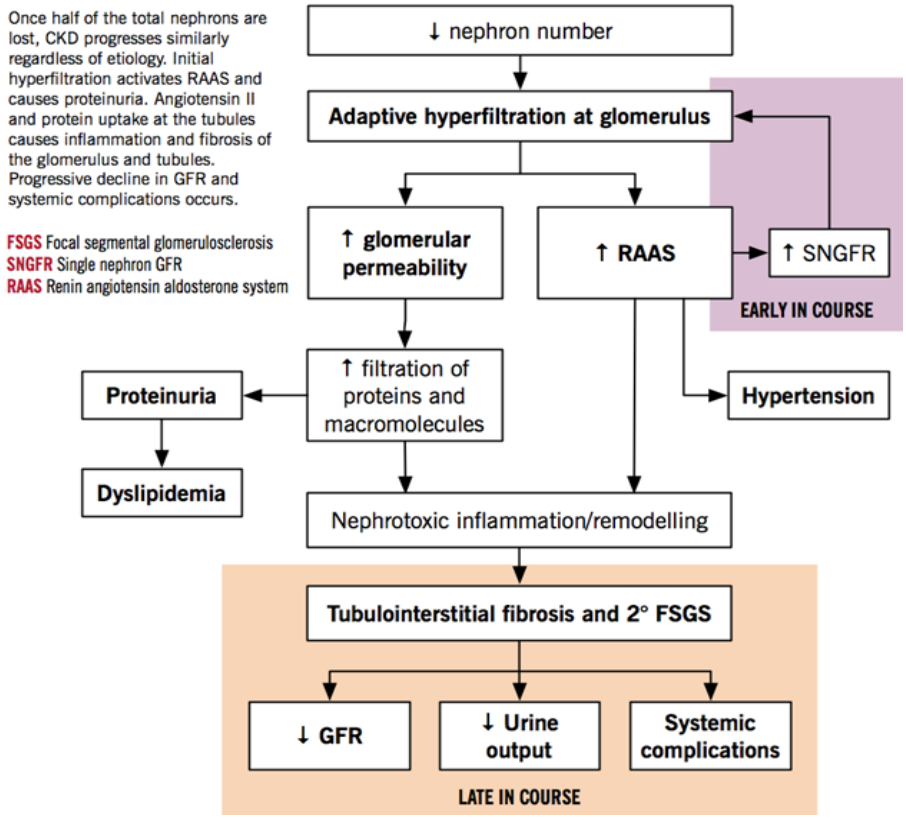
Unit V – Problem 11 – Physiology: Pathophysiology of Chronic Renal Failure

- **What is Chronic kidney disease?**
  - Kidney damage for ≥ 3 months, as defined by structural or functional abnormalities of the kidney, with or without decreased GFR; manifest by either:
    - ✓ Pathological abnormalities.
    - ✓ Markers of kidney damage, including abnormalities in the composition of the blood or urine, or abnormalities in imaging tests.
  - GFR < 60 ml/min/1.73m^2 for ≥ 3 months, with or without kidney damage.
  - **Simply, chronic renal disease is a progressive deterioration in:**
    - ✓ Glomerular filtration.
    - ✓ Tubular reabsorptive capacity.
    - ✓ Endocrine functions.
- **What are the causes of chronic kidney disease?**
  - **Metabolic disorders**: diabetes mellitus and obesity.
  - **Hypertension.**
  - **Immunologic disorders**: glomerulonephritis.
  - **Renal vascular disorders**: atherosclerosis and nephrosclerosis-hypertension.
  - **Infections.**
  - **Urinary tract obstruction.**
  - **Congenital disorders.**
- **What are the stages of chronic kidney disease?**

Stage	Description	GFR (ml/min/1.73m^2)
1	Kidney damage with normal or ↑ GFR	≥ 90
2	Kidney damage with mild ↓ GFR	60-89
3	Moderate ↓ GFR	30-59
4	Severe ↓ GFR	15-29
5	Kidney failure	< 15 (or dialysis)

- **Pathophysiology of chronic kidney disease:**
  - It results from progressive and irreversible loss of nephrons (> 70%). Therefore, adaptive changes will occur in the remaining nephrons and this will result in compensatory increase in GFR and hyperfiltration.



- **Chronic kidney disease results in azotemia:**
  - ✓ At ≤ 50% GFR.
  - ✓ Waste products (urea, uric acid and creatinine) will accumulate in proportion to the number of nephrons that have been destroyed.
  - ✓ The overall condition can result in uremia if not well-controlled! Uremia is characterized by the following:
    - ❖ Very low GFR (< 15 ml/min).
    - ❖ Uremic toxins (urea, phenols and β_2-microglobulin).
- **Volume and electrolyte imbalance:**
  - ✓ There is an ability to compensate if there are more than 25% functional nephrons.
  - ✓ Inability to regulate sodium excretion and inability to excrete free water will lead to extracellular fluid expansion and edema.
- **Hyperkalemia (occurs when GFR < 5 ml/min):**
  - ✓ When GFR is > 5 ml/min, there is a compensatory aldosterone-mediated potassium secretion in distal convoluted tubules (DCT).
  - ✓ Exacerbation of hyperkalmeia:
    - ❖ Exogenous factors: K^+-rich diet.
    - ❖ endogenous factors: infection and trauma.
- **Metabolic acidosis:**
  - ✓ Initially, there is failure to secrete hydrogen ions and decreased capacity to generate enough ammonia from cells of proximal tubule.
  - ✓ With progression, accumulation of phosphate and other organic acids (sulfuric acid, hippuric acid and lactic acid) creates an increased anion-gap metabolic acidosis.
- **Calcium and phosphate homeostasis:**
  - ✓ Hyperphosphatemia due to ↓GFR.
  - ✓ Hypocalcemia: due to impaired ability of the diseased kidney to synthesize 1,25-dehydroxivitamin D (the active form of vitamin D).
- **Hyperparathyroidism and bone disease:**
  - ✓ ↑PTH (Parathyroid Hormone).
  - ✓ Disordered vitamin D metabolism (as mentioned above).
  - ✓ Chronic metabolic acidosis: bone is a large reservoir of alkaline salts (calcium phosphate, calcium carbonate); dissolution of this buffer source probably contributes to: renal and metabolic osteodystrophy.
- **Hematologic abnormalities:**
  - ✓ Normochromic normocytic anemia with a low reticulocyte count.
  - ✓ Due to reduced production of erythropoietin from kidneys resulting in decreased erythropoesis.
- **Cardiovascular abnormalities:**
  - ✓ Elevated serum triglycerides and accelerated atherosclerosis.
  - ✓ Congestive heart failure.
  - ✓ Pulmonary edema
  - ✓ Pericarditis resulting from irritation and inflammation of the pericardium by uremic toxins.
- **Endocrine abnormalities:**
  - ✓ Prolonged half-life of insulin due to reduced clearance.
  - ✓ Amenorrhea and pregnancy failure due to low estrogen levels.
  - ✓ Impotence, oligospermia and germinal cell dysplasia due to low testosterone levels.
- **Abnormalities in skin integrity:**
  - ✓ Pallor (due to anemia).
  - ✓ Hematomas (due to clotting abnormalities).

- ✓ Pruritis (due to high phosphate levels and phosphate crystals formed by hyperparathyroidism).
- ✓ When urea concentrations are extremely high, evaporation of sweat leaves a residue of urea termed “uremic frost”.

- **Gastrointestinal abnormalities:**
  - ✓ Anorexia, nausea and vomiting (due to uremia).
  - ✓ Metallic taste in the mouth (depressing appetite).
  - ✓ Ulceration and bleeding of GI mucosa.
- **Neuromuscular abnormalities:**
  - ✓ <u>Features of uremia:</u>
    - ❖ Asterixis.
    - ❖ Myoclonus.
    - ❖ Chorea.
    - ❖ Stupor.
    - ❖ Seizures.
    - ❖ Coma.
  - ✓ <u>Peripheral neuropathy</u>: atrophy and demyelination of nerve fibers.