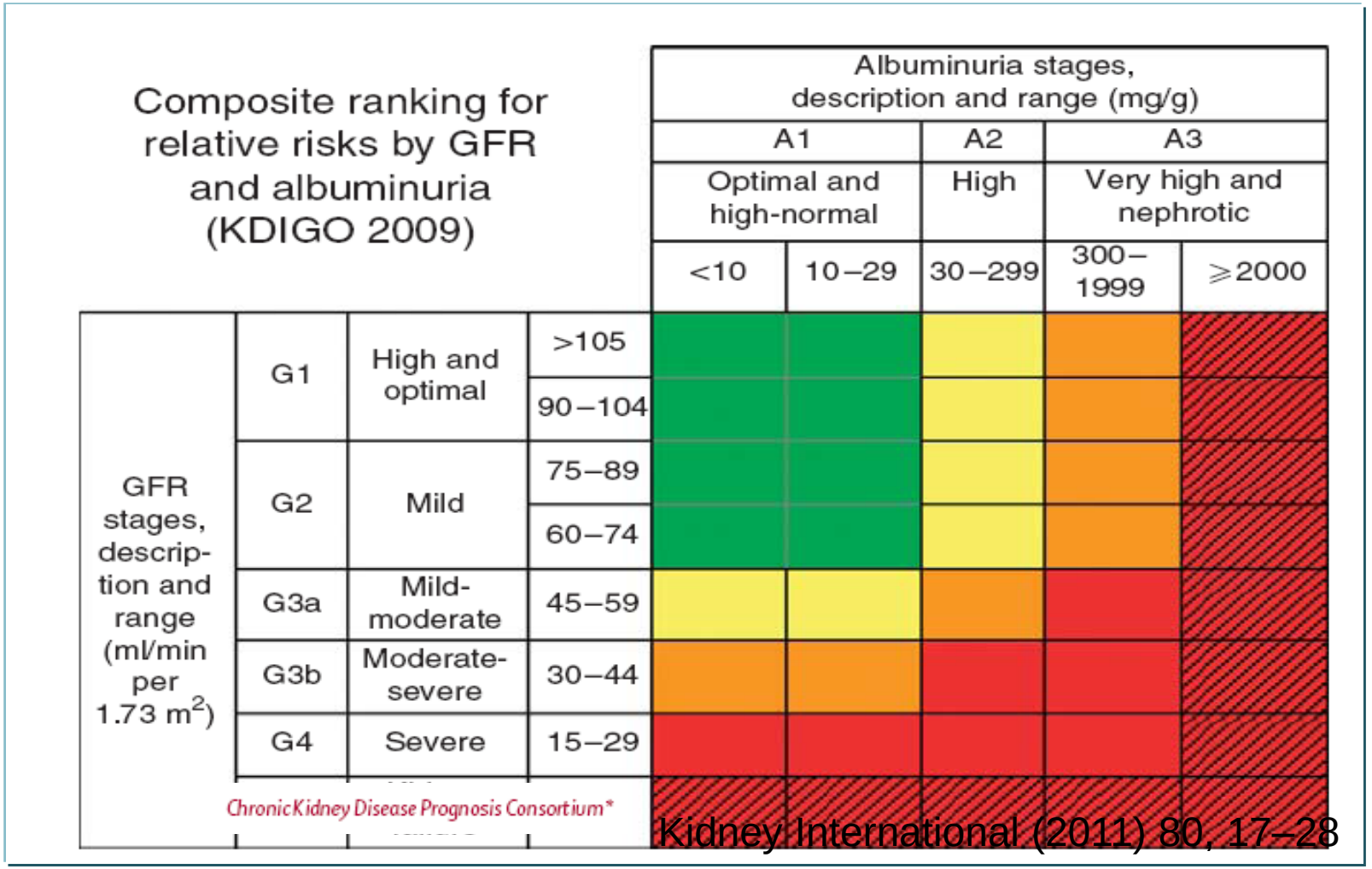
Also CKD is considered when GFR <60m^2 /1.73m^2 for≥3months, with or without kidney damage.

Classification of CKD based on GFR as proposed by the Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines

CKD Stage	Description
1	Normal or increased GFR; some evidence of kidney damage reflected by microalbuminuria/proteinuria, hematuria, or histologic changes
2	Mild decrease in GFR (89–60 ml/min/1.73 m^2)
3	Moderate decrease in GFR (59–30 ml/min/1.73 m^2)
4	Severe decrease in GFR (29–15 ml/min/1.73 m^2)
5	GFR <15 ml/min/1.73 m^2; when renal replacement therapy in the form of dialysis or transplantation has to be considered to sustain life

Evolution of CKD Staging

The two key markers for CKD are urine albumin and eGFR.



Kidney International (2011) 80, 17–28

INCIDENCE OF CRF IS INCREASING

- **Environmental pollution.**
- **Drug abuse.**
- **Others.**

Causes of CKD

Major Causes of Severe Chronic Kidney Disease

Cause	Percent of Cases†
Diabetes mellitus	44.9
Type 1	3.9
Type 2	41.0
Hypertension	27.2
Glomerulonephritis	8.2
Chronic interstitial nephritis or obstruction	3.6
Hereditary or cystic disease	3.1
Secondary glomerulonephritis or vasculitis	2.1
Neoplasms or plasma-cell dyscrasias	2.1
Miscellaneous conditions‡	4.6
Uncertain or unrecorded cause	5.2

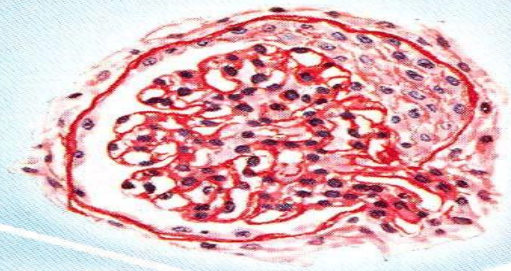
Major causes of ESRD presenting to dialysis in USA

	Prevalence %	Incidence %
Diabetes	33.2	41.8
Hypertension	24	25.4
GN	17.2	9.3
Cystic disease	4.6	2.2

ETIOLOGY OF CHRONIC RENAL FAILURE

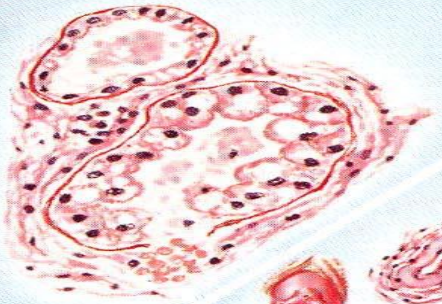
1: PRIMARILY GLOMERULAR DISEASE

ACUTE GLOMERULONEPHRITIS
ANTIGLOMERULAR BASEMENT MEMBRANE DISEASE
CHRONIC GLOMERULONEPHRITIS
FOCAL GLOMERULONEPHRITIS
GOODPASTURE'S SYNDROME
INTERCAPILLARY GLOMERULOSCLEROSIS
RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS



2: PRIMARILY TUBULAR DISEASE

CHRONIC HYPERCALCEMIA
CHRONIC POTASSIUM DEPLETION
FANCONI SYNDROME AND VARIANTS
HEAVY METAL POISONING (LEAD, CADMIUM, etc.)



3: VASCULAR DISEASE

ISCHEMIC DISEASE OF KIDNEYS, CONGENITAL OR ACQUIRED
- BILATERAL RENAL ARTERY STENOSIS;
- BILATERAL FIBROMUSCULAR HYPERPLASIA

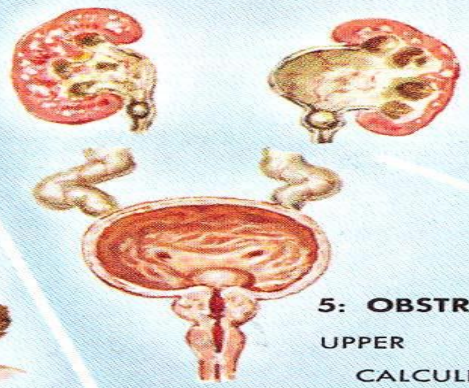
MALIGNANT PHASE OF ESSENTIAL HYPERTENSION

NEPHROSCLEROSIS

4: INFECTIONS

CHRONIC PYELONEPHRITIS

TUBERCULOSIS



5: OBSTRUCTIVE DISEASE

UPPER
- CALCULI
- NEOPLASMS
- RETROPERITONEAL FIBROSIS

LOWER
- CONGENITAL ANOMALIES OF BLADDER NECK AND/OR OF URETHRA
- PROSTATIC ENLARGEMENT
- URETHRAL STRICTURE

6: COLLAGEN DISEASE

DIFFUSE SYSTEMIC SCLEROSIS (SCLERODERMA)

DISSEMINATED (SYSTEMIC) LUPUS ERYTHEMATOSUS

POLYARTERITIS NODOSA

7: METABOLIC RENAL DISEASE

AMYLOIDOSIS

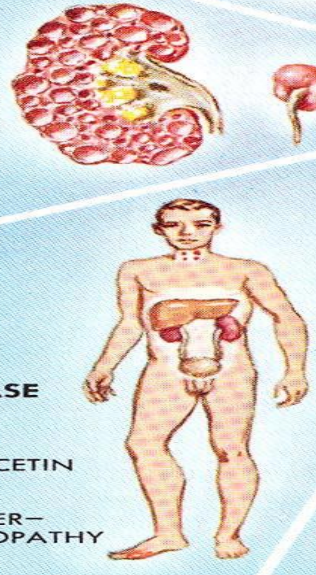
CHRONIC PHENACETIN OVERDOSAGE

GOUT WITH HYPERURICEMIC NEPHROPATHY

PRIMARY HYPERPARATHYROIDISM

MILK–ALKALI SYNDROME

SARCOIDOSIS



8: CONGENITAL ANOMALIES OF KIDNEYS

HYPOPLASTIC KIDNEYS

MEDULLARY CYSTIC DISEASE

POLYCYSTIC KIDNEYS

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ETIOLOGY OF CKD

Primary glomerular disease

Such as MCGN and FSGS.

Tubulointerstitial disease

Such as NSAIDs abuse, heavy metals hypercalcaemia, hypokalaemia.

Renal vascular disease

Such as renal artery stenosis and renal vein thrombosis.

Chronic pyelonephritis

ETIOLOGY OF CKD

Chronic urinary tract obstruction

Collagen disease

Such as SLE, PAN.

Metabolic disease

Such as DM, amyloidosis, gout, NSAIDs abuse.

PATHOLOGY OF CKD

Gross appearance:

Size is decreased except in PCKD, DM, amyloidosis, hydronephrosis.

Microscopic appearance:

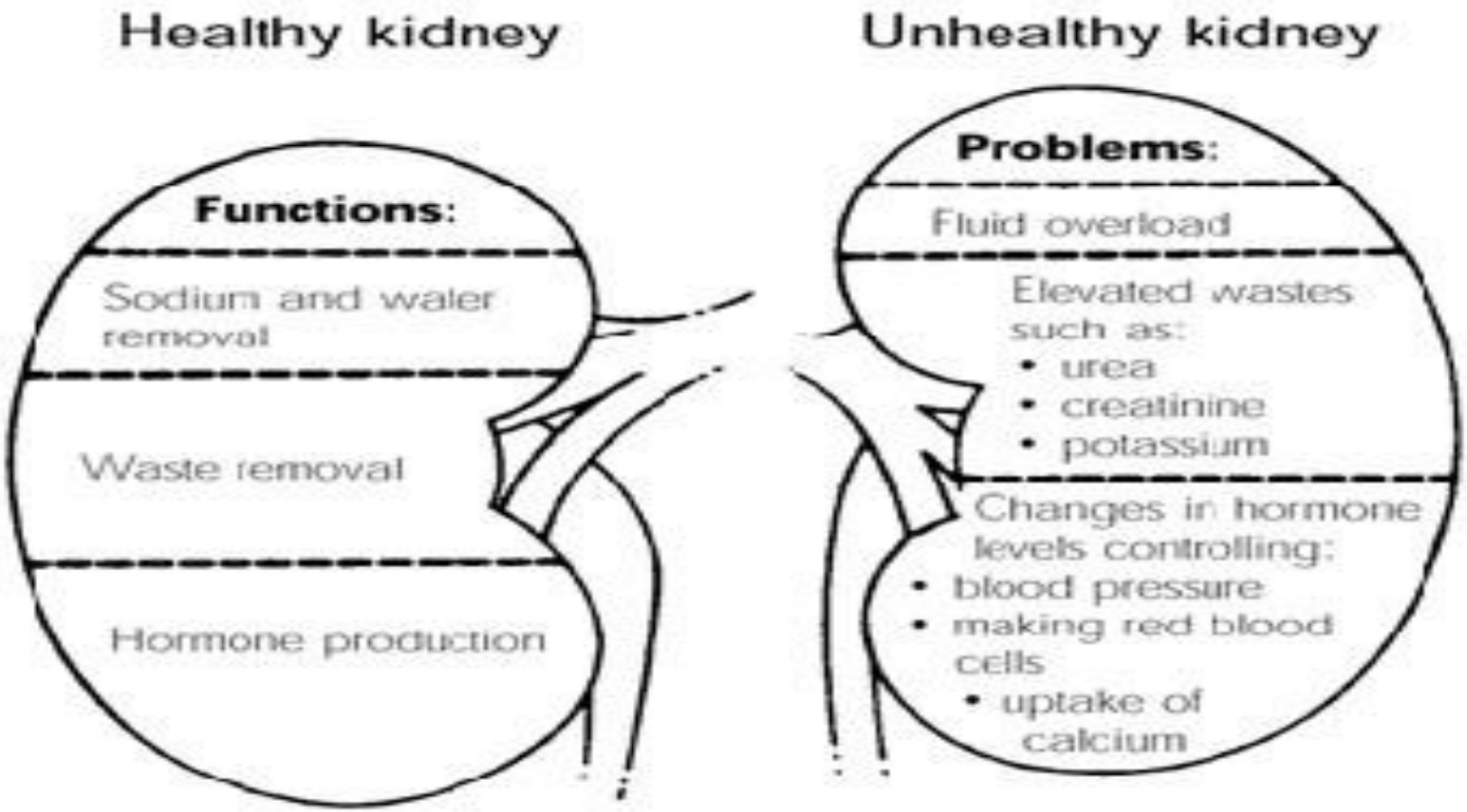
Tubular atrophy, interstitial fibrosis and glomerulosclerosis.

LATE STAGE OF CHRONIC GLOMERULONEPHRITIS

CONTRACTED, PALE, COARSELY GRANULAR KIDNEY

GLOMERULI IN VARIOUS STAGES OF OBSOLESCENCE; DEPOSITION OF PAS–STAINING MATERIAL, HYALINIZATION, FIBROUS CRESCENT FORMATION, TUBULAR ATROPHY, INTERSTITIAL FIBROSIS

PATHOPHYSIOLOGY OF CKD



PATHOPHYSIOLOGY OF CKD

I. **Disturbance of water excretion.**
II. **Disturbance of sodium excretion.**
III. **Disturbance of potassium excretion.**
IV. **Disturbance of acid-base balance.**
V. **Disturbance of calcium-phosphate metabolism.**
VI. **Retention of uraemic toxins.**
VII. **Failure of renal endocrine functions.**

DISTURBANCE OF WATER EXCRETION

1. **Loss of the renal ability to concentrate urine:** **Occurs early in uremia, manifest as polyuria and nocturia. Caused by osmotic overload of the remaining nephrons.**

2. **Loss of the renal ability to dilute urine:**

Occurs late in uremia.

DISTURBANCE OF SODIUM EXCRETION

- Most pts remain in sodium balance until GFR is very low → ↑ solute excretion /nephron.

- Salt loosing nephropathy (e.g. analgesic nephropathy , chronic obstructive uropathy)

DISTURBANCE OF POTASIUM EXCRETION

Hyperkalaemia occurs only if:

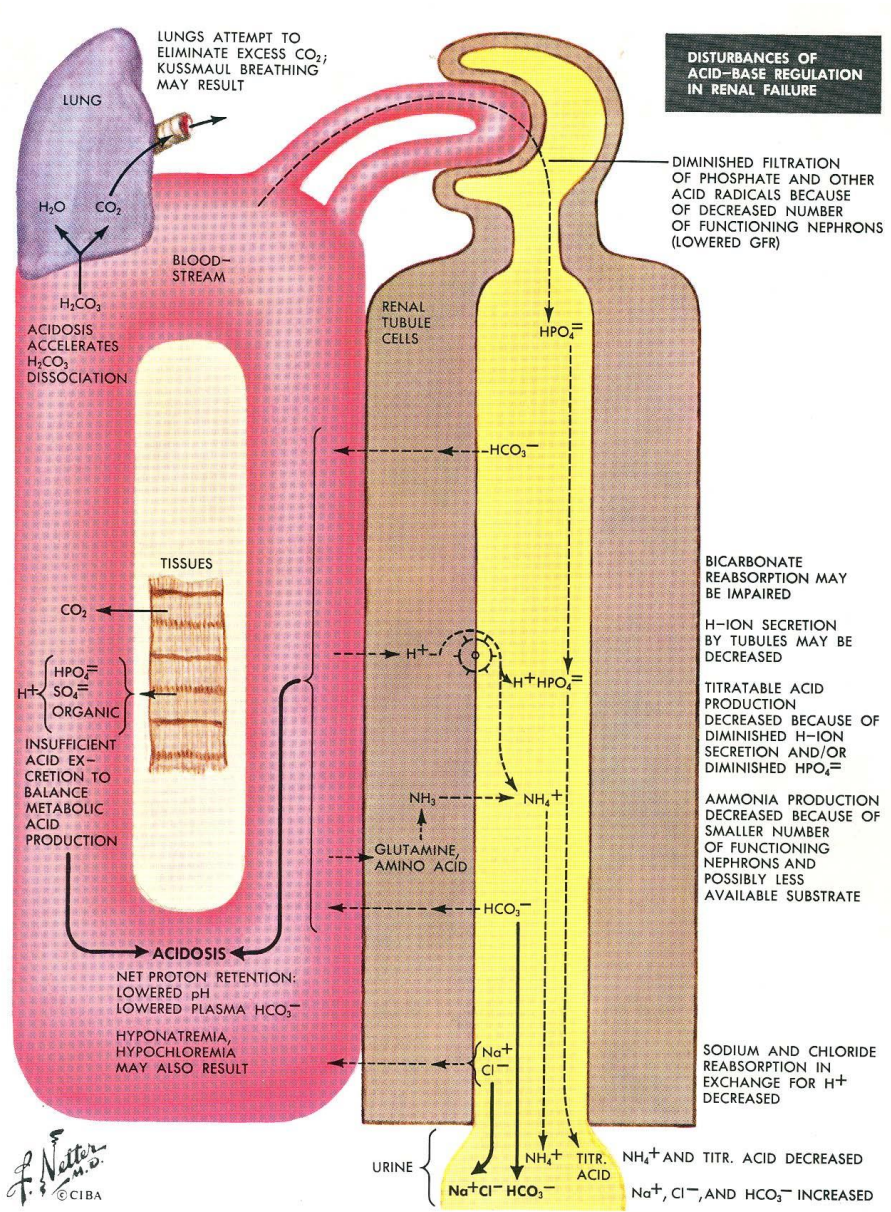
1. **GFR < 10 ml/min**
2. **Excess K load**
3. **Severe acidosis .**
4. **Drugs as ACEIs, ARBs, Aldosterone antagonists.**

Hypokalaemia occurs in cases with salt loosing nephropathy

DISTURBANCE OF H+ EXCRETION

- **Metabolic acidosis may occur due to:**
  1. **Hco_3 wastage**
  2. **Inability to secrete H+.**
  3. **Retention of titratable acids.**
  4. **Decreased ammonia production.**

- **May be more severe with tubulo interstitial diseases, hypercatabolic states, and in children.**
- **May aggravate bone disease.**


DISTURBANCES OF ACID–BASE REGULATION IN RENAL FAILURE
LUNGS ATTEMPT TO ELIMINATE EXCESS CO_2; KUSSMAUL BREATHING MAY RESULT
LUNG
H_2O
CO_2
H_2CO_3
BLOOD–STREAM
ACIDOSIS ACCELERATES H_2CO_3 DISSOCIATION
RENAL TUBULE CELLS
DIMINISHED FILTRATION OF PHOSPHATE AND OTHER ACID RADICALS BECAUSE OF DECREASED NUMBER OF FUNCTIONING NEPHRONS (LOWERED GFR)
$HPO_4^=$
HCO_3^-
TISSUES
CO_2
H^+
$HPO_4^=$
$SO_4^=$
ORGANIC
INSUFFICIENT ACID EXCRETION TO BALANCE METABOLIC ACID PRODUCTION
H^+
$H^+HPO_4^=$
BICARBONATE REABSORPTION MAY BE IMPAIRED
H–ION SECRETION BY TUBULES MAY BE DECREASED
TITRATABLE ACID PRODUCTION DECREASED BECAUSE OF DIMINISHED H–ION SECRETION AND/OR DIMINISHED $HPO_4^=$
NH_3
NH_4^+
GLUTAMINE, AMINO ACID
AMMONIA PRODUCTION DECREASED BECAUSE OF SMALLER NUMBER OF FUNCTIONING NEPHRONS AND POSSIBLY LESS AVAILABLE SUBSTRATE
HCO_3^-
ACIDOSIS
NET PROTON RETENTION: LOWERED pH LOWERED PLASMA HCO_3^-
HYPONATREMIA, HYPOCHLOREMIA MAY ALSO RESULT
Na^+
Cl^-
SODIUM AND CHLORIDE REABSORPTION IN EXCHANGE FOR H^+ DECREASED
URINE
NH_4^+
TITR. ACID
Na^+Cl^- HCO_3^-
NH_4^+ AND TITR. ACID DECREASED
Na^+, Cl^-, AND HCO_3^- INCREASED
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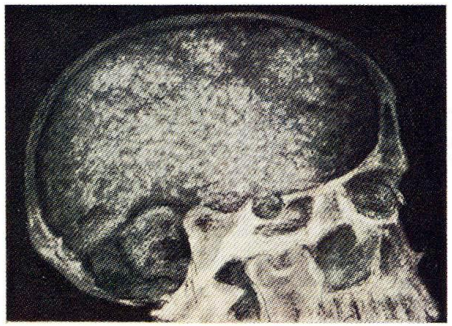
DISTURBANCE OF CALCIUM-PHOSOPHATE METABOLISM

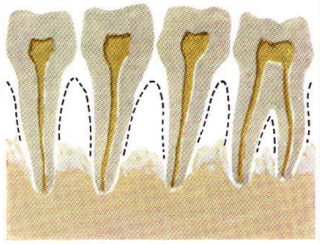
1. **Retention hyperphosphataemia.**
2. **Hypocalcaemia(due to ↓active vit.D ,↑phosphate)**
3. **Secondary hyperparthyrodism.**
4. **Bone disease and soft tissue calcification.**

BONE MANIFESTATIONS OF SECONDARY HYPERPARATHYROIDISM IN CHRONIC RENAL DISEASE

"BANDED SCLEROSIS" OF SPINE, SCLEROSIS OF UPPER AND LOWER MARGINS OF VERTEBRAE WITH RAREFACTION BETWEEN. NOTE COMPRESSION FRACTURE

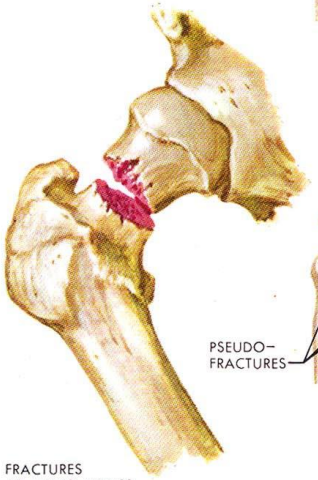


SPOTTY DEMINERAL-IZATION OF SKULL

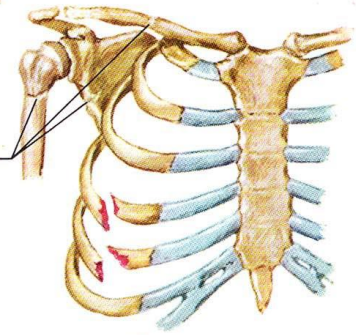


LOSS OF LAMINA DURA OF TEETH (BROKEN LINES INDICATE NORMAL CONTOURS)

SUBPERIOSTEAL RESORPTION OF PHALANGES (CHIEFLY ON PALMAR ASPECT OF MIDDLE PHALANX)

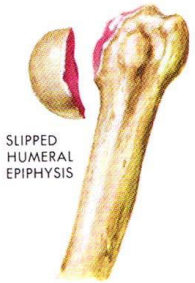


FRACTURES OF LONG BONES



PSEUDO-FRACTURES

RESORPTION OF LATERAL END OF CLAVICLE; RIB FRACTURES



SLIPPED HUMERAL EPIPHYSIS

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CLINICAL FEATURES OF CKD

- Early stages of CKD (stage 1&2) are usually asymptomatic.
- Patients in stage 3 starts to show some manifestations of uremic syndrome.
- Full-blown picture of uremia is seen in patients of stage 4&5.
- At 1st nocturia & polyuria due to impaired concentrating ability.
- Severe depression of GF can result in oliguria

Gastrointestinal manifestations of uremia

a. Anorexia, nausea, vomiting
b. Hiccough
c. Ammoniacal smell
d. Coated tongue
e. Change of bowel habits
f. GIT hge

Neurological manifestations:

Cerebral:

- Headache, intellectual deterioration
- Drowsiness , coma
- Insomnia, reversal of sleep rhythm.

Neuromuscular:

- Flapping tremors
- Restless leg syndrome
- Peripheral neuropathy
- Muscle twitches
- Convulsions

CV manifestations:

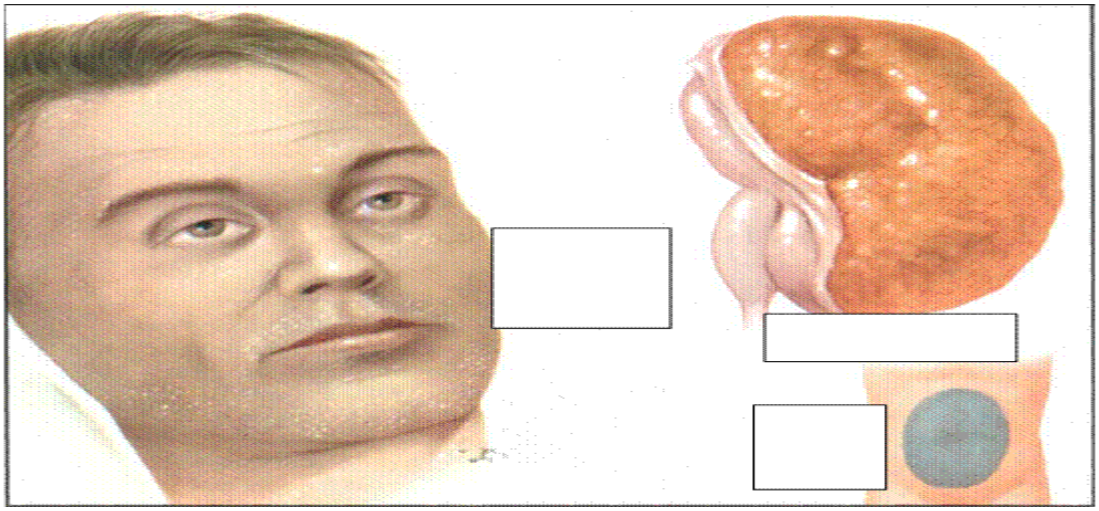
a. Hypertension.
b. Uremic pericarditis
c. Cardiac tamponade

Respiratory manifestations:

a. Acidotic breathing
b. Recurrent infection.
c. Dyspnea.
d. Pleurisy

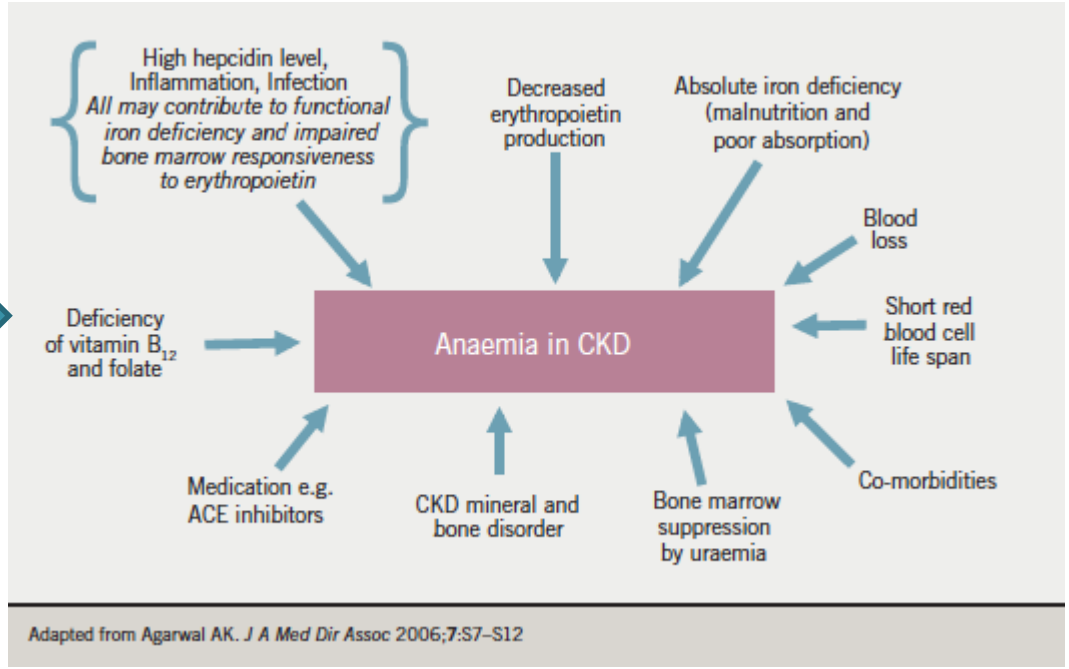
Cutaneous manifestations:

a. **Pale & yellow (sallow face)**
b. **Dry skin**
c. **Bruises.**
d. **Pruritis.**
e. **Purpura.**
f. **Urea frost.**



Hematologic manifestations:

Anemia



Bleeding tendency:

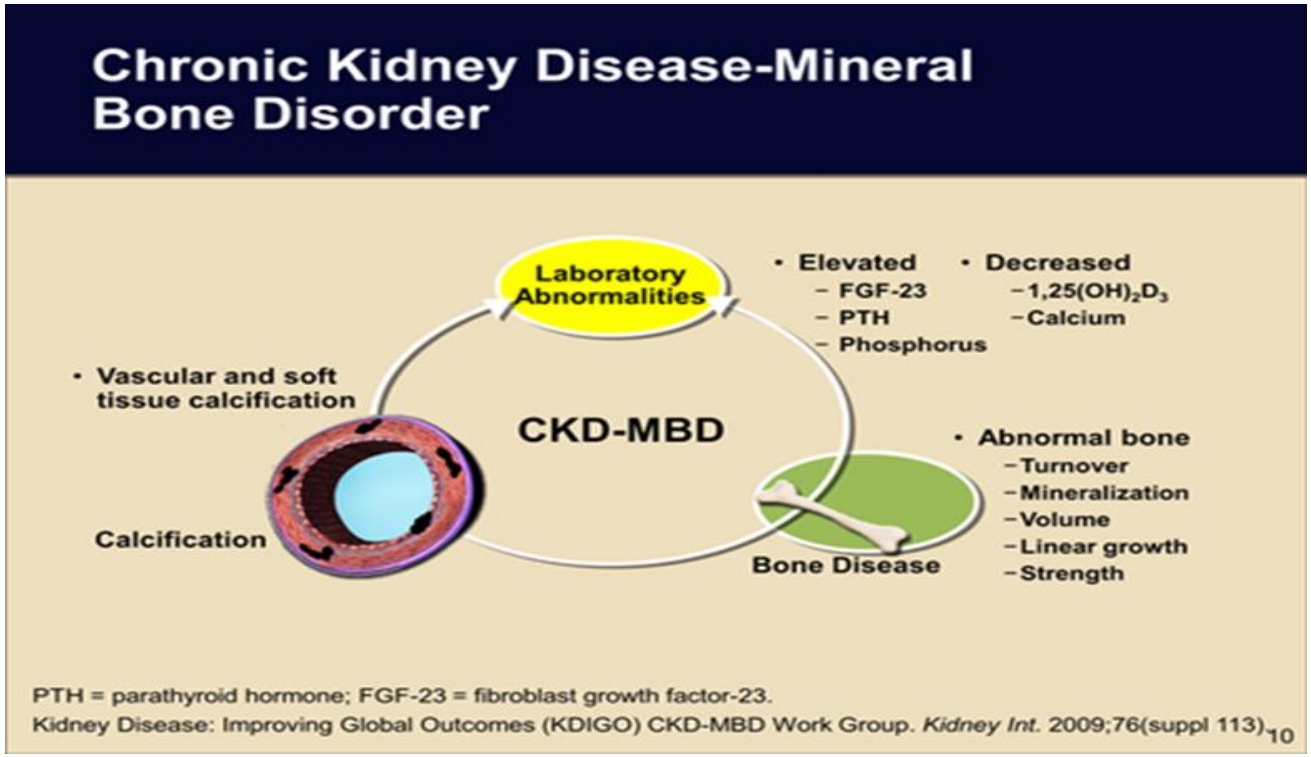
- Defective platelet function
- Heparin during dialysis

Musculo-skeletal manifestations:

a. **Muscle fatigue, wasting**

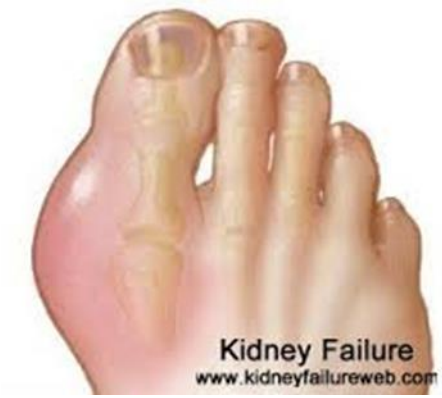
b. **Bone aches, fractures, deformity in children.**

c. **Soft tissue calcification.**



Metabolic manifestations :

a. Gout
b. Dyslipedemia.



Gonadal manifestations:

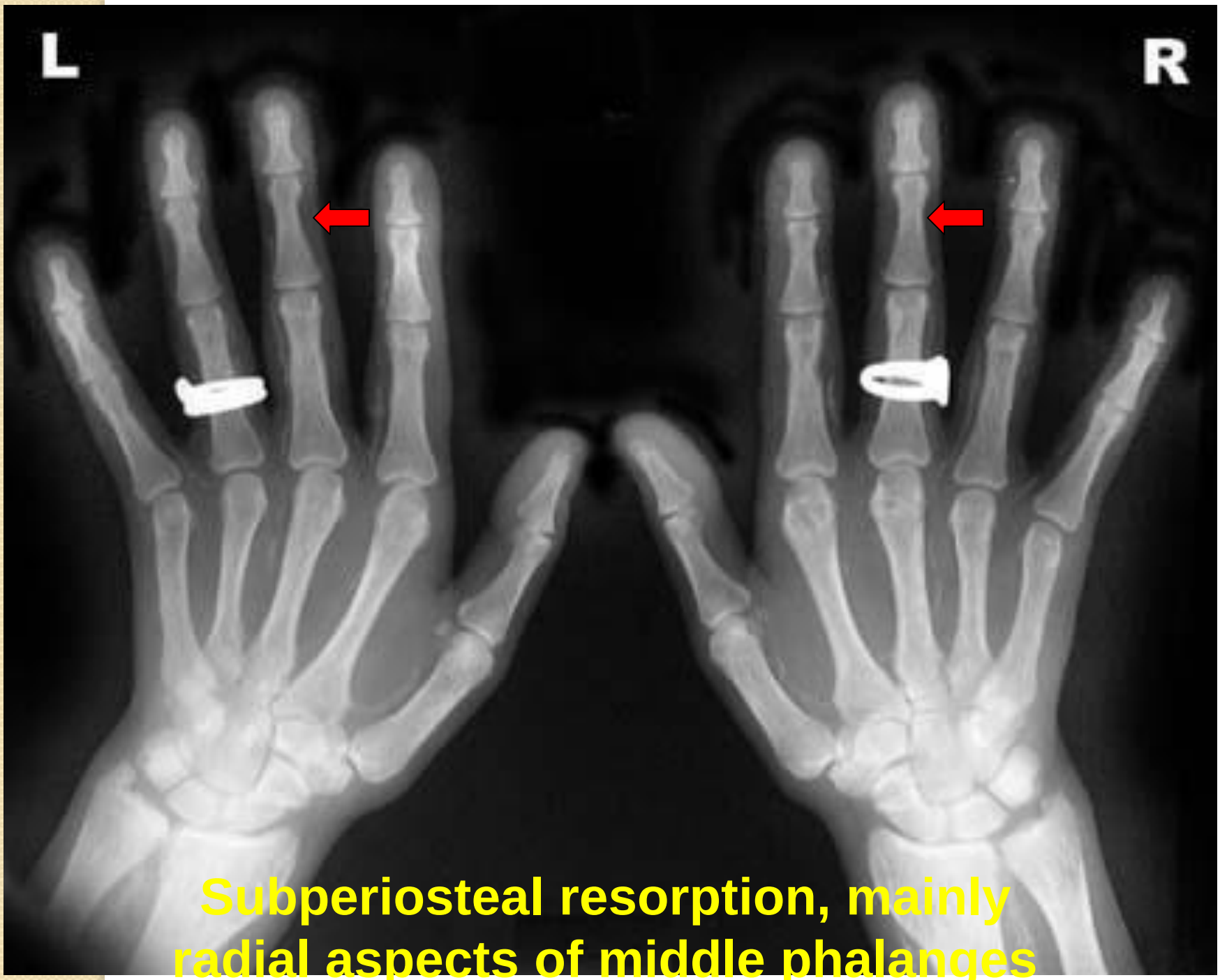
a. Decreased libido, impotence, gynecomastia
b. Infertility, menstrual disorders.

Endocrine disorders in uraemia:

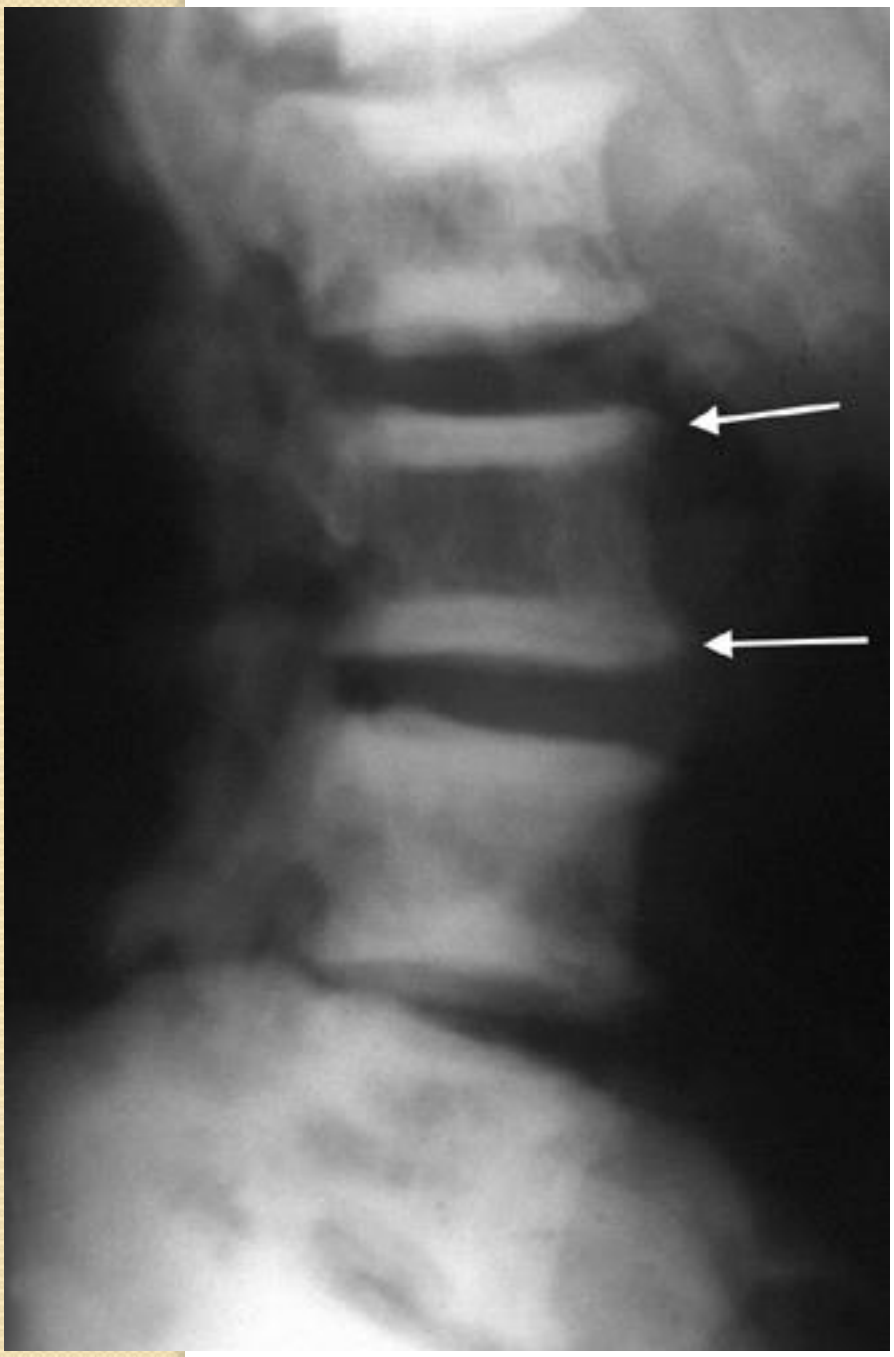
a. Hyperparathyoidism.
b. Lack of EPO.
c. Lack of active vit.D.
d. Increased renin activity.
e. Decreased testosterone.
f. Increased prolactin and LH.
g. Insulin increased peripheral resistance and half life.

Features of the underlying disease:

Such as DM, SLE, Stone disease.


L
R
Subperiosteal resorption, mainly radial aspects of middle phalanges

A patient with renal failure reveals subperiosteal resorption along the radial aspect of the middle phalanx (arrows), as well as resorption of the distal tuft (arrowheads).



Endplate sclerosis (arrows) referred to as rugger-jersey spine

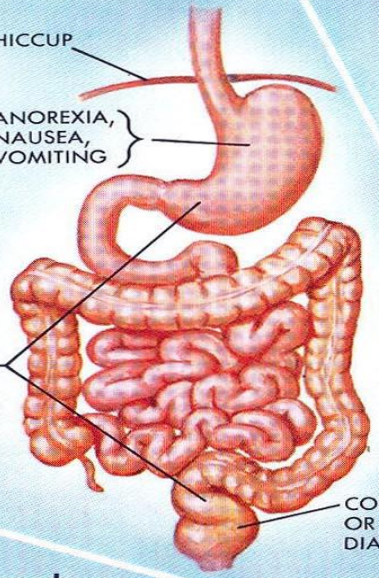
UREMIA:
MANIFESTATIONS WHICH MAY BE PRESENT IN VARIABLE DEGREE

GASTROINTESTINAL

COATED TONGUE, AMMONIACAL OR UNPLEASANT TASTE IN MOUTH

HICCUP

ANOREXIA, NAUSEA, VOMITING



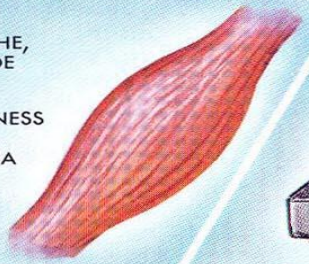
GASTROINTESTINAL BLEEDING

CONSTIPATION OR DIARRHEA

NEURAL

HEADACHE, LASSITUDE

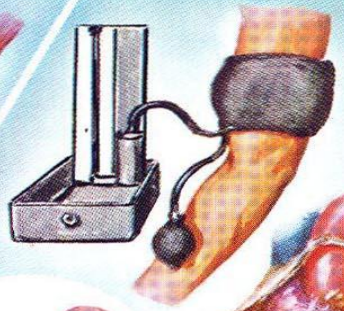
DROWSINESS OR/AND INSOMNIA



MUSCLE TWITCHING, WEAKNESS

CONVULSIONS OR COMA

CARDIOVASCULAR

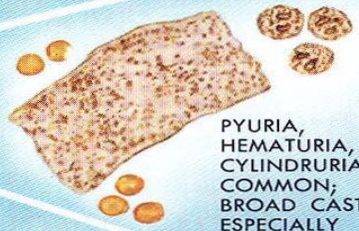


HYPERTENSION USUAL BUT NOT INVARIABLE

SEROFIBRINOUS PERICARDITIS (OCCASIONALLY)

ANEMIA; NORMOCHROMIC, NORMOCYTIC (BURR CELLS MAY APPEAR)
POLYCYTHEMIA RARELY

URINARY



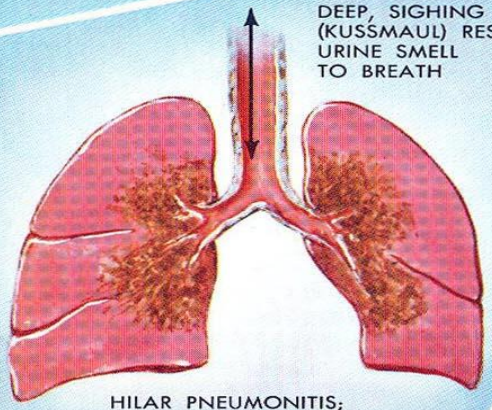
PYURIA, HEMATURIA, CYLINDRURIA COMMON; BROAD CASTS ESPECIALLY SIGNIFICANT

PROTEINURIA USUAL BUT NOT IN PROPORTION TO DEGREE OF FAILURE; NEPHROTIC SYNDROME MAY IMPROVE WHEN RENAL FAILURE APPEARS

BIOCHEMICAL

GFR ↓
CREATININE CLEARANCE ↓
UREA CLEARANCE ↓
BUN ↑ URIC ACID ↑
PLASMA CREATININE ↑
URINE CONCENTRATING ABILITY ↓
URINE DILUTING ABILITY ↓ (LATER);
DISTURBANCES OF Na, K, Ca, PO_4, AND GLUCOSE METABOLISM;
ACIDOSIS

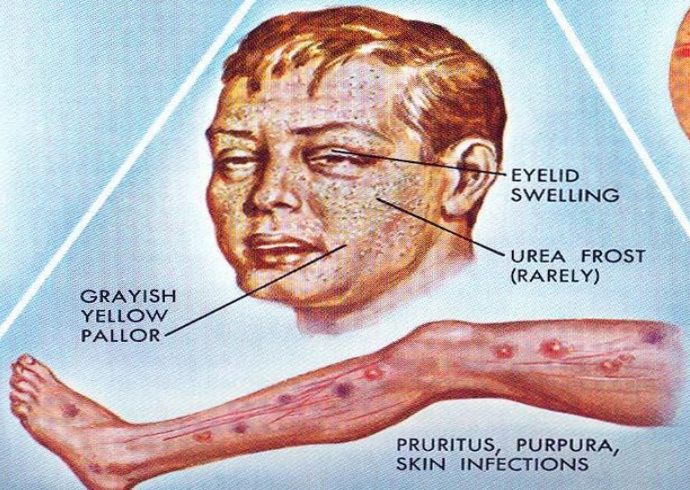
RESPIRATORY



DEEP, SIGHING (KUSSMAUL) RESPIRATION; URINE SMELL TO BREATH

HILAR PNEUMONITIS; "BAT-WING" OPACITY ON X-RAY (UREMIC LUNG)

DERMAL



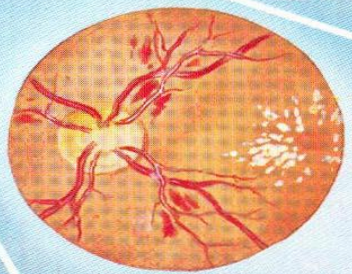
EYELID SWELLING

UREA FROST (RARELY)

GRAYISH YELLOW PALLOR

PRURITUS, PURPURA, SKIN INFECTIONS

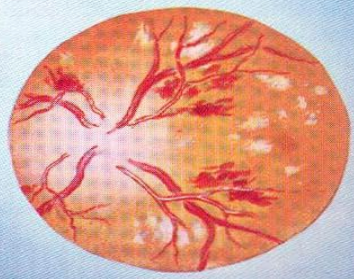
RETINAL



ARTERIOSCLEROTIC RETINOPATHY

OR/AND

HYPERTENSIVE RETINOPATHY



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Causes of acute deterioration in chronic kidney disease

- **Systemic infection - eg, urinary tract infection (UTI), chest infection, central line.**
- **Drugs - eg, diuretics, angiotensin-converting enzyme (ACE) inhibitors, aminoglycosides.**
- **Dehydration.**
- **Urinary tract obstruction**
- **Renal hypoperfusion secondary to dehydration**
- **Progression of underlying diseases - eg, relapse of glomerulonephritis.**
- **Development of accelerated-phase hypertension.**

Renal failure

Differentiation between acute and chronic renal failure

	Acute	*Chronic*
History	Short (days-week)	Long (month-years)
Haemoglobin concentration	Normal	Low
Renal size	Normal	Reduced
Renal osteodystrophy	Absent	Present
Peripheral neuropathy	Absent	Present
Serum Creatinine concentration	Acute reversible increase	Chronic irreversible


THANK
You