Chronic Kidney Disease

AND

Anemia
Metabolic acidosis
Cardiovascular complications

Mojgan Mortazavi,
professor of nephrology,
Isfahan kidney diseases research center
Isfahan university of medical sciences

Aim of this lesson

- Cardiovascular complications
- Anemia
- Metabolic acidosis
- **Interventions for Slowing Progression of Chronic Kidney Disease**
- **Overview of Chronic Kidney Disease Management by Stage**

CKD

- **Chronic renal failure is defined as progressive and irreversible loss of renal function.**

Risk factors

- Small for gestation birth weight
- Childhood obesity
- Hypertension
- Diabetes mellitus
- Autoimmune disease
- Advanced age
- African ancestry
- Family history of kidney disease
- A previous episode of acute kidney injury
- Presence of proteinuria, abnormal urinary sediment, or structural abnormalities of the urinary tract

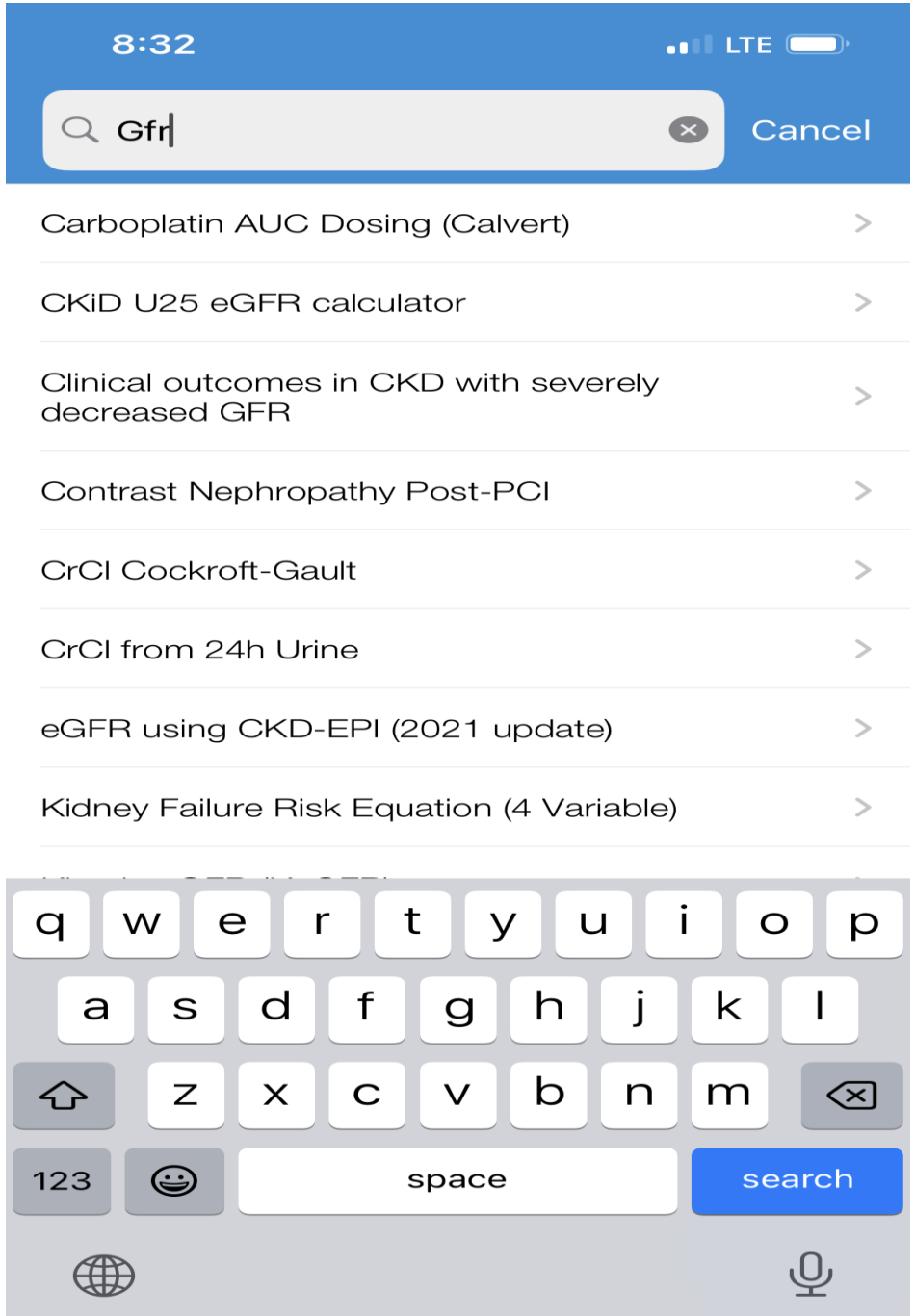
Leading Categories of Etiologies of CKD

- Diabetic nephropathy
- Hypertension-associated CKD
- Glomerulonephritis
- Autosomal dominant polycystic kidney disease
- Other cystic and tubulointerstitial nephropathy

KDIGO classification of chronic kidney disease (CKD)

- 1- SCr
- GFR calculation
  - Equation from the Modification of Diet in Renal Disease study (MDRD)
  - CKD-EPI equation
- 2- Albuminuria


8:32
LTE
Games
Calculator
Extras
Files
Calculate
My Files
Inbox:9656unr...
Find My
Shortcuts
Freeform
Translate
Books
PDMed
Skype
Apple Store
Clips
Connect
Music
GarageBand
iMovie
iTunes U
Keynote
WhatsApp
Search


8:32
LTE
Gfr
Cancel
Carboplatin AUC Dosing (Calvert)
CKiD U25 eGFR calculator
Clinical outcomes in CKD with severely decreased GFR
Contrast Nephropathy Post-PCI
CrCl Cockroft-Gault
CrCl from 24h Urine
eGFR using CKD-EPI (2021 update)
Kidney Failure Risk Equation (4 Variable)
q w e r t y u i o p
a s d f g h j k l
z x c v b n m
123
space
search

Questions

Gender?	Unanswered >
Age?	Unanswered >
Creatinine?	Unanswered >

Results

Please answer all questions

Stages of CKD*

Stage	Description	GFR, mL/min/1.73 m²
1	Kidney damage† with normal or increased GFR	≥90
2	Kidney damage† with mild decreased GFR	60–89
3	Moderately decreased GFR	30–59
4	Severely decreased GFR	15–29
5	Kidney failure	<15 (or dialysis)

GFR categories (ml/min/1.73 m²) description and range			
	G1	Normal or high	≥90
	G2	Mildly decreased	60–89
	G3a	Mildly to moderately decreased	45–59
	G3b	Moderately to severely decreased	30–44
	G4	Severely decreased	15–29
	G5	Kidney failure	<15

Persistent albuminuria categories description and range		
A1	**A2**	**A3**
Normal to mildly increased	Moderately increased	Severely increased
<30 mg/g <3 mg/mmol	30–300 mg/g 3–30 mg/mmol	>300 mg/g >30 mg/mmol

CRF

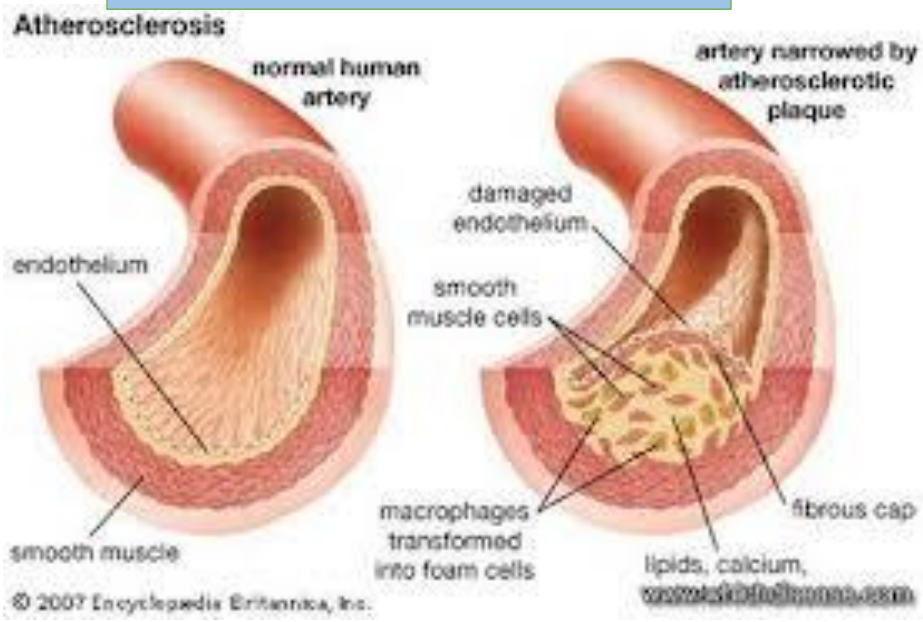
- Stages 1 and 2 CKD are usually not associated with any symptoms arising from the decrement in GFR.
- If the decline in GFR progresses to stages 3 and 4, clinical and laboratory complications of CKD become more prominent

Systemic manifestation of uremia

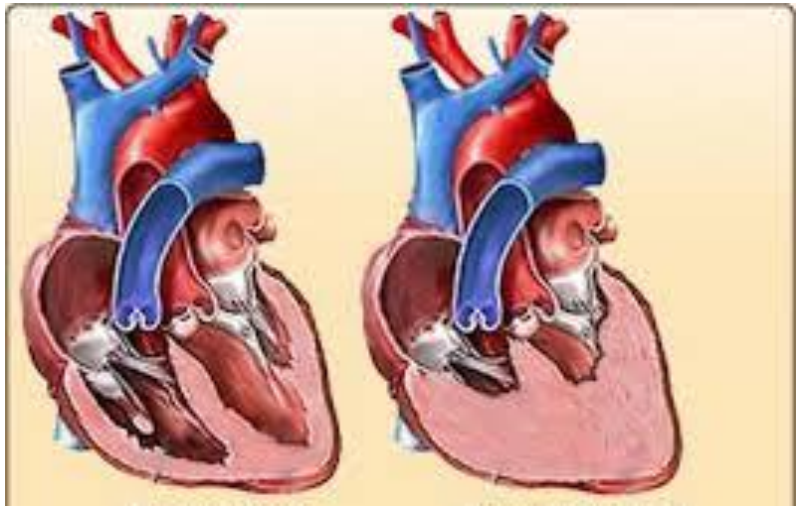
Cardiovascular disturbances

Arterial hypertension
Congestive heart failure or pulmonary edema
Pericarditis
Hypertrophic or dilated cardiomyopathy
Uremic lung
Accelerated atherosclerosis
Hypotension and arrhythmias (D)
Vascular calcification

Arterial hypertension

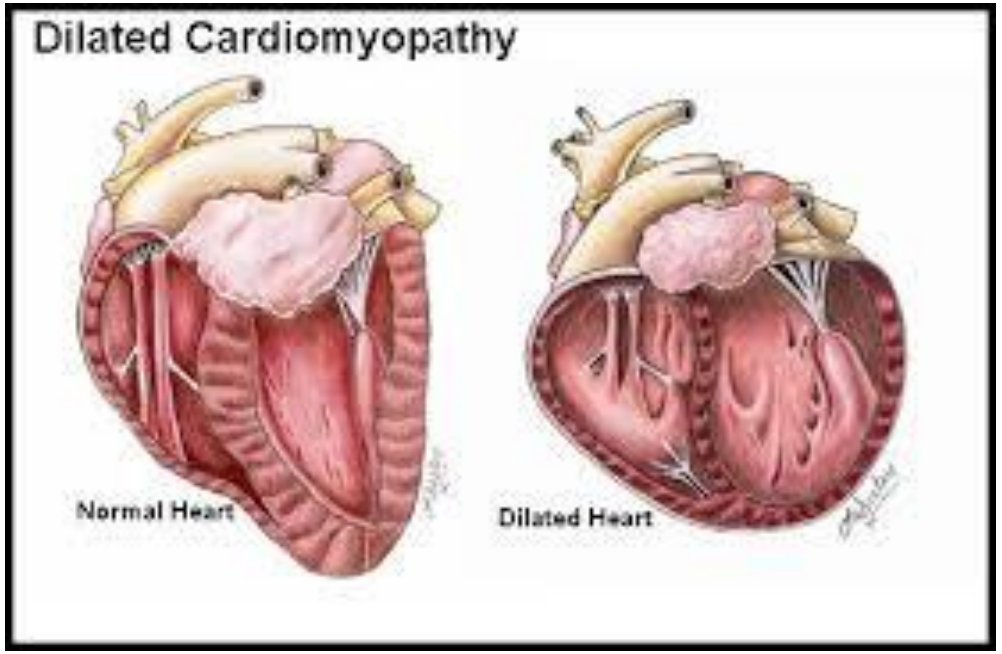


Congestive heart failure

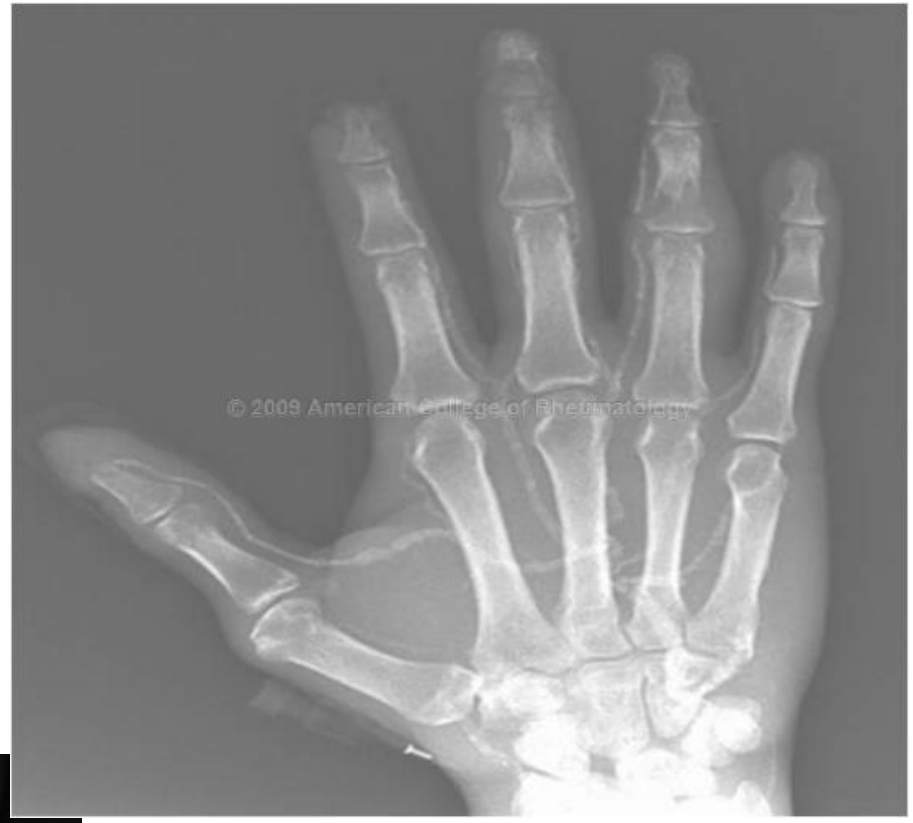


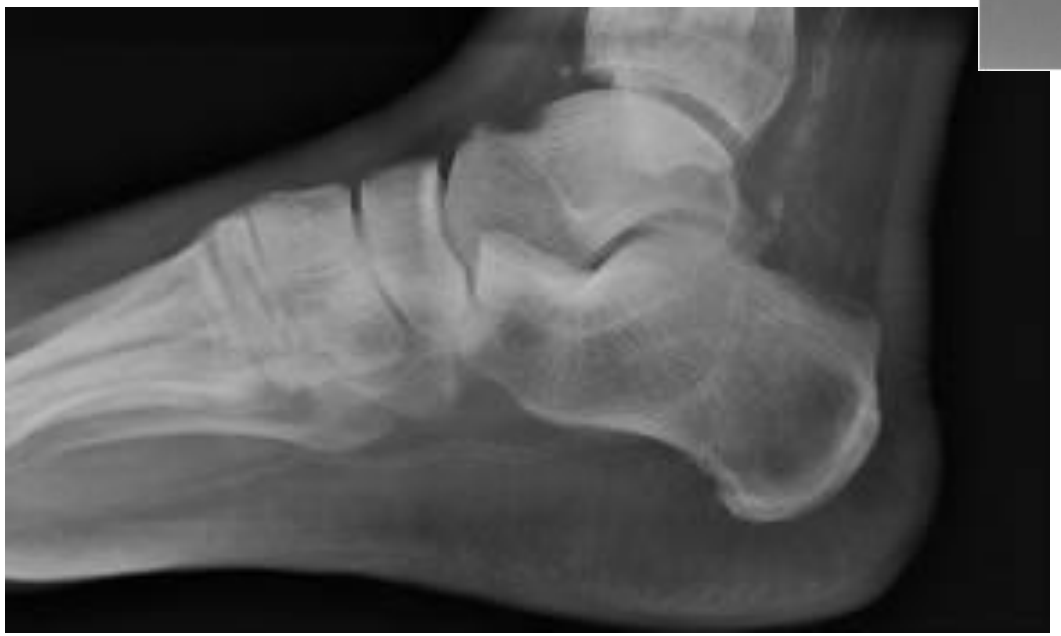
Normal

Hypertophic cardiomyopathy



Vascular calcification





Gastrointestinal disease

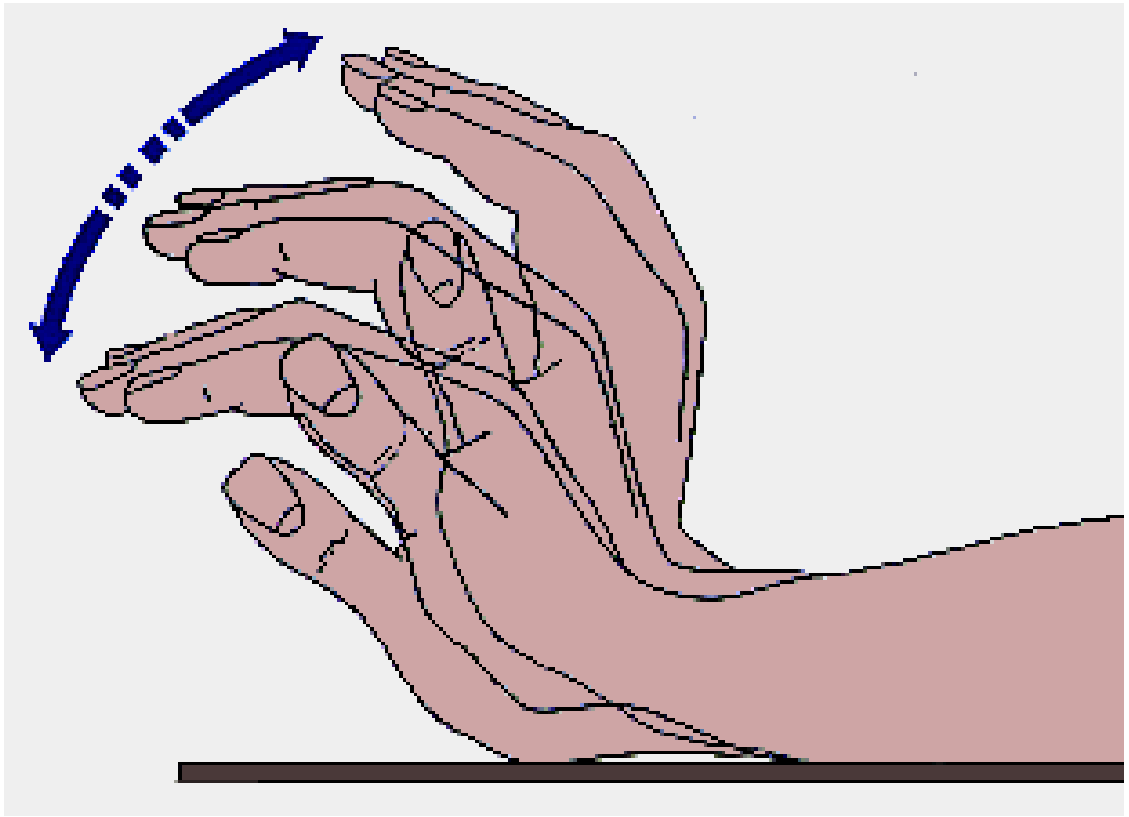
- **Anorexia**
- **Nausea**
- **Vomiting**
- **Disturbance of taste**
- **Gastritis**
- **Peptic ulcer**
- **GI bleeding**

Neurologic manifestations

- **Irritability**
- **Insomnia**
- **Lethargy**
- **Anorexia**
- **Seizures**
- **Coma**
- **Glove and stocking sensory loss**
- **Restless leg**
- **Foot drop or wrist drop**

Recognizing asterixis

In asterixis, the patient's wrists and fingers are observed to "flap" because of a brief, rapid relaxation of wrist dorsiflexion.



Musculoskeletal manifestations

- **Muscle weakness**
- **Gout and pseudogout**
- **Renal osteodystrophy**

Hematologic effects

Hematologic and immunologic disturbances

Anemia (I)
Lymphocytopenia (P)
Bleeding diathesis (I or D)
Increased susceptibility to infection (I or P)

Hematologic Abnormalities

Anemia

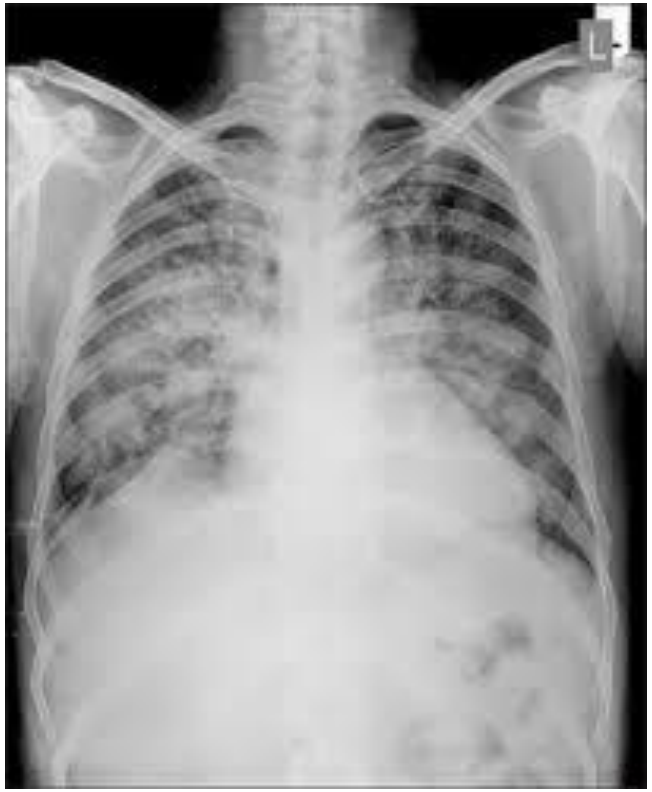
Causes:

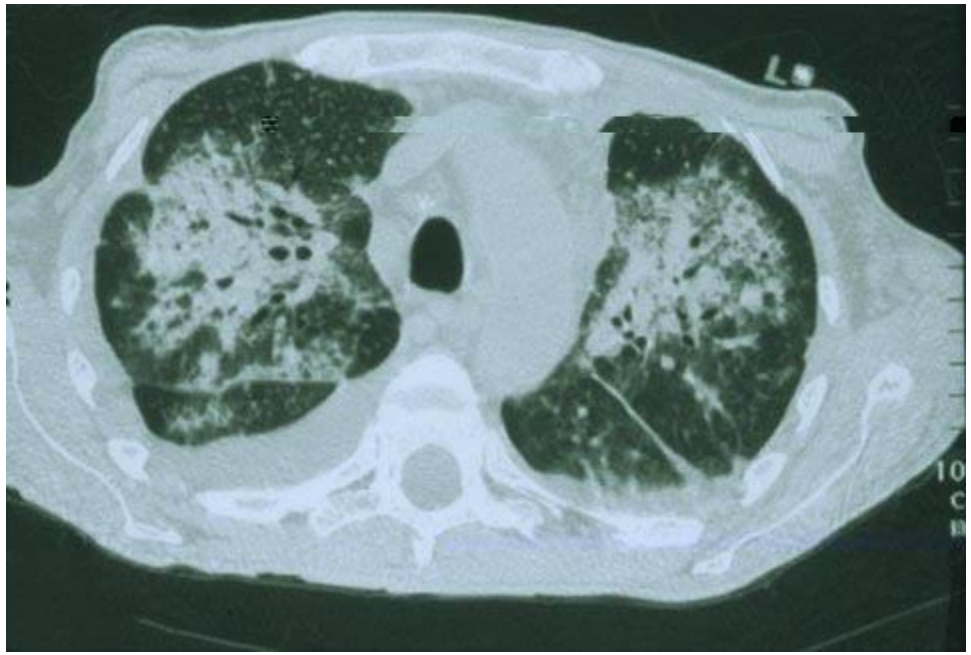
Relative deficiency of erythropoietin
Diminished red blood cell survival
Bleeding diathesis
Iron deficiency
Hyperparathyroidism/bone marrow fibrosis
"Chronic inflammation"
Folate or vitamin B12 deficiency

Pulmonary effects

- **Noncardiogenic pulmonary edema**
- **Pneumonitis**
- **Pleuritis**

Uremic lung

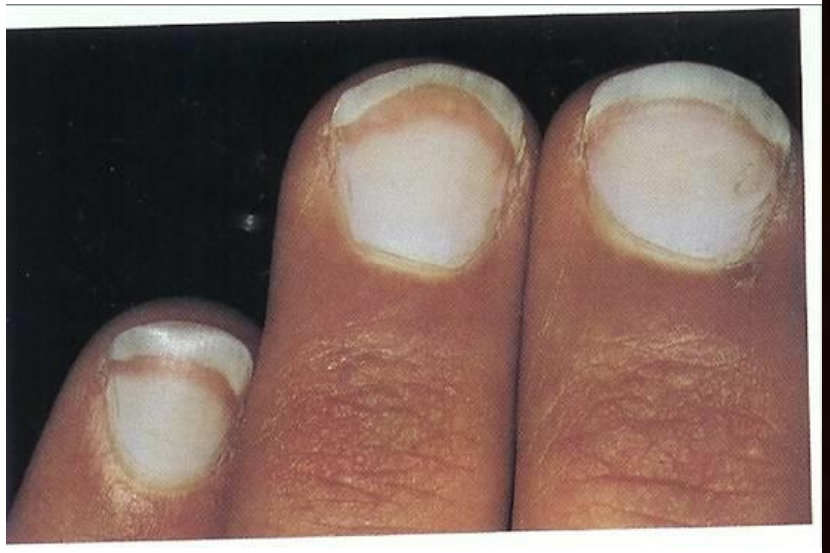


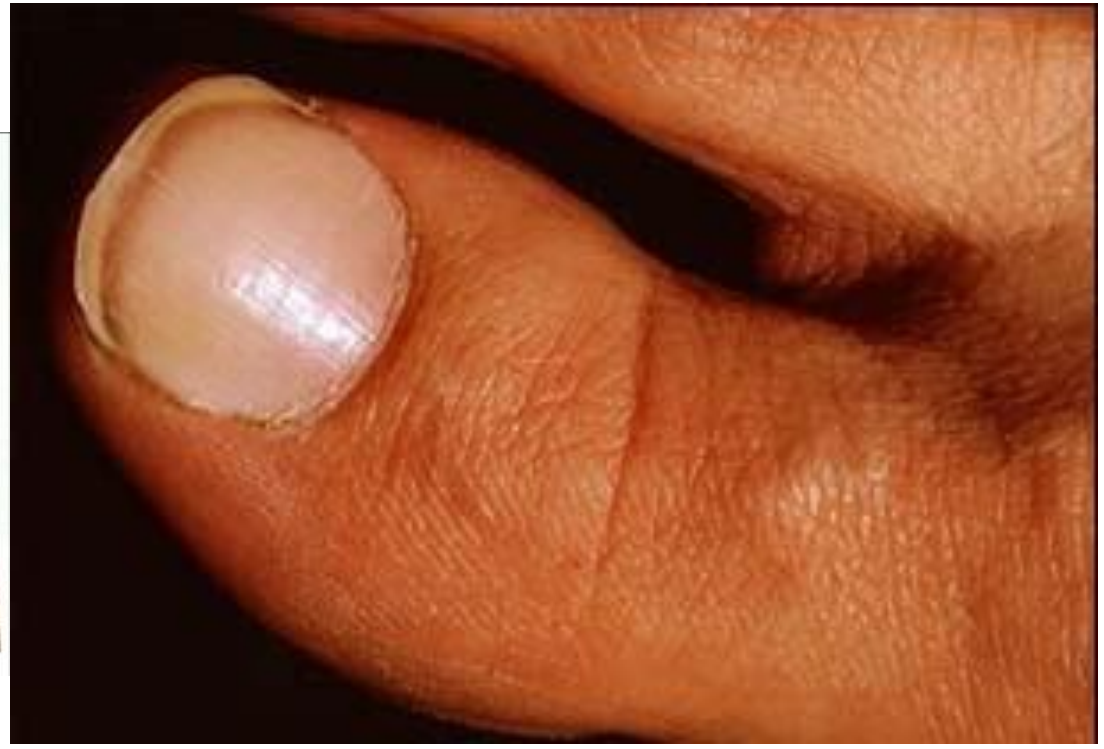


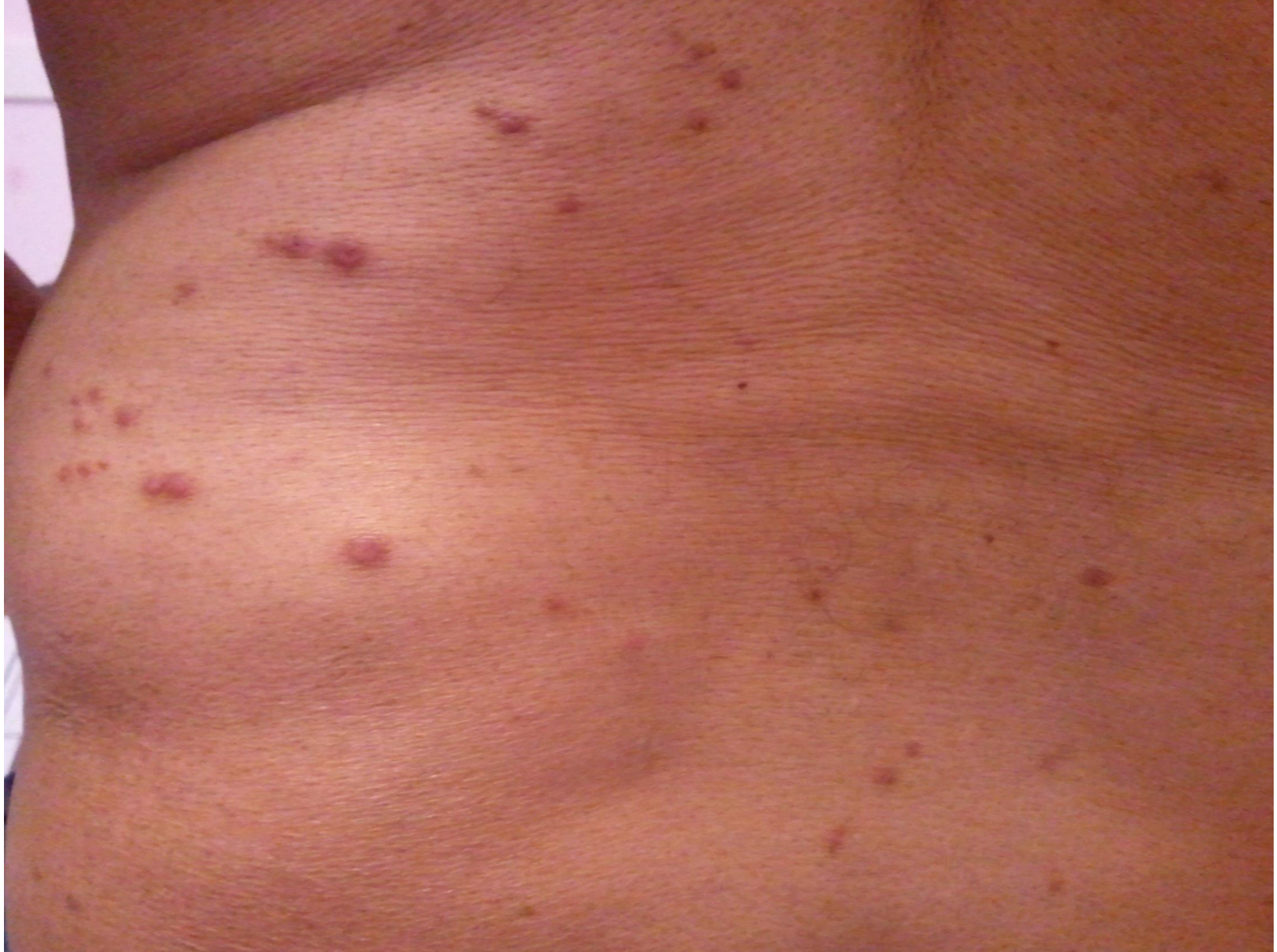
Dermatologic disturbances

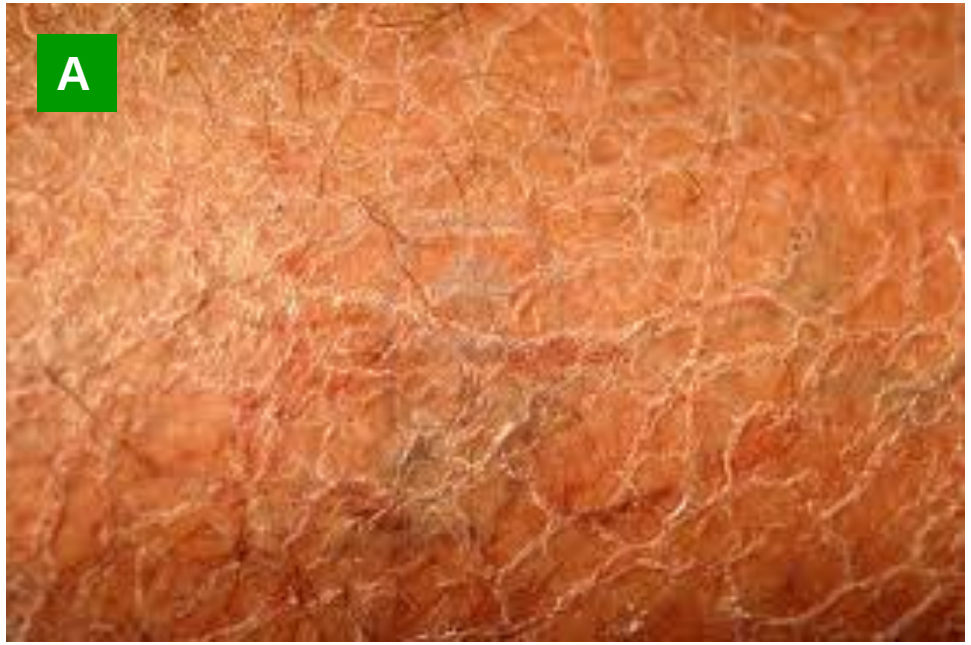
Pallor (I)[b]
Hyperpigmentation
Pruritus
Ecchymoses
Nephrogenic fibrosing
Dermopathy (D)
Uremic frost

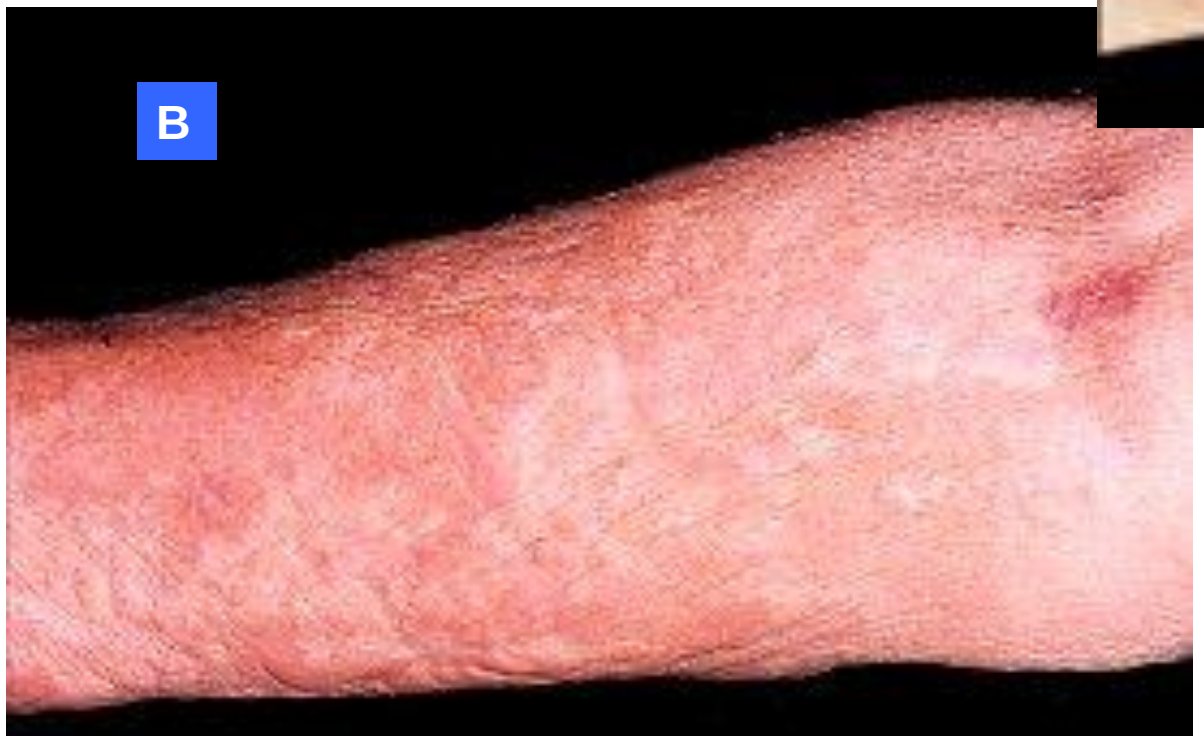
Half and half nail



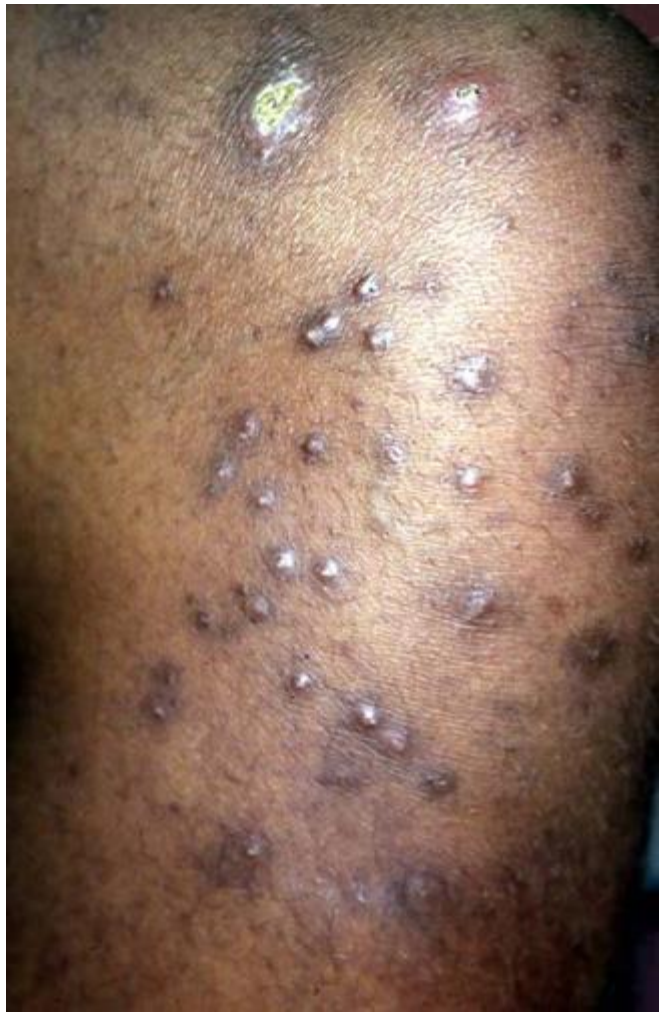








A- Dry skin
B-Nephrogenic systemic fibrosis



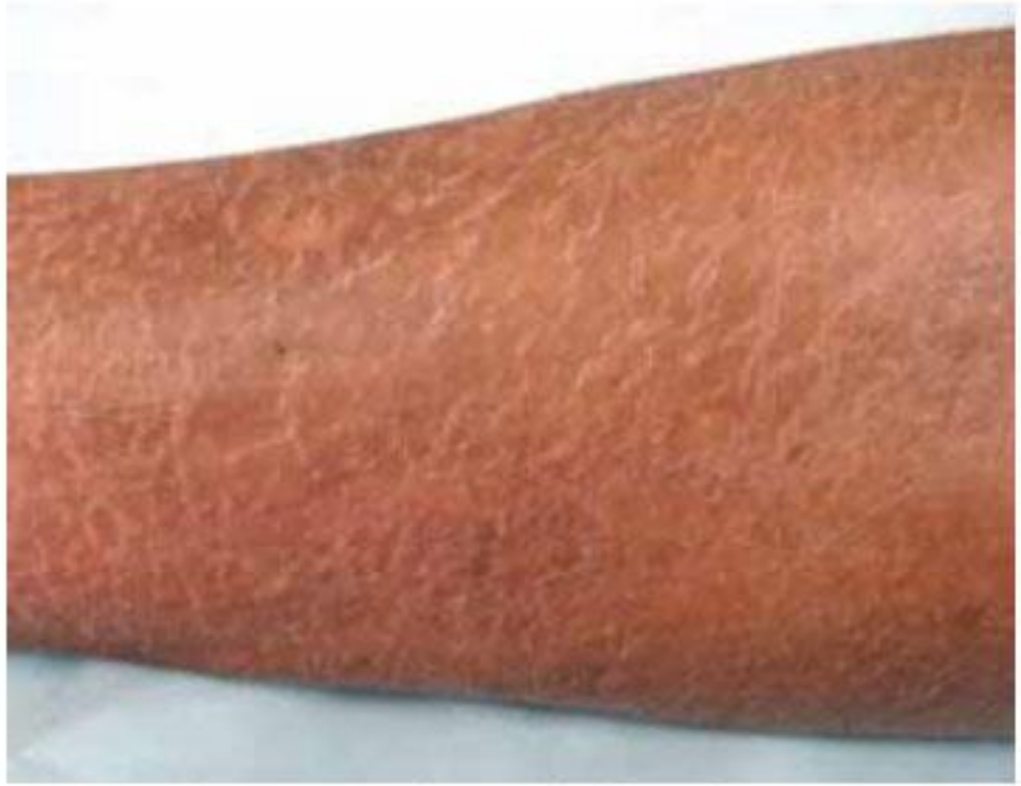
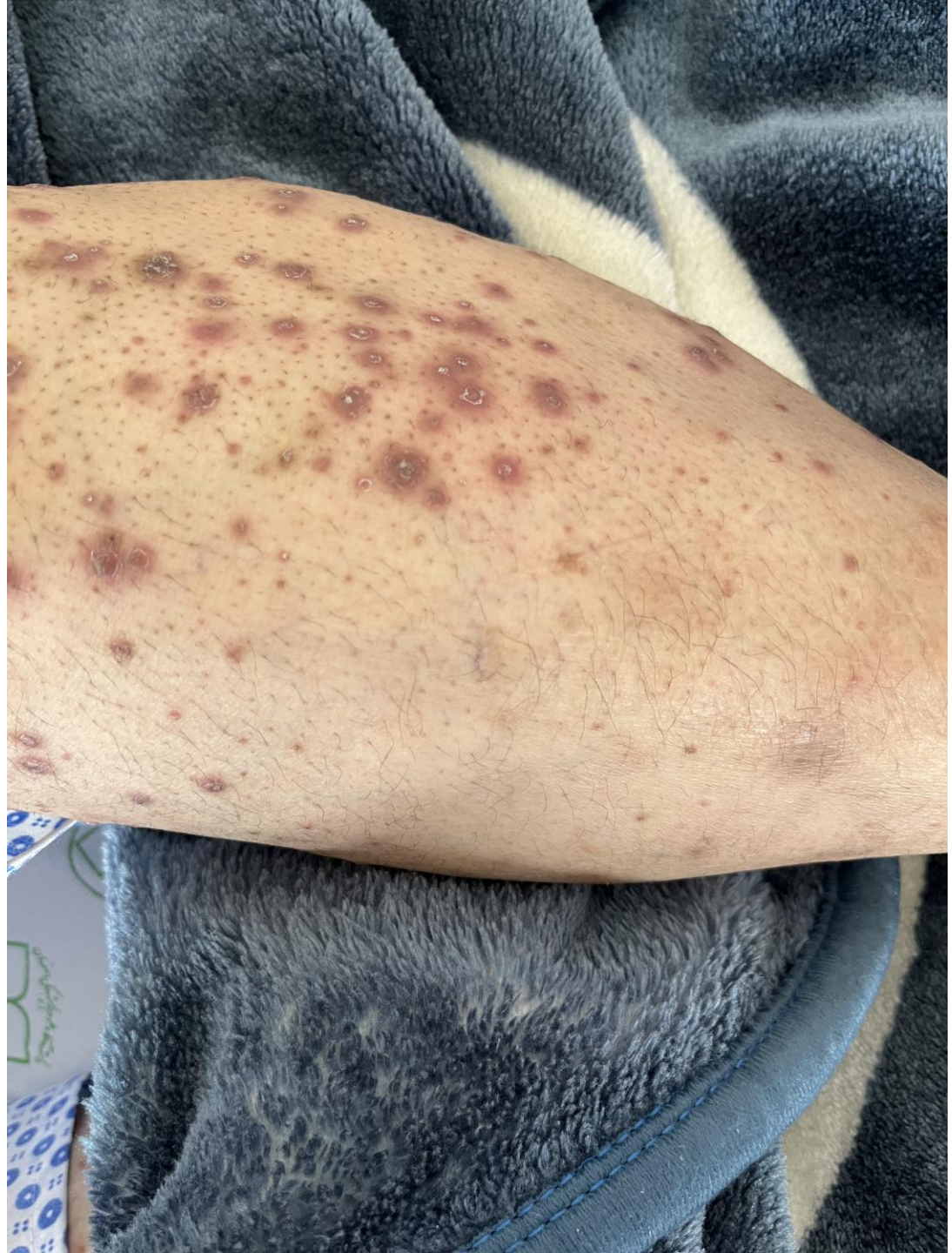


FIGURE 3: Skin xerosis evolving with ichthyosiform appearance in the lower limb of a chronic renal patient



Acid-Base/ electrolytes

- **Anion gap acidosis**
- **Hyperkalemia**
- **Fluid overload**
- **Hypocalcemia**
- **Hyperphosphatemia**
- **Hyermagnesemia**

Metabolic Acidosis

1. **CKD patients produce less ammonia.**
2. **Hyperkalemia, if present, further depresses ammonia production.**
3. **Metabolic acidosis is mild; the pH is rarely <7.35 and can usually be corrected with oral sodium bicarbonate supplementation.**

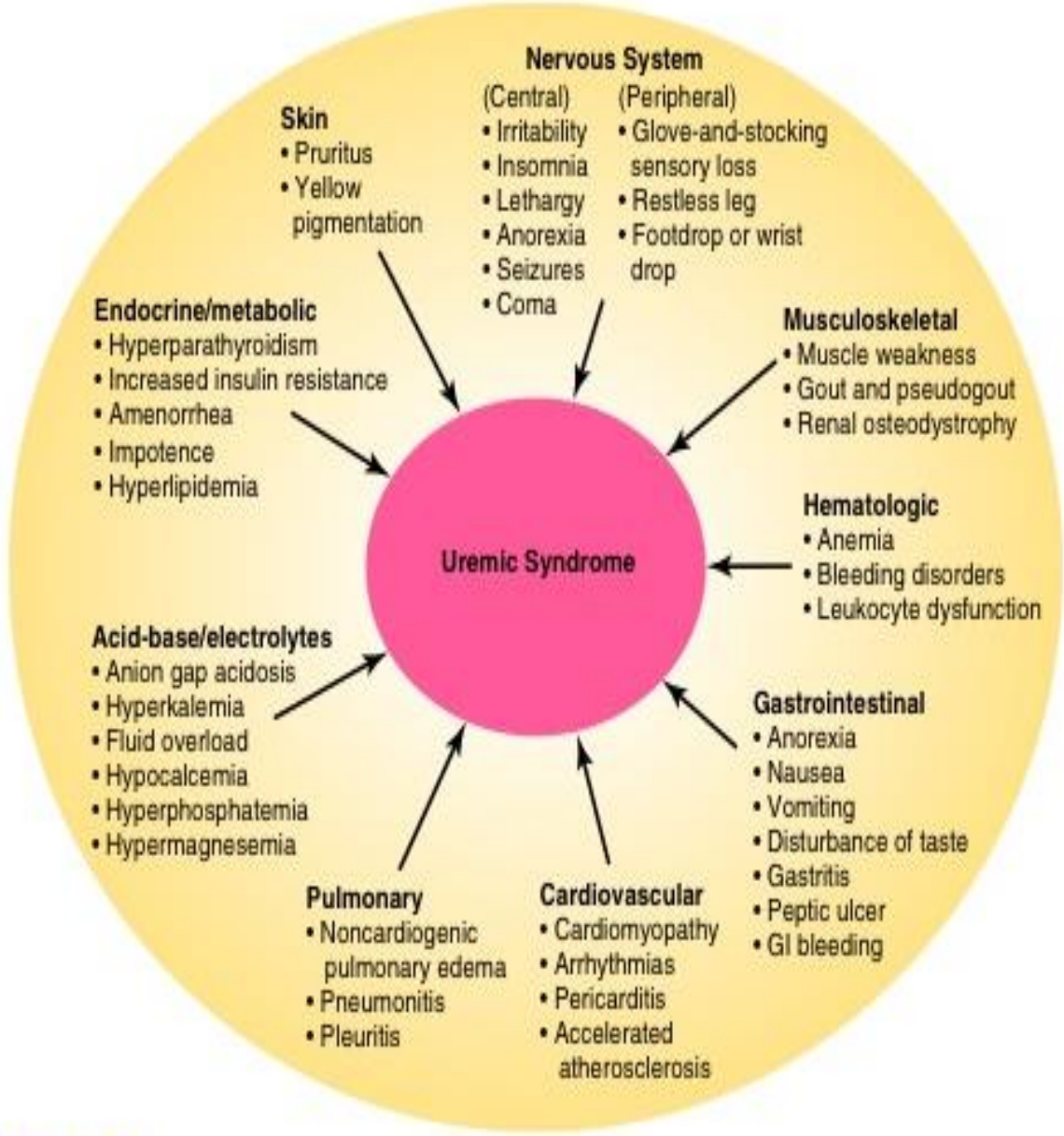
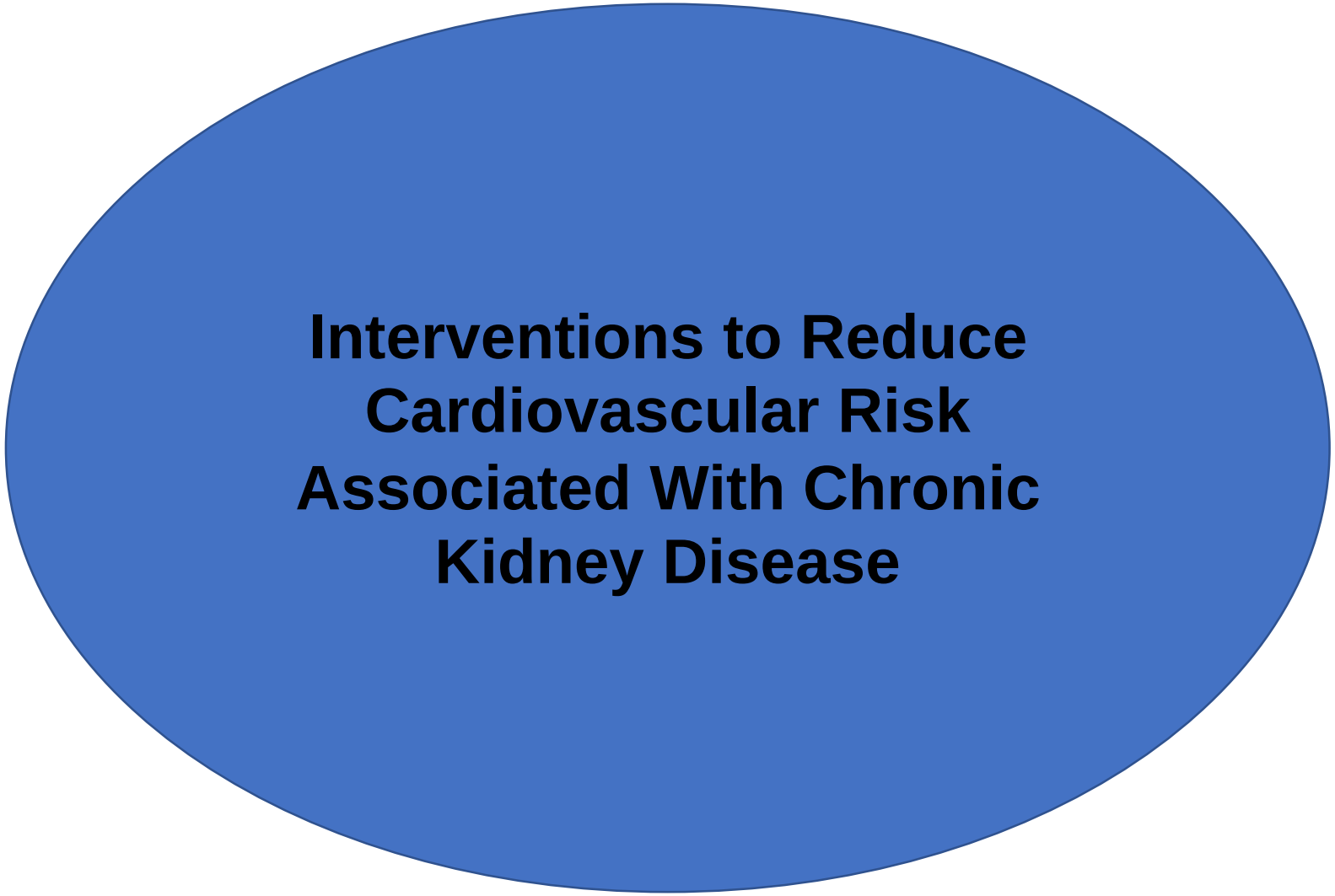


FIGURE 32-3 Diagrammatic summary of the major manifestations of the uremic syndrome. GI, Gastrointestinal.

CHRONIC RENAL FAILURE (CRF)

- RENAL INSUFFICIENCY -

- Edema
- Headaches
- GFR - progressively decreases from 90 to 30 ml/min
- ↓ Ability to Concentrate Urine
- Mild Anemia
- Polyuria → Oliguria
- ↑ BP
- ↑ BUN & Serum Creatinine
- Weakness & Fatigue


Interventions to Reduce Cardiovascular Risk Associated With Chronic Kidney Disease

When cardiovascular complications is expressed?

- Following a seminal report in the early 1970s describing accelerated atherosclerosis in persons receiving maintenance hemodialysis, a large body of research has focused on the relationship between CKD and cardiovascular disease.
- It is now clear that increased cardiovascular mortality is expressed early in the course of CKD, for example, in the setting of microalbuminuria in persons with diabetes and when the GFR starts to decline in stage 3 CKD.

What should we do?

- lifestyle measures including smoking cessation, weight loss, and dietary sodium restriction afford both renal and cardiovascular protection.
- In addition, the treatment of hypertension with RAAS inhibitors and a lower blood pressure target of 130/80 mm Hg, central to achieving renoprotection, also reduces cardiovascular risk
- All persons with chronic kidney disease should be regarded as having a high risk of cardiovascular disease and management offered to reduce this risk, including treatment with a statin.

Metabolic Acidosis

- As the number of functioning nephrons declines, CKD leads to net retention of hydrogen ions, which begins when GFR falls below 40 to 50 mL/min/1.73 m2.
- Among persons in whom GFR decreases from 90 to less than 20 mL/min/1.73 m2, the prevalence of metabolic acidosis rises from 2% to 39% and is higher among younger persons and those with diabetes.
- As the patient approaches ESKD, the plasma bicarbonate concentration tends to stabilize between 15 and 20 mEq/L.
- Chronic metabolic acidosis has multiple adverse consequences, including increased protein catabolism, increased bone turnover, induction of inflammatory mediators, insulin resistance, and increased production of corticosteroids and parathyroid hormone.

Metabolic Acidosis

- Western diets are typically acid producing, but the addition of significant portions of fruits and vegetables can move this to a base-producing state.

- The KDIGO guidelines recommend bicarbonate supplementation for persons with levels below 22 mEq/L.

Anemia

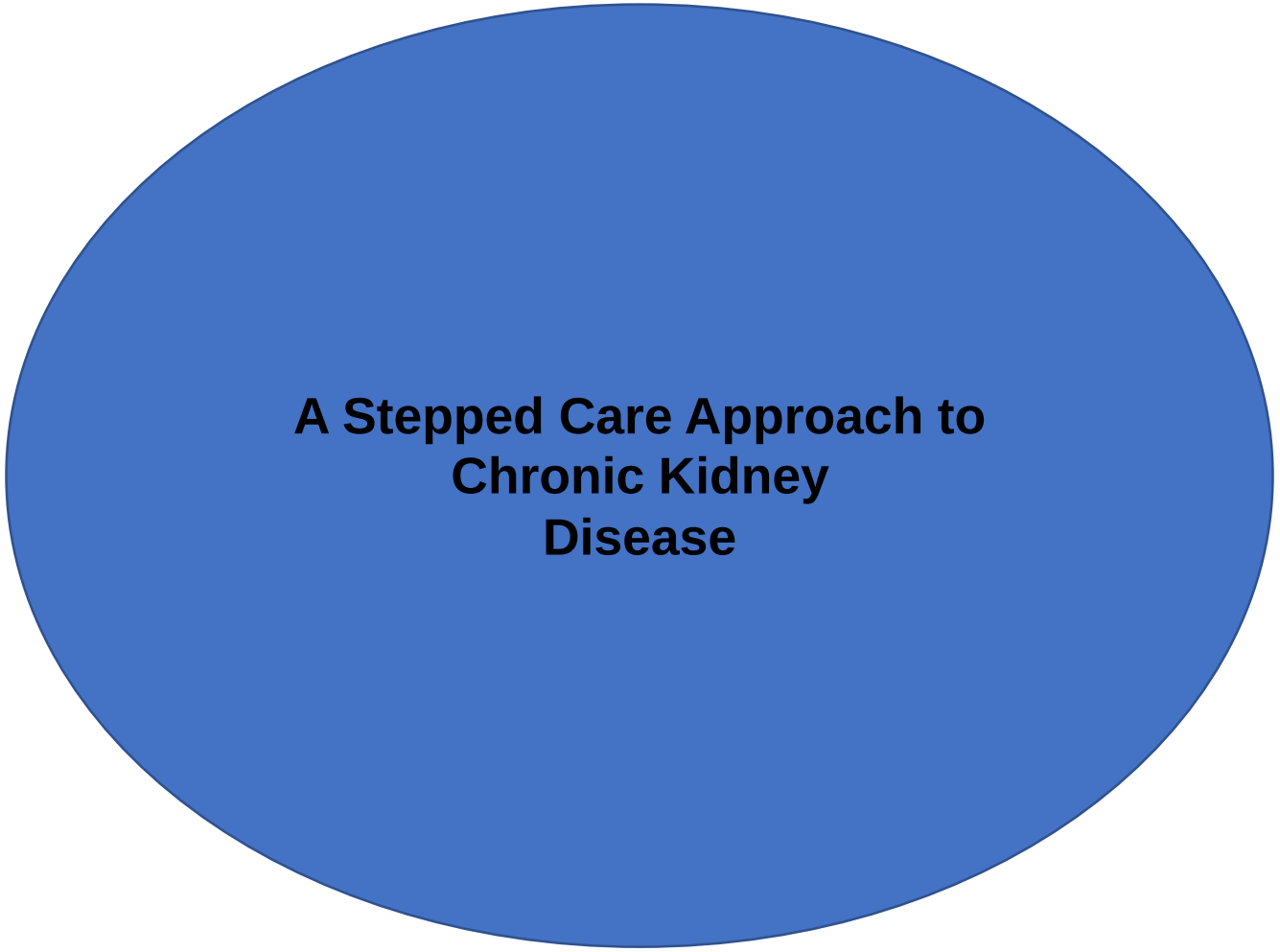
- The anemia of CKD results from a combination of reduced renal erythropoietin production (presumed reflection of the reduction in functioning renal mass), shortened red blood cell survival, and functional iron deficiency.
- Anemia— defined as a hemoglobin count lower than 13 g/dL in men and lower than 12 g/dL in women—can develop well before the onset of uremic symptoms.
- In cross-sectional studies, associations between anemia and an increased risk of morbidity and mortality, caused principally by cardiac disease and stroke, have been described in persons on dialysis.

Anemia

- In addition, anemia may influence the progression of CKD.
- By contrast, prevention of anemia in the remnant kidney model by administration of erythropoietin resulted in increased systemic and glomerular blood pressures and markedly increased glomerulosclerosis .
- Despite the apparently favorable hemodynamic effects of anemia in experimental models of CKD, some human studies suggest that anemia may in fact accelerate CKD progression.
- In persons with inherited hemoglobinopathies, chronic anemia is associated with glomerular hyperfiltration that eventuates in proteinuria, hypertension, and ESKD.
- In several longitudinal studies, lower hemoglobin value was identified as a risk factor for CKD progression and ESKD.

Anemia

- Moreover, in the Cardiovascular Risk Reduction by Early Anemia Treatment with Epoetin Beta (CREATE) study, achievement of a higher hemoglobin target (13–15 mg/dL) was associated with a shorter time to initiation of dialysis than was achievement of the lower target (**10.5–11.5 mg/dL**).
- Further concern was provoked by serious adverse effects associated with higher hemoglobin targets, including increased rate of mortality and increased risk of stroke.
- Current KDIGO recommendations are therefore to treat symptomatic anemia in CKD with erythropoietin or iron supplementation, or both, to partially correct the hemoglobin and achieve a range of 10 to 11.5 mg/dL.
- Hemoglobin value should not exceed 13 g dL.


A Stepped Care Approach to
Chronic Kidney
Disease

Stages 1 and 2

- At these stages of CKD, the diagnosis is based on the presence of albuminuria, hematuria, or structural kidney disease, and an eGFR above 60 mL/min/1.73 m2.

- Persons with stages 1 and 2 disease do not have specific symptoms or complications of renal failure such as anemia or bone and mineral disorder.

- The majority of persons with stages 1 and 2 CKD are detected by routine or health care insurance–mandated screening and are visiting primary care or other physicians;

A Stepped Care Approach to Chronic Kidney Disease: Stages 1 and 2

- The following initial investigations are appropriate for assisting with risk assessment :

- 1. Estimation of urinary albumin or protein excretion by measurement of ACR or PCR on a random urine sample.
- Persons with a urine protein measurement equivalent to 0.5 g/day (UACR, 300 mg/g or 30 mg/mmol) or greater should be referred for investigation by a nephrologist.

A Stepped Care Approach to Chronic Kidney Disease: Stages 1 and 2

- 2. Further urinalysis is needed to detect hematuria.
- For painless but visible hematuria, serious urologic causes—such as bladder, renal cell, and, less often, prostatic cancers—must be confirmed or ruled out, particularly in persons older than age 50 years, smokers, and those with a family history of renal tract malignancy.
- . Painless microscopic hematuria (nonvisible hematuria) is much more likely to be caused by glomerular disease, but referral to a urologist may be necessary to confirm or rule out renal tract malignancy

A Stepped Care Approach to Chronic Kidney Disease: Stages 1 and 2

- 3. Abdominal ultrasonography to exclude structural abnormalities and determine the bipolar diameter of the kidneys is indicated if urinalysis results are abnormal, if there is a strong family history of CKD, or if there is significant hypertension.

- In general, persons with stages 1 and 2 CKD, who do not have a specific renal disease or significant proteinuria, require only annual monitoring of blood pressure, eGFR, and proteinuria.

Stage 3

- In stage 3 CKD, GFR is between 30 and 59 mL/min/1.73 m2.
- This is a significant stage because it represents the majority of persons in whom CKD is identified (stages 1 and 2 often remain undetected unless urinalysis is performed) and because many of the complications start to manifest once the GFR drops below 45 mL/min/1.73 m2.
- In addition, the rate of cardiovascular mortality increases substantially among persons with a GFR lower than

45 mL/min/1.73 m2.

- Monitoring of blood pressure, eGFR, and serum biochemistry profile, as well as complete blood cell count and evaluation for proteinuria, should be performed every 3 to 12 months, depending on risk profile and clinical circumstances.

Stage 4

- Persons with stage 4 CKD have a high cumulative risk of cardiovascular death and progression to ESKD.
- Almost 66% of such persons experience either a renal event or a CVE over 5 years after diagnosis.
- Achieving renoprotection remains an important goal to delay the onset of RRT for as long as possible, as does minimizing cardiovascular risk.
- Blood pressure, eGFR, and serum biochemistry profile, including level of parathyroid hormone as well as complete blood cell count, should be monitored every 3 to 6 months.

Stage 4….

- As the GFR declines to below 20 mL/min/1.73 m2, the focus should change to treating the complications of CKD and planning for RRT.
- Effective preparation for RRT requires input from multiple staff disciplines (medical, nursing, pharmacy, dietetics, psychology, and social work) and is best delivered in a multidisciplinary clinic.

- It is clear that late referral (less than 3 months before initiation of dialysis) for dialysis preparation is associated with significantly higher rates of mortality and lower quality of life.
-

Hepatitis B Vaccination

- persons with CKD in whom dialysis is anticipated should be screened for hepatitis B and C, as well as human immunodeficiency virus infection.
- Persons who are seronegative for hepatitis B surface antigen and hepatitis B surface antibody should be immunized and their antibody levels measured after vaccination.
- Because seroconversion rates decrease with GFR, immunization should ideally occur in stage 3 in persons with a high risk of progression; however, in view of the large number of persons and lack of precision in predicting outcomes, it is usually delayed until stage 4.
- Seroconversion rates are low once dialysis has commenced, particularly in older persons.

Stage 5

- Once GFR declines to below 15 mL/min/1.73 m2, priorities include maintaining optimal health and function as well as achieving a planned and uncomplicated initiation of RRT.

Stage 5….

- We therefore recommend that the initiation of RRT should be individualized but in general should occur when the GFR falls below 10 mL/min/1.73 m2 but before significant uremic symptoms or malnutrition occurs.
- In order to facilitate this timing, the frequency of monitoring of GFR, serum biochemistry, and hemoglobin, together with clinical assessment, should increase to every 1 to 3 months.
- Persons who decline RRT should continue to be treated for complications of CKD to optimize their quality of life and, if necessary, be referred to a palliative care service to allow adequate planning of their care once they develop symptomatic uremia.

Recommended Frequency of Monitoring by Stage of Chronic Kidney Disease

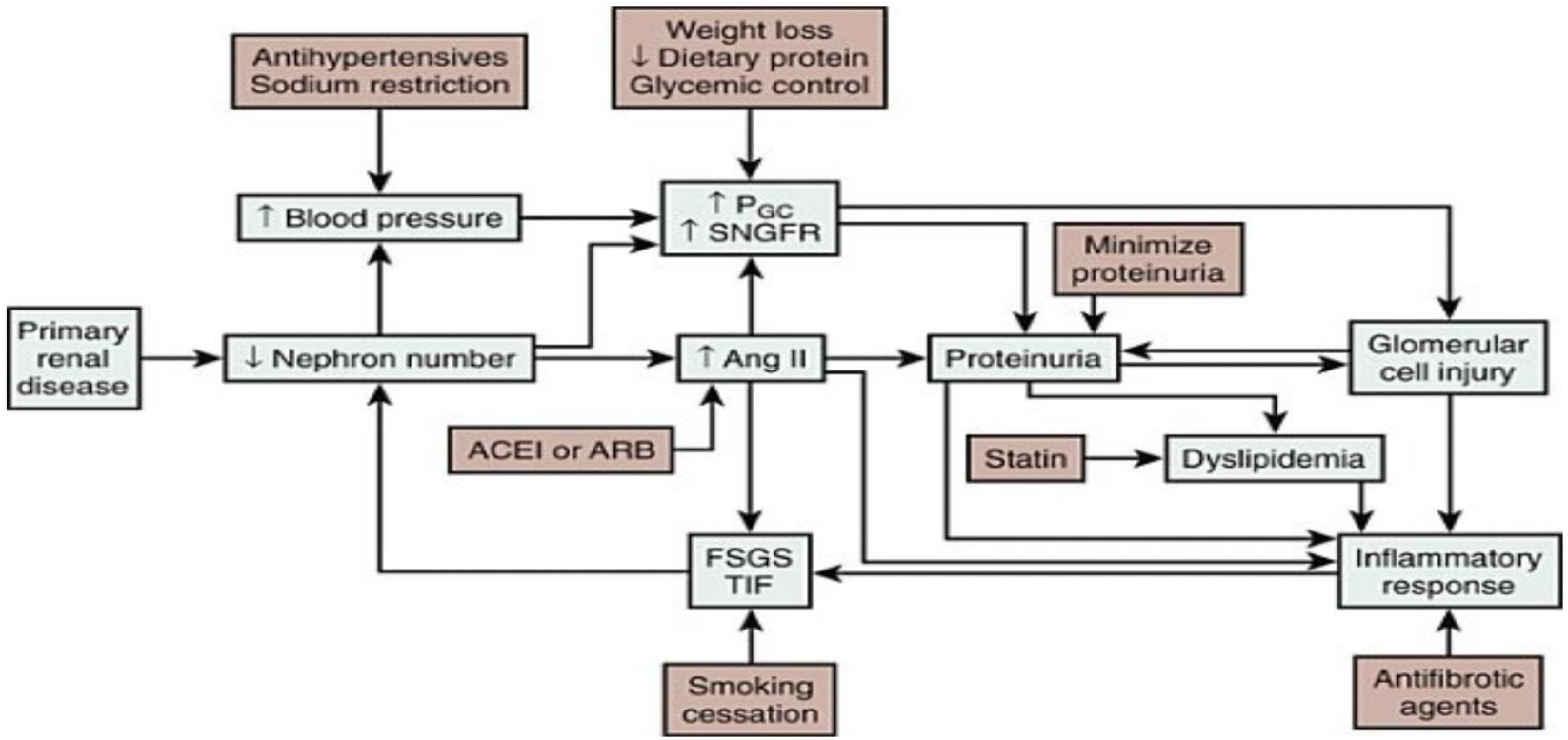
Variable	Stage 1 and 2	Stage 3	Stage 4	Stage 5
GFR and electrolytes	Every 12 months	Every 3–12 months	Every 3–6 months	Every 1–3 months
Proteinuria with ACR or PCR testing	Every 12 months	Every 3–12 months	Every 3–6 months	Every 3–6 months
Blood pressure	Each visit	Each visit	Each visit	Each visit
Calcium and phosphate levels	Every 12 months	Every 12 months	Every 3–6 months	Every 3 months
Parathyroid hormone level	—	Every 12 months	Every 3–6 months	Every 3–6 months[a]
Hemoglobin	Every 12 months	Every 12 months	Every 3–6 months	Every 1–3 months[a]

[a]Monitoring of parathyroid hormone and anemia should depend on the previous results and specific treatment, if any, for these conditions. Stable values with no specific treatment require

Interventions for Slowing Progression of Chronic Kidney Disease

- Lifestyle Interventions
- Smoking Cessation
- Weight Loss
- Dietary Sodium Restriction
- Dietary Protein Restriction
- Glycemic Control in Persons With Diabetes
- Antihypertensive Therapy

A common pathway of mechanisms that result in a vicious circle of nephron loss in chronic kidney disease (CKD).



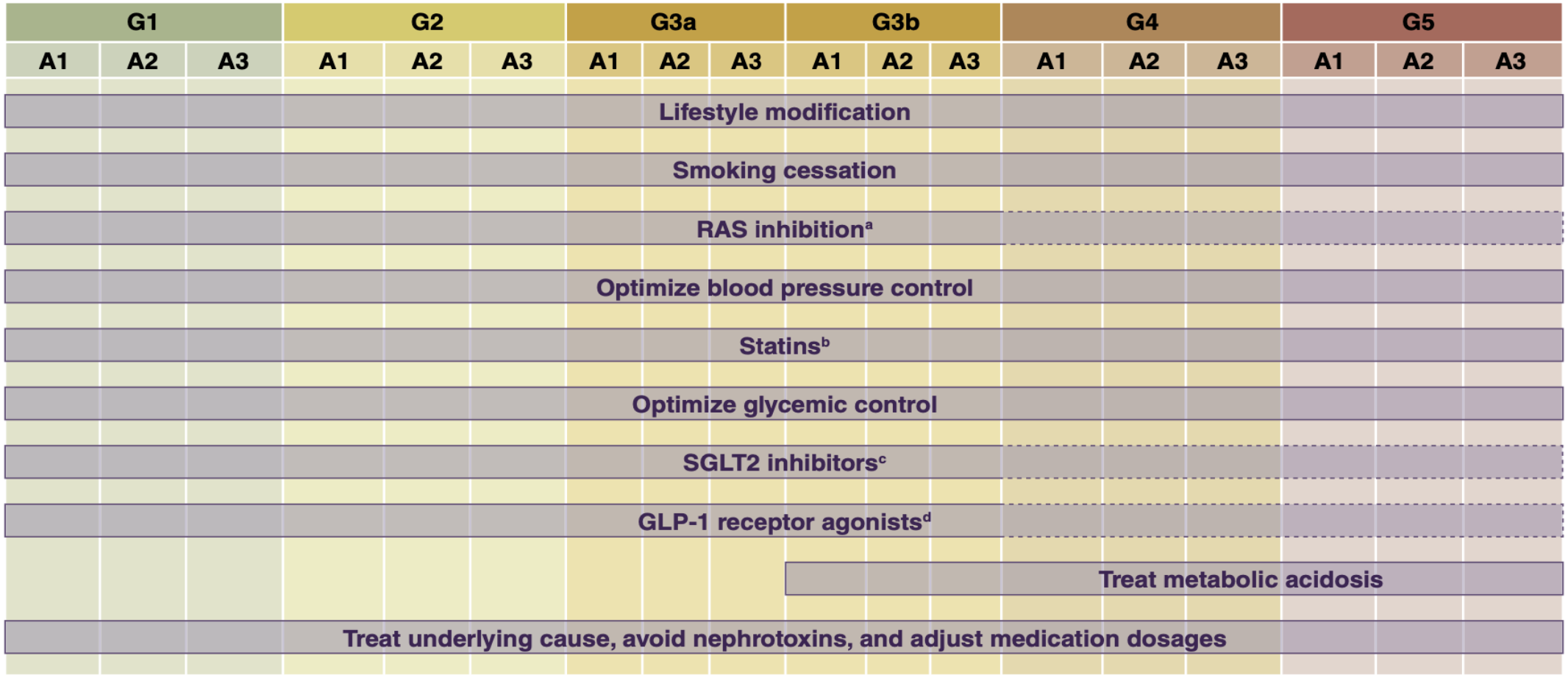


Figure 3 | Interventions to slow chronic kidney disease (CKD) progression and/or reduce cardiovascular risk. [a]Unclear if and when to

Thanks for attention