

SYSTEMIC DISEASES AFFECTING KIDNEYS

DR ANJUM

LEARNING OBJECTIVES

- **How different systemic diseases can affect renal function**
 - Diabetes..... Diabetic nephropathy
 - Cardiovascular disorders..... Hypertension , Chronic heart failure
 - Immunological disorders..... SLE , glomerulonephritis
 - Hematological disorders..... Sickle cell anemia, HUS

DIABETES AND THE KIDNEY

- **Diabetes**is a serious, life-long condition where **glucose levels in the blood are too high.**
- If untreated, it can lead to serious health complications including damage to the **eyes, nerves, heart and kidney.**
- One of the complications of diabetes is kidney disease, also called **DIABETIC NEPHROPATHY**



DIABETIC NEPHROPATHY

- Affect up to a **third of people** who have diabetes.
- It develops **over many years** and can affect anyone with diabetes.
- This is caused by damage to the small blood vessels in the kidneys.
- A kidney affected by diabetes can look normal under an ultrasound but under the microscope the kidney can show **damage to the filtering units.....**
- causes protein to leak into the urine, which is an important marker for **diabetic kidney disease...EARLIEST SIGN**

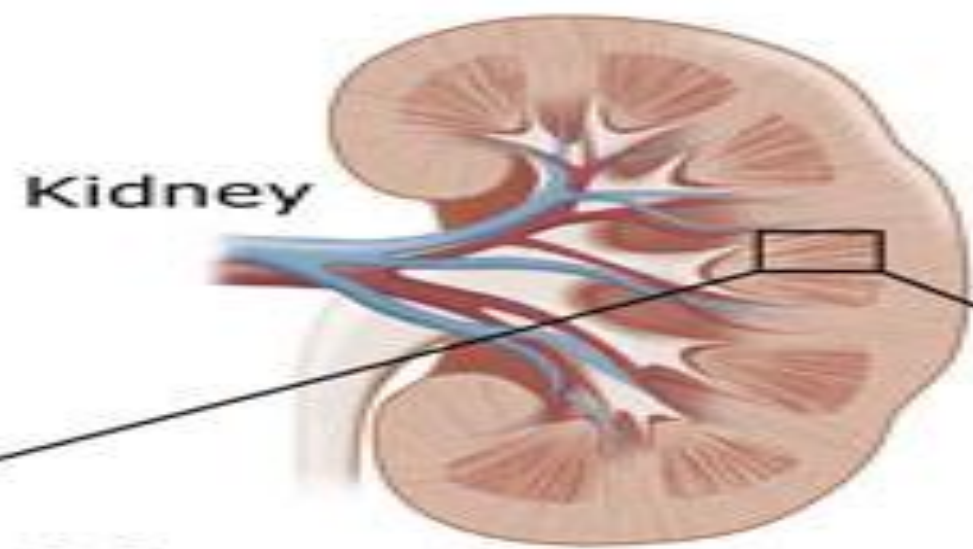
DIABETIC NEPHROPATHY

- About **25% of people who have type 2 diabetes**, will have small amounts of protein leak from diabetic nephropathy after 10 years.
- This over time contributes to **gradual reduction in the function** of the kidneys.
- However, only a few people will end up needing **dialysis**.
- **Renal failure requiring dialysis is the end result of chronic kidney disease.**

CHARACTERISTICS OF DIABETIC NEPHROPATHY

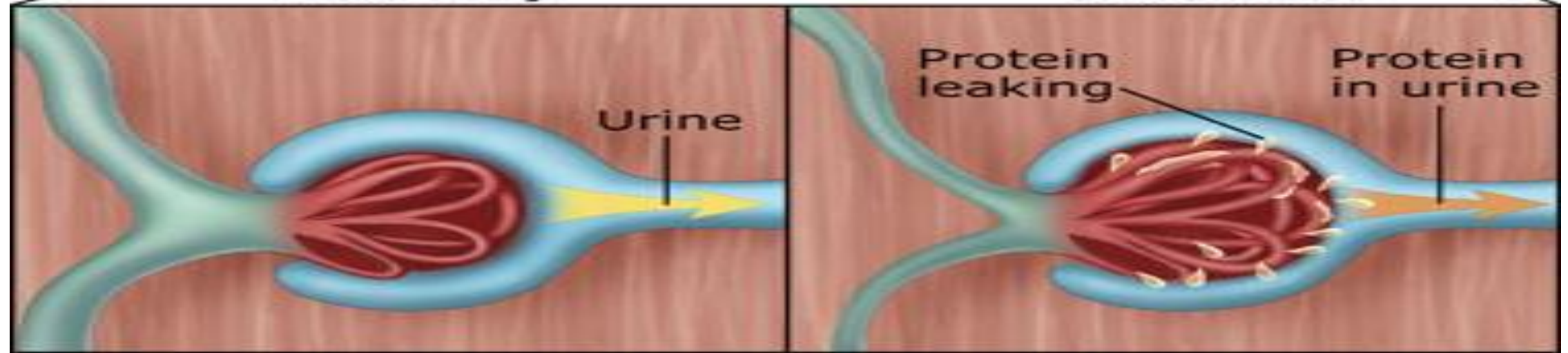
- Micro albuminuria..... **20 – 300 mg**
- **> 300 mg** Diabetic Nephropathy
- GFR gradually decreases
- Blood pressure increases

Diabetes Affects the Kidney



Healthy

Diabetes



STRUCTURAL CHANGES

- **Earliest consistent change** thickening of glomerular basement membrane, which is apparent within 1.5–2 years of DM 1 diagnosis.
- It is paralleled by capillary and tubular basement membrane thickening .
- **Other glomerular changes**.... include loss of endothelial fenestrations, mesangial matrix expansion, and loss of podocytes with effacement of foot processes .
- Development of Kimmelstiel–Wilson nodules and micro aneurysms

STRUCTURAL CHANGES

- **Sub endothelial deposits of plasma proteins**, which form periodic acid–Schiff-positive (PAS) and electron-dense deposits.....
- Accumulate in small arterial branches, arterioles, and glomerular capillaries as well as micro aneurysms.
- Result in luminal compromise (*e.g.*, **hyaline arteriosclerosis**).
- Similar **subepithelial deposits** are seen in Bowman's capsule (**capsular drop lesion**) and proximal renal tubules.

STRUCTURAL CHANGES

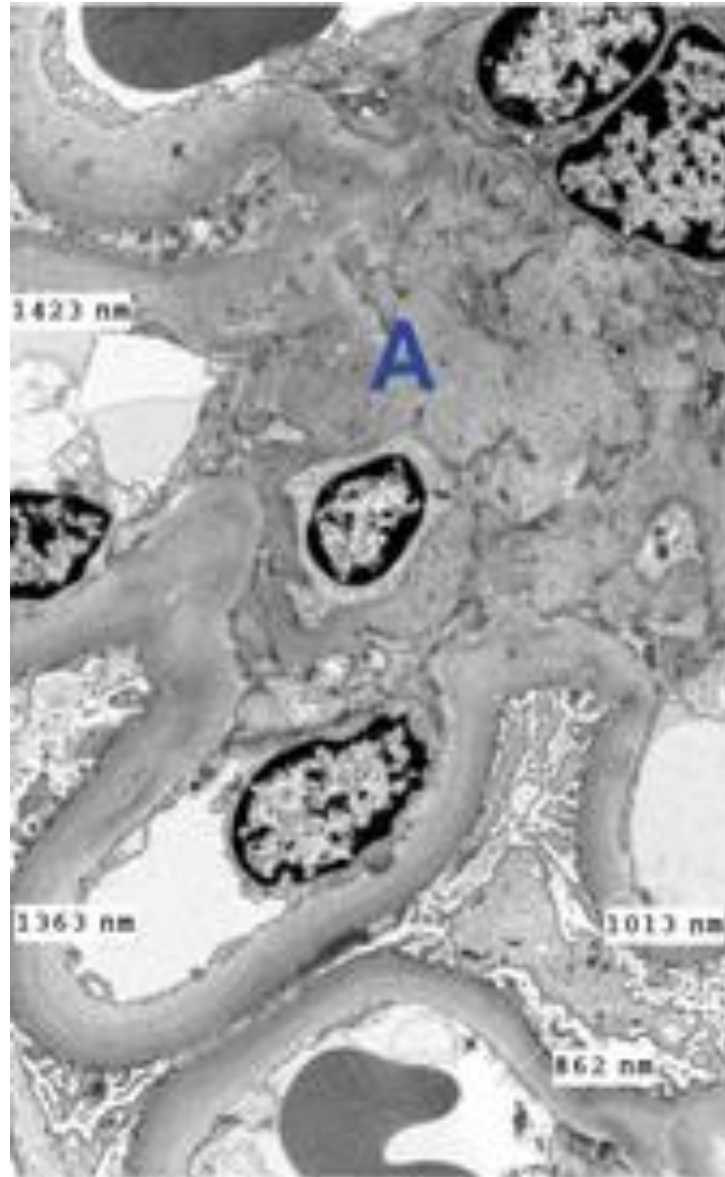
- **In later stages of diabetes....** segmental and global sclerosis.
- **In patients with DM1.....** GFR, albuminuria, and hypertension are strongly correlated with mesangial expansion and somewhat less strongly associated with glomerular basement membrane width

Electron microscope images of structural changes in diabetic kidney disease.

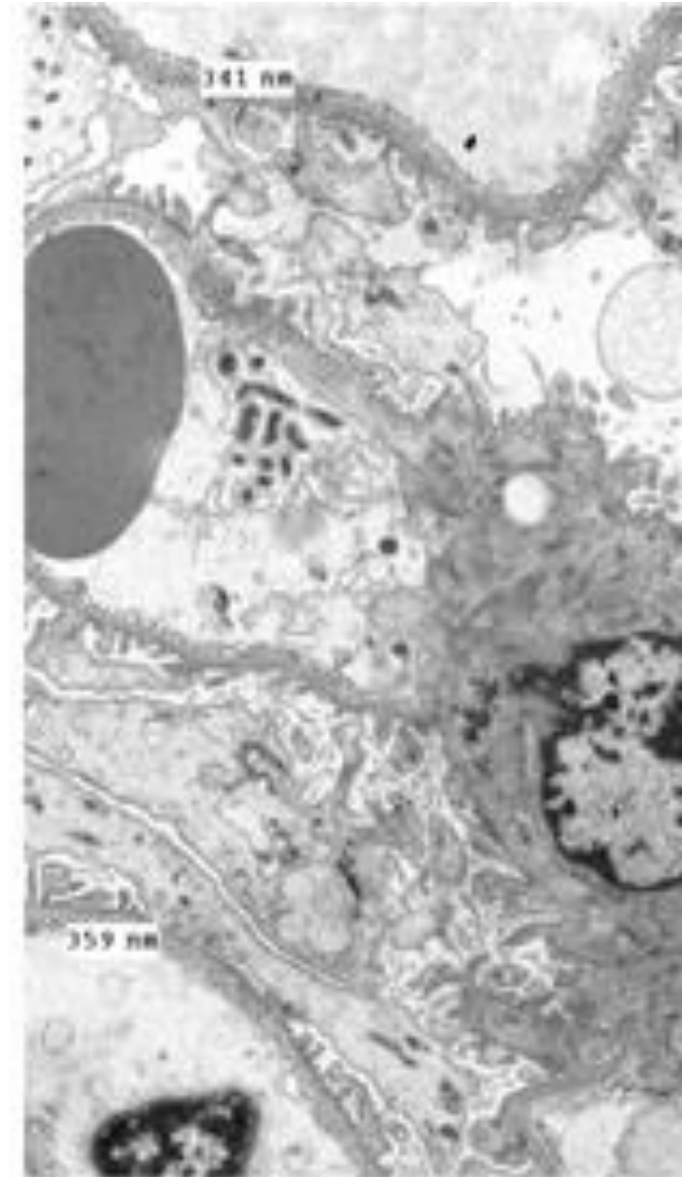
A... indicates marked expansion of the mesangium.

B... indicates marked diffuse thickening of capillary basement membranes (to three times the normal thickness in this case).

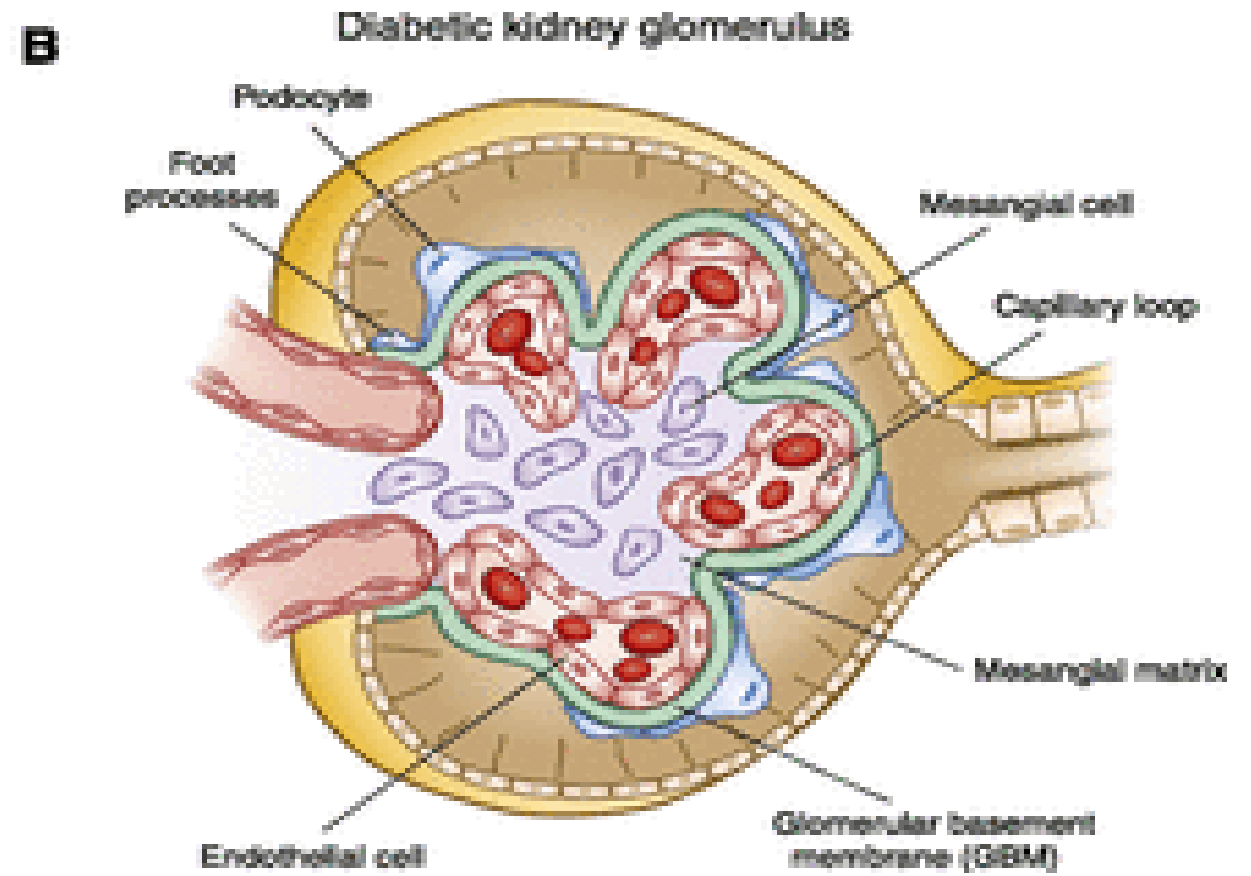
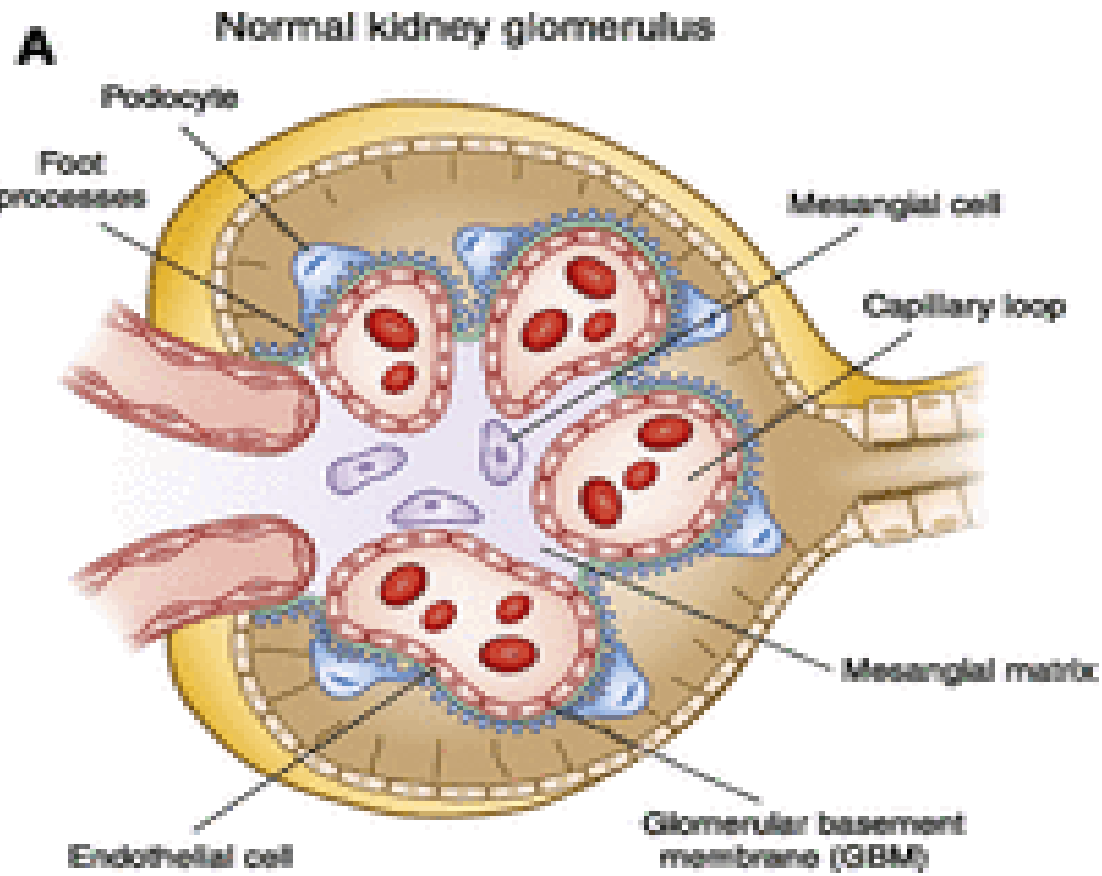
C... indicates segmental effacement of the visceral epithelial foot processes.



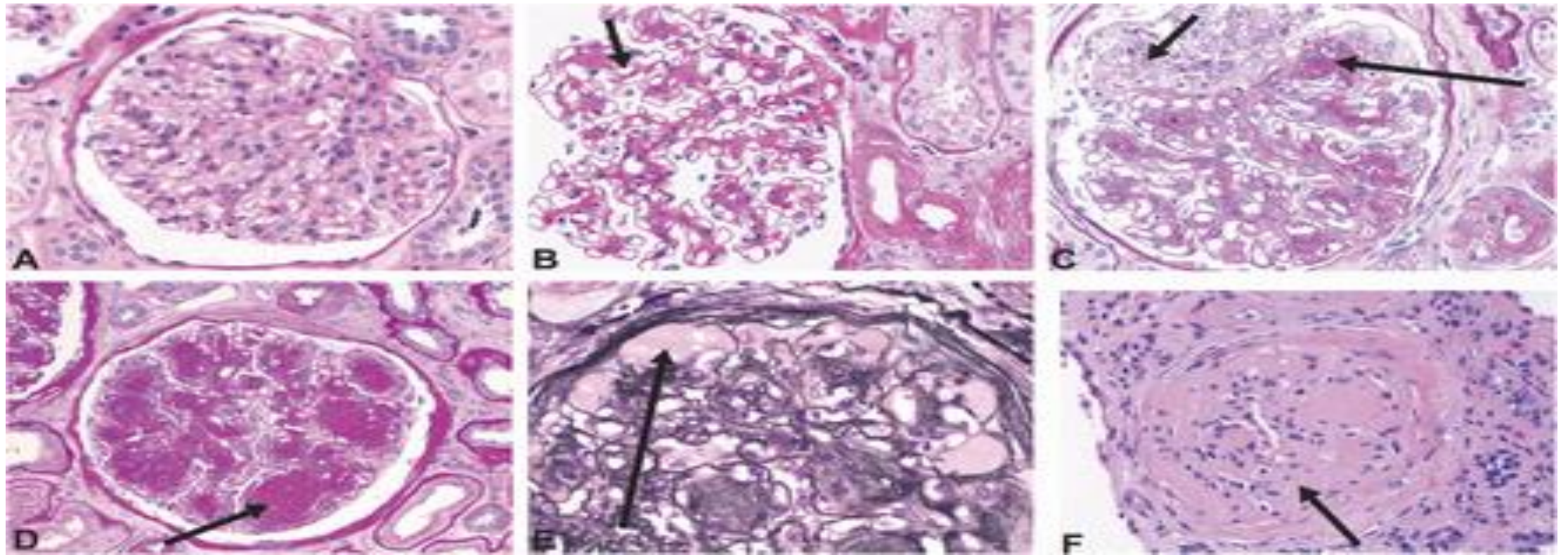
Diabetic Glomerulopathy



Normal Glomerulus



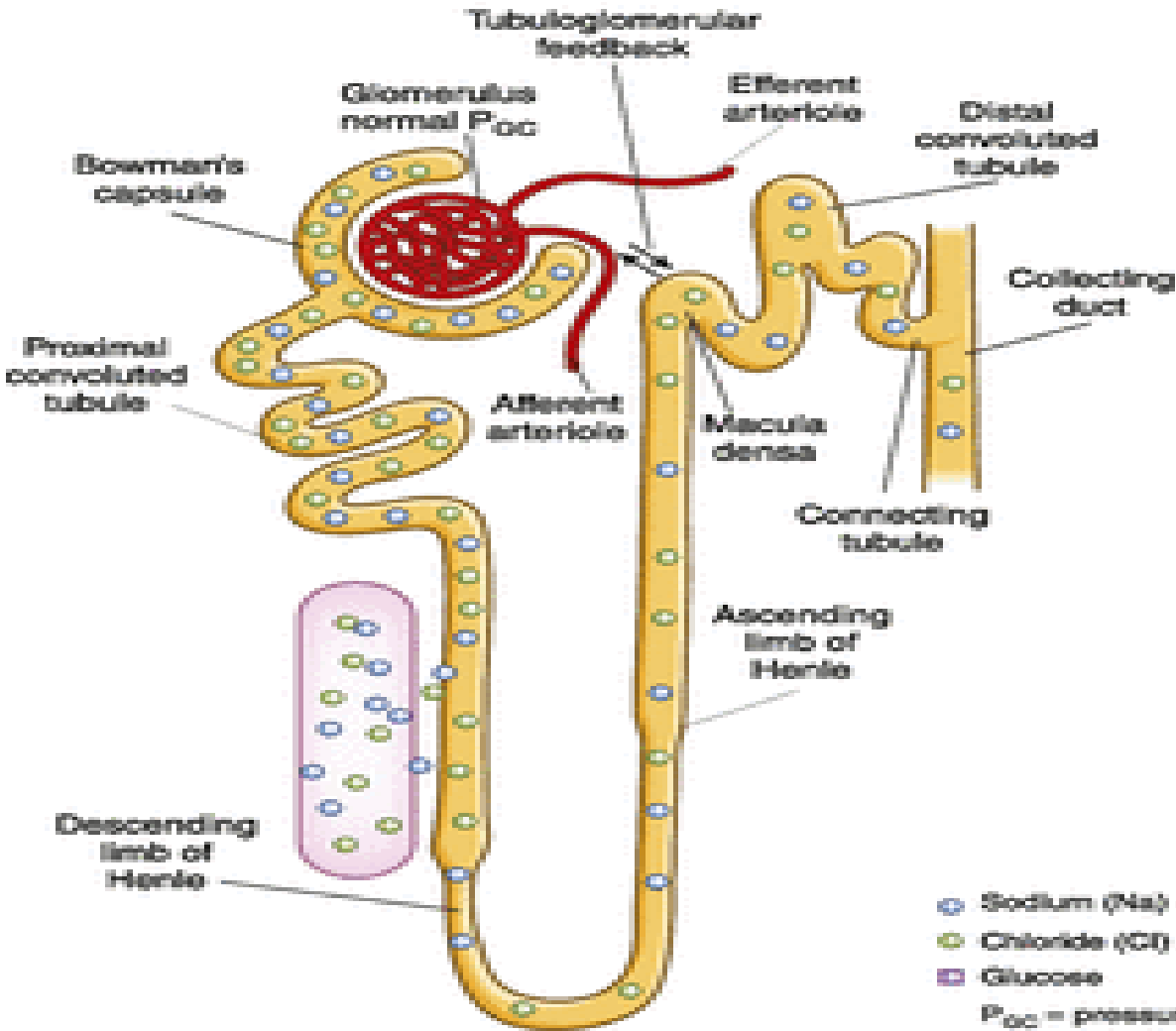
- **Normal kidney morphology and structural changes in diabetes mellitus.** Diabetic kidney disease induces structural changes, including thickening of the glomerular basement membrane, fusion of foot processes, loss of podocytes with denuding of the glomerular basement membrane, and mesangial matrix expansion.



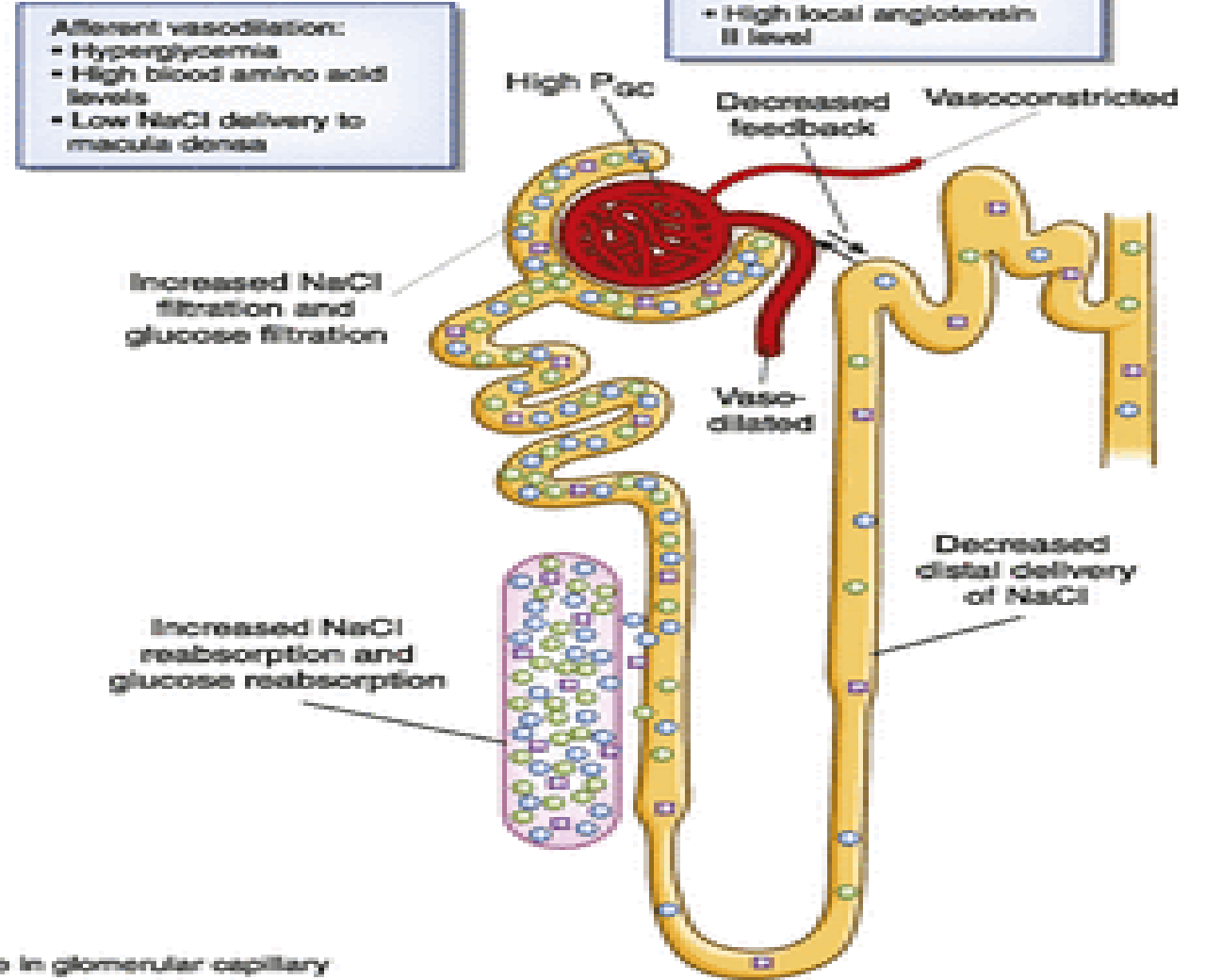
- **Diabetic glomerulopathy.** Changes in glomerular histology in diabetic glomerulopathy **(A) Normal glomerulus.**
- **(B)** Diffuse mesangial expansion with mesangial cell proliferation.
- **(C)** Prominent mesangial expansion with early nodularity and mesangiolytic changes.
- **(D)** Accumulation of mesangial matrix forming Kimmelstiel–Wilson nodules.
- **(E)** Dilated capillaries forming microaneurysms, with subintimal hyaline (plasmatic insudation).
- **(F)** Obsolescent glomerulus. A–D and F were stained with period acid–Schiff stain, and E was stained with Jones stain.

Normal and diabetic nephron with altered renal hemodynamics.

A Normal



B Diabetes



STEPS YOU CAN TAKE TO PREVENT DIABETIC NEPHROPATHY.

- Control blood glucose.
- Control blood pressure.
- Control blood cholesterol
- Quit smoke
- Avoid pain medications that can hurt your kidneys (such as **non-steroidal anti-inflammatory drugs**)
- Test urine for kidney function and urine micro albumin / creatinine ratios yearly..... **Normal kidney function** (Urine microalbumin/Cr ratio: less than 30 mg/g Cr)
- **Early Nephropathy** (Urine microalbumin/Cr ratio: 30-300 mg/g Cr)
- **Late Nephropathy** (Urine microalbumin/Cr ratio: more than 300 mg/g Cr)

CARDIOVASCULAR DISORDERS..... HTN, CHF

- **Cardiovascular disease (CVD)..... the leading cause of death.**
- **CVD and kidney disease....** are closely interrelated and **disease of one organ cause dysfunction of the other, ultimately leading to the failure of both organs.**
- **Patients with end-stage renal disease (ESRD)....** are at much higher risk of mortality due to CVD.
- **Cardiovascular diseases** are the **main cause of morbidity and mortality in CKD patients**

CARDIOVASCULAR DISORDERS..... HTN, CHF

- Kidney disease and heart disease share two of the same main causes [diabetes](#) , [high blood pressure](#).

☐ High Blood Pressure

- **Blood pressure....** is the force of your blood pushing against the walls of your blood vessels.
- **With high blood pressure**, your heart works harder to pump blood, which can strain your heart.
- **High blood pressure can damage your blood vessels.**
- If high blood pressure damages the small blood vessels in your kidneys, your kidneys will not filter your blood as efficiently as they should.

CARDIOVASCULAR DISORDERS..... HTN, CHF

- **High blood pressure** is not only a cause of kidney disease; kidney disease is also a cause of high blood pressure.
- When you have **damaged kidneys**, they may be unable to filter extra water and salt from your body.
- The high blood pressure that results can then make kidney disease worse.
- Worsening kidney disease can raise blood pressure again.....**A dangerous cycle results as each disease makes the other worse.**

HOW THEY WORK TOGETHER... HEART AND KIDNEYS

- ❑ **HEART**...send a continuous supply of oxygenated blood around the body..
- ❑ **THE KIDNEY**.... filters the blood, extracting waste in the form of urine and also helps regulate the [water](#) and [salt](#) levels to control blood pressure.
- ❑ **HEART FAILURE**.... is a significant risk factor for kidney disease.
 - When the heart is no longer pumping efficientlyit becomes congested with blood, causing pressure to build up in the main vein connected to the kidneys and leading to congestion of blood in the kidneys, too.
 - The kidneys also suffer from the **reduced supply of oxygenated blood**.

HOW THEY WORK TOGETHER... HEART AND KIDNEYS

- **When the kidneys become impaired**, the hormone system, which regulates [blood pressure](#), goes into **overdrive** in an attempt to increase blood supply to the kidneys.
- The heart then has to pump against higher pressure in the arteries, and eventually suffers from the increase in workload.
- It's routine for doctors to check your kidney function if they believe you may have heart disease.
- A simple blood test can check if the **level of creatinine**, a waste product usually secreted by the kidneys, is raised, suggesting impairment

HOW YOU CAN REDUCE YOUR RISK

- Be a non-smoker.
- Eat a low-salt diet.
- Weigh yourself regularly at home to warn of fluid overload or dehydration.
- Get to know your drugs – ask your doctor, specialist nurse or pharmacist to explain.
- Exercise regularly – swimming, [cycling](#), dancing or power [walking](#) all help to lower blood pressure and improve heart and muscle function.

IMMUNOLOGICAL DISORDERS.....SLE, GN

- **The kidney**, like most other organs, is a target of autoimmunity.
- As a consequence of **systemic autoimmunity**, such as [systemic lupus erythematosus \(SLE\)](#) which causes [nephritis](#) in **35%–55%** of the patients due to an abnormal inflammation in the [glomerulus](#).
- In other instances, kidney disorders are caused by **deposits of nonspecific autoantibodies** in the glomerulus as in cases of and **IgA glomerulopathies**.

IMMUNOLOGICAL DISORDERS.....SLE, GN

- **The kidney** is also the target of autoantibodies that attack specific cell types in the glomerulus.
- These include membranous nephropathy and glomerular basement membrane nephropathy.
- **Lupus nephritis.....** is a frequent complication in people who have **systemic lupus erythematosus** — more commonly known as **lupus**.

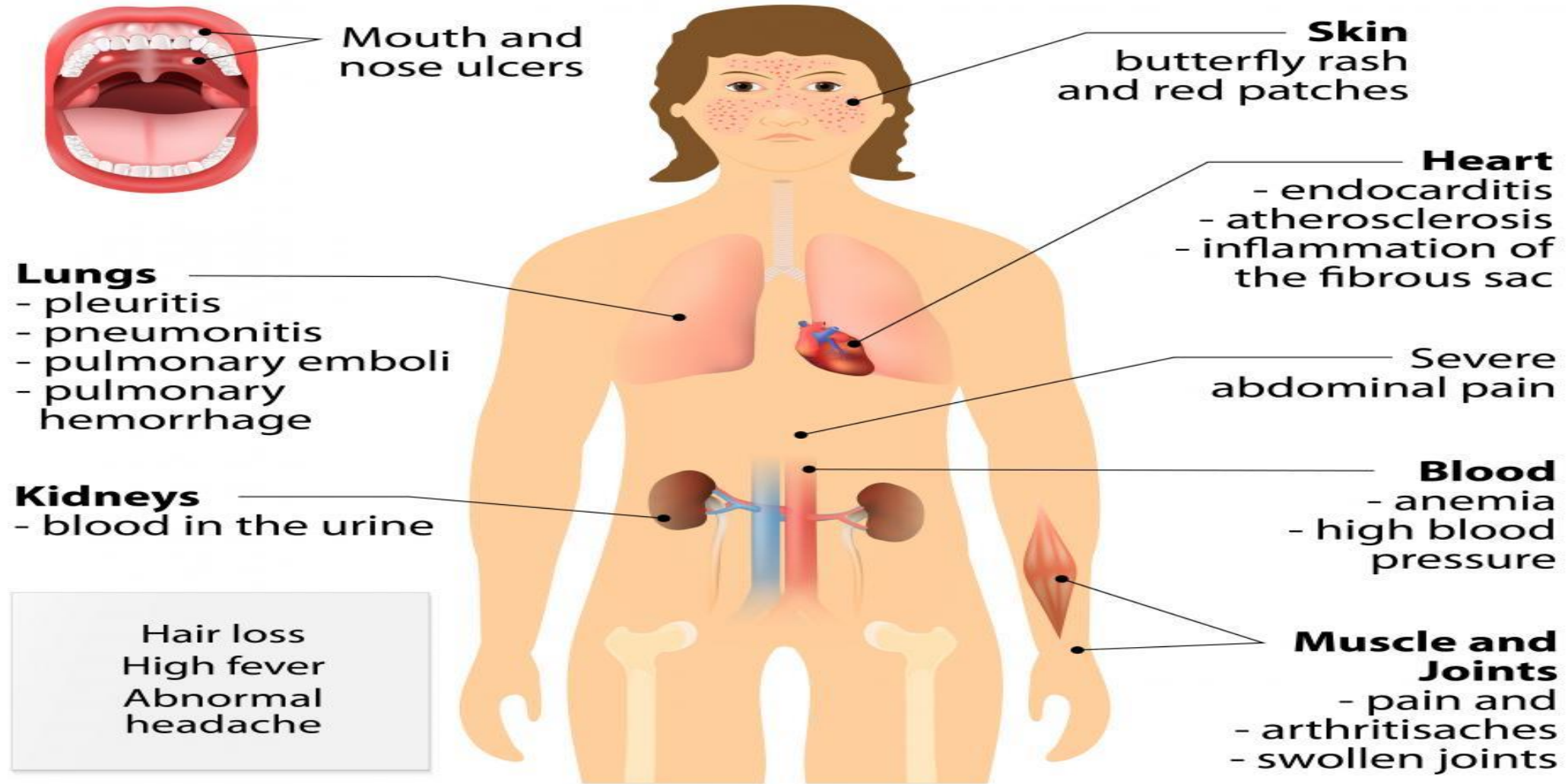
SLE (SYSTEMIC LUPUS ERYTHEMATOSIS)

- **Lupus.....** is an autoimmune disease.
- It causes your immune system to produce proteins called **autoantibodies** that attack your own tissues and organs, including the kidneys.
- **Lupus nephritis**occurs when **lupus autoantibodies** affect structures in your kidneys that filter out waste.
- This causes kidney **inflammation** and may lead to **blood in the urine, protein in the urine, high blood pressure, impaired kidney function or even kidney failure.**

RISK FACTORS

- **Sex.** Although women are more likely to get lupus , men get lupus nephritis more than women.
- **Race or ethnicity.** Blacks, Hispanics/Latinos and Asian Americans are more likely to have lupus nephritis than whites.

Systemic lupus erythematosus

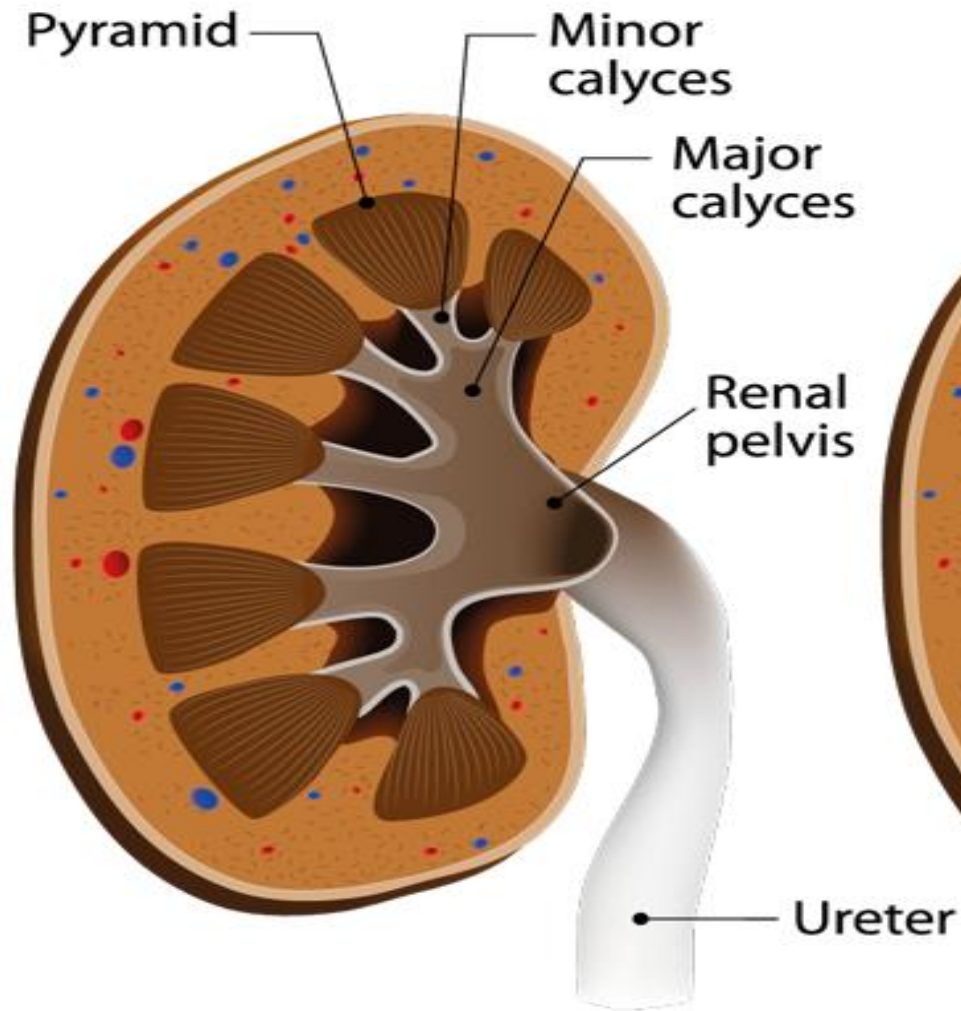


AUTOIMMUNE GLOMERULONEPHRITIS

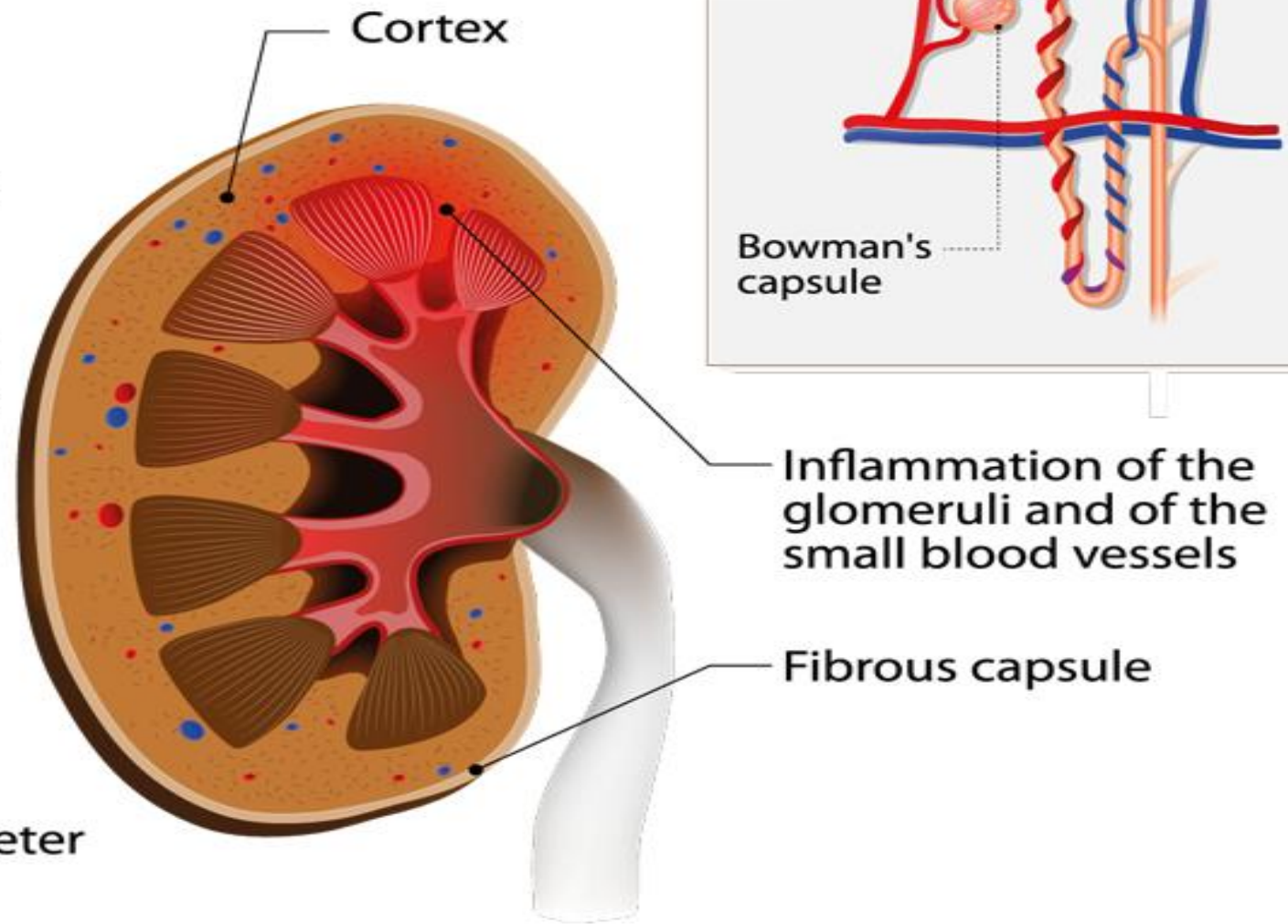
- **Autoimmune glomerulonephritis**, the body's own immune system attacks the blood vessels of the glomeruli, the part of the kidney that filters the blood.
- This condition is **life-threatening**, but current treatments are limited and carry a high risk of serious side-effects.
- **Glomerulonephritis**is a form of kidney disease that causes damage to the glomeruli, hindering their ability to carry out their essential functions.

AUTOIMMUNE GLOMERULONEPHRITIS

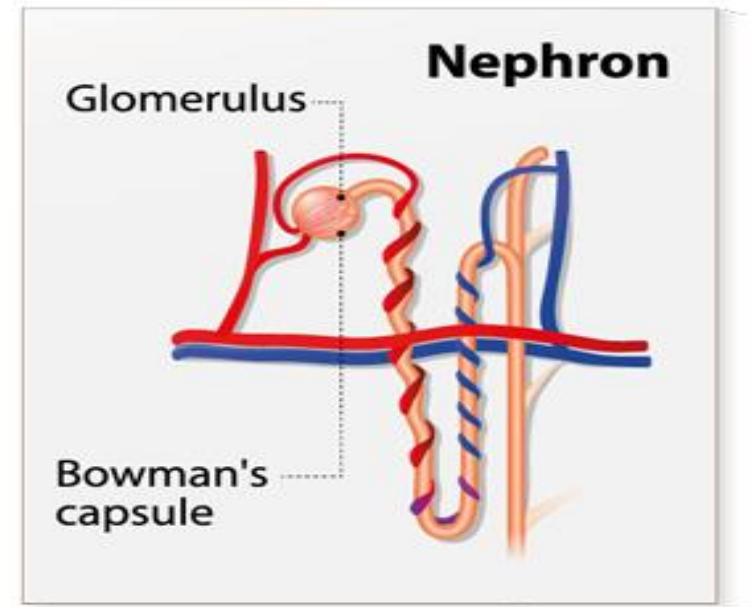
- This damage takes the **form of vasculitis**, which causes changes in the walls of blood vessels, potentially hindering blood flow.
- **Then kidneys cannot effectively remove waste products (such as urea) and excess fluids from the blood.**
- While some types of glomerulonephritis do not necessarily cause serious symptoms, some forms of the condition can be devastating and even life-threatening, damaging the kidney to the point where dialysis or even a transplant are necessary.



Normal kidney



Glomerulonephritis



HEMATOLOGICAL DISORDERS...SICKLE CELL ANEMIA, HUS

- Renal diseases are associated with a variety of haemopoietic changes.
- **Anemia...** parallels the degree of renal impairment and its most **important** cause is failure of renal erythropoietin secretion.
- **Other factors** depressed red cell production and reduced red cell survival.

ANEMIA AND KIDNEY DISEASE

- **ANEMIA**.... when your red blood cells are in short supply.
- Red blood cells (RBCs).... carry oxygen from your lungs to all parts of your body, giving you the energy you need for your daily activities.
- **Anemia can cause** pale Look, Feel tired , little energy for your daily activities
- Have a poor appetite, Have trouble sleeping, Have trouble thinking clearly
- Feel dizzy or have headaches, Have a rapid heartbeat
- Feel short of breath

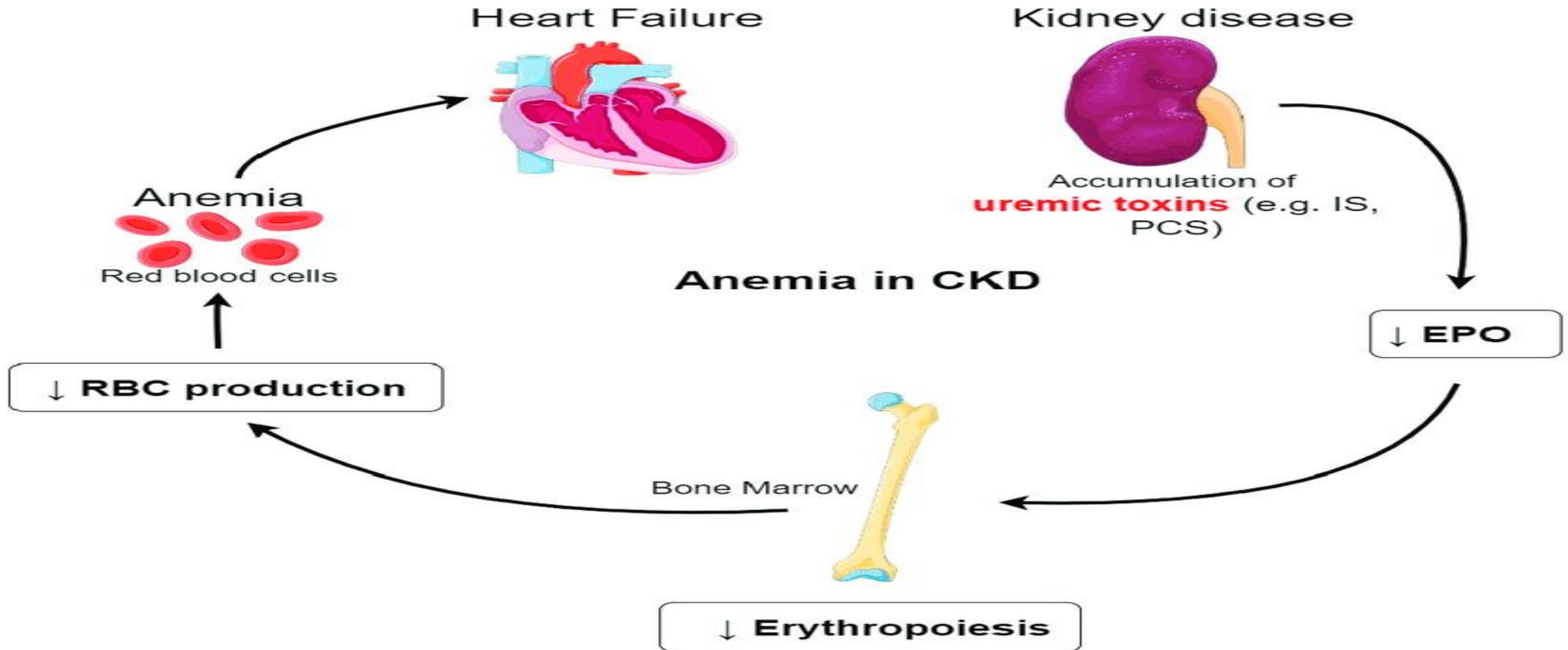
WHY DO PEOPLE WITH KIDNEY DISEASE GET ANEMIA?

- Kidneys make an important hormone called **erythropoietin (EPO)**.
- Hormones are **chemical messengers** that travel to tissues and organs to help you stay healthy.
- **EPO**tells your body to make red blood cells.
- **When you have kidney disease, your kidneys cannot make enough EPO. Low EPO levels cause your red blood cell count to drop and anemia to develop.**

ANAEMIA AND RENAL FAILURE

- **Linear relationship between anemia and renal impairment** at blood urea nitrogen levels of less than 150 mg/100 m.
- A similar relationship exists between the **hematocrit and creatinine clearance**.
- In renal failure the degree of anemia may be exaggerated or minimised by fluid retention and dehydration causing fluxes in plasma volume.
- Most people with kidney disease will develop anemia. Anemia can happen early in the course of kidney disease and grow worse as kidneys fail and can no longer make EPO.

Anemia in CKD. Accumulation of uremic toxins induces a decrease of EPO production in the kidney. The decreased EPO synthesis compromises erythropoiesis in the bone marrow. This in turn results in a decrease of RBCs production leading to CKD-associated anemia.



Key Points: Anemia of Chronic Kidney Disease

Causes and Effects

- **↓ EPO production**
- **↑ hepcidin**
 - Due to ↓ renal clearance and ↑ IL-6
 - Leads to:
 - iron sequestration in macrophages
 - iron-restricted erythropoiesis, resistance to EPO
- **True iron deficiency**
 - Due to increased blood loss and hepcidin-mediated decrease in intestinal iron absorption)
- **Suppression of erythropoiesis by inflammatory cytokines** (important in acute inflammation)
- **Shortened erythrocyte lifespan**
 - Due to inflammation and uremia

Treatments and Modulators

- **Exogenous EPO/Erythropoietin Stimulating Agents (ESAs)**
 - Causes pulsatile erythropoiesis and transient high demand for iron
 - High doses ↓ hepcidin but at the cost of side effects
- **Iron**
 - Overcomes hepcidin-induced blockade of iron release from macrophages
 - Decreases resistance to EPO
- **HIF-PHD Inhibitors**
 - Increases uptake of iron
 - Increases endogenous EPO release, leads to:
 - Inhibition of downstream effects of hepcidin

HUS.....HEMOLYTIC UREMIC SYNDROME

- **Hemolytic uremic syndrome or HUS....** is a rare condition that mainly affects children under the age of 10. It often causes:
 - Damage to the lining of blood vessel walls
 - Destruction of red blood cells
 - Kidney failure
- **Hemolytic uremic syndrome (HUS)....** is a condition that can occur when the small blood vessels in your kidneys become damaged and inflamed.
- This damage can cause **clots to form in the vessels**. The clots clog the filtering system in the kidneys and lead to kidney failure, which could be life-threatening.

WHAT CAUSES HUS?

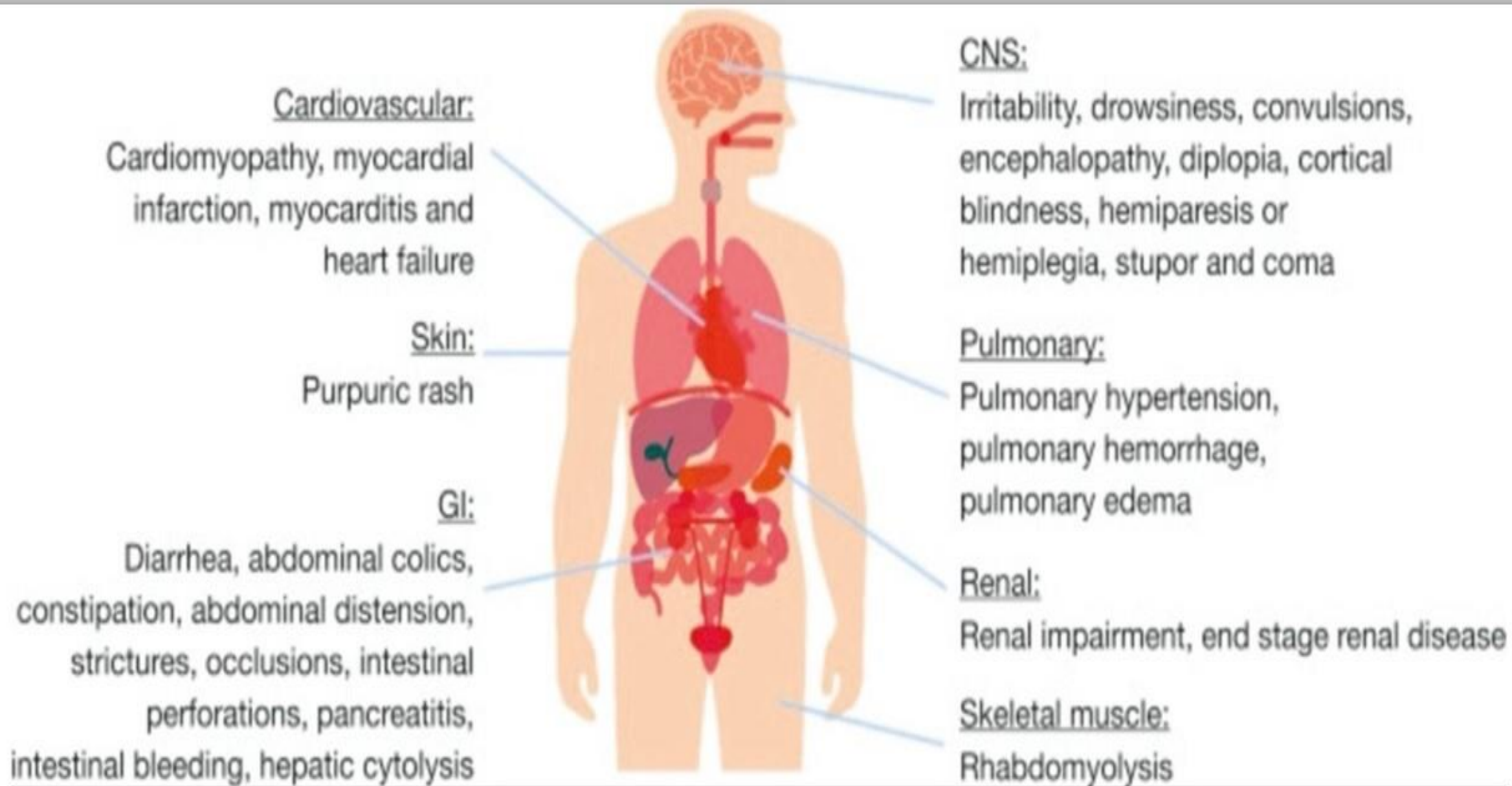
- **Most cases of HUS occur after an infection in the digestive tract caused by the *E. coli* bacterium**
- **Diarrhea and upper respiratory infections** are the most common factors leading to HUS.
- **This type of *E. coli* can be found in undercooked meat and is one of the causes of restaurant-related food poisoning outbreaks.**
- **HUS is less common in adults**, but may occur more often in **pregnant women**, women who have been taking **birth control pills**, and women who have recently had a **baby or have birth-related problems**.

HAEMOLYTIC URAEMIC SYNDROME (HUS)

- **HUS**associated with **acute severe damage to small blood vessels**.
- **In HUS....** glomerular capillaries are the major site of vascular injury and renal failure and hemolytic anemia are the presenting features.
- The **pathogenesis** of this diseases is ill understood but an **abnormal plasma factor which causes aggregation of platelets**.
- **Focal intravascular coagulation**contributes to vascular injury with deposition of fibrin in the microcirculation.

HOW DOES HUS AFFECT THE KIDNEYS?

- **In HUS.....** the tiny filter units in the kidneys known as glomeruli become clogged with platelets and damaged red blood cells.
- This leads to problems with the kidney's ability to filter and eliminate waste products.
- **HUS causes mild kidney failure.....**fluid volume management may be all that is necessary for adequate treatment.
- **When it causes severe kidney failure** (when kidney function is less than 10 percent of normal)..... **dialysis** may be needed to do the work of the kidneys.



Hemolytic Uremic Syndrome (HUS)

Most common cause of acute renal failure in children



***E. coli* H7:0157**

Other causes
Complement-mediated
Strep. pneumoniae
HIV
Drug toxicity

Shiga-like
toxin
(Verotoxin)

@medical_treat

HUS Triad



Microangiopathic
hemolytic anemia
(Schistocytes)



Thrombocytopenia



Renal
insufficiency

Epidemiology

- Primarily affects children under the age of five years

Clinical

- Prodrome of abdominal pain, vomiting, bloody diarrhea
- Hemolytic anemia, thrombocytopenia, acute kidney injury (Triad)
- Seizures, lethargy

Treatment

- Mainly supportive
- No antibiotics
- Plasma infusion and plasma exchange
- Eculizumab (in severe CNS involvement)

THANK
You!