IN THE NAME OF GOD

RENAL PATHOLOGY

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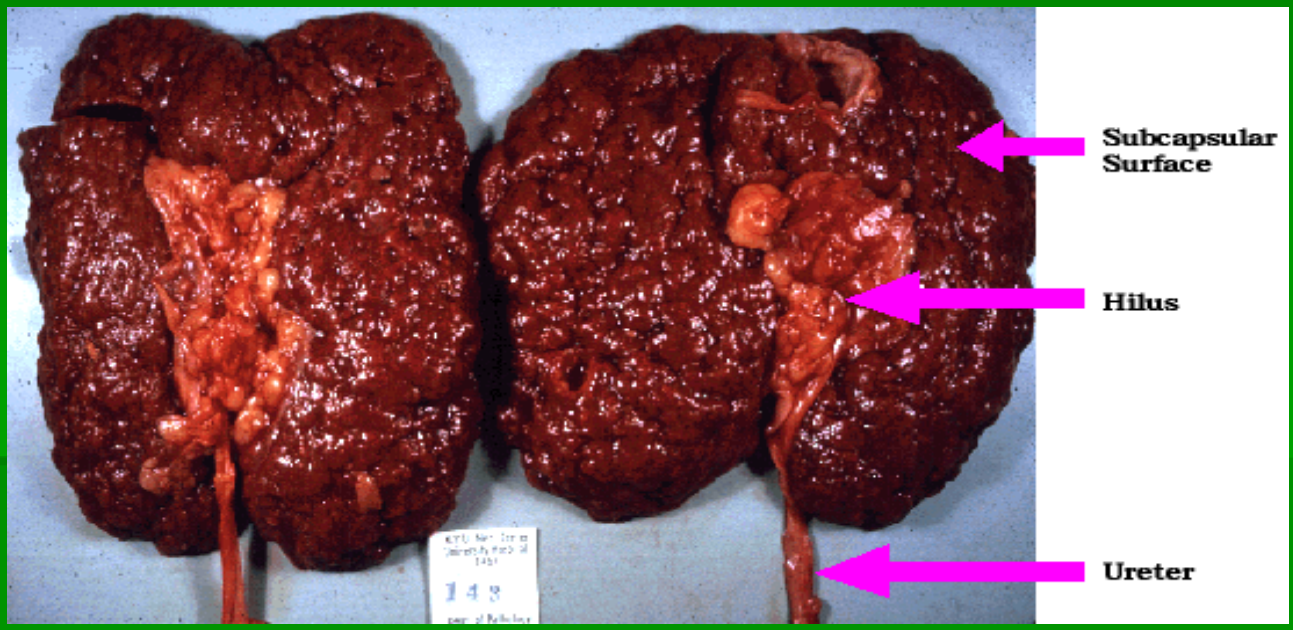
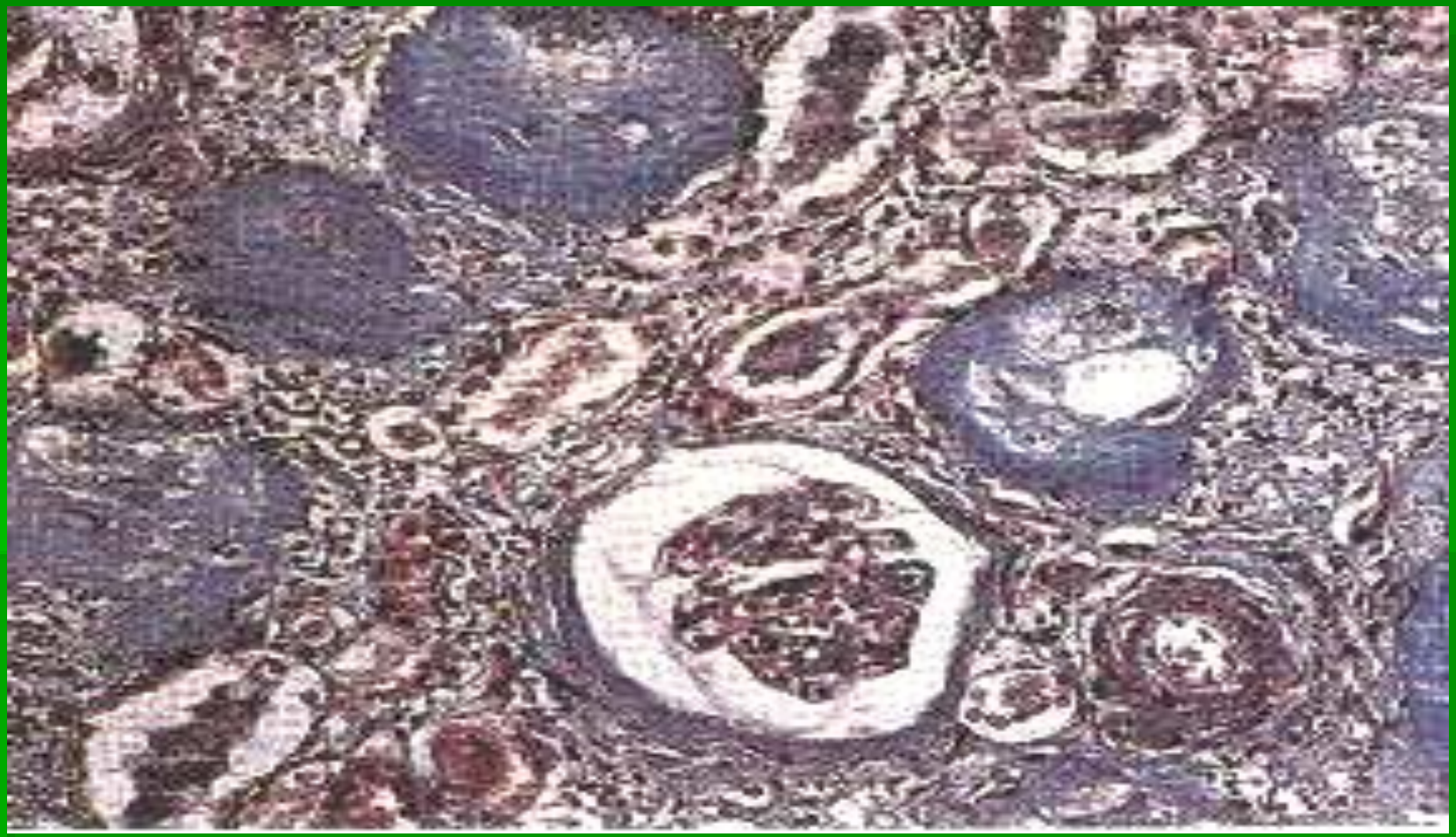
CHRONIC GLOMERULONEPHRITIS

- Can result from just about ANY of the previously described acute ones
  - THIN CORTEX
  - HYALINIZED (fibrotic) GLOMERULI
  - OFTEN SEEN IN DIALYSIS PATIENTS

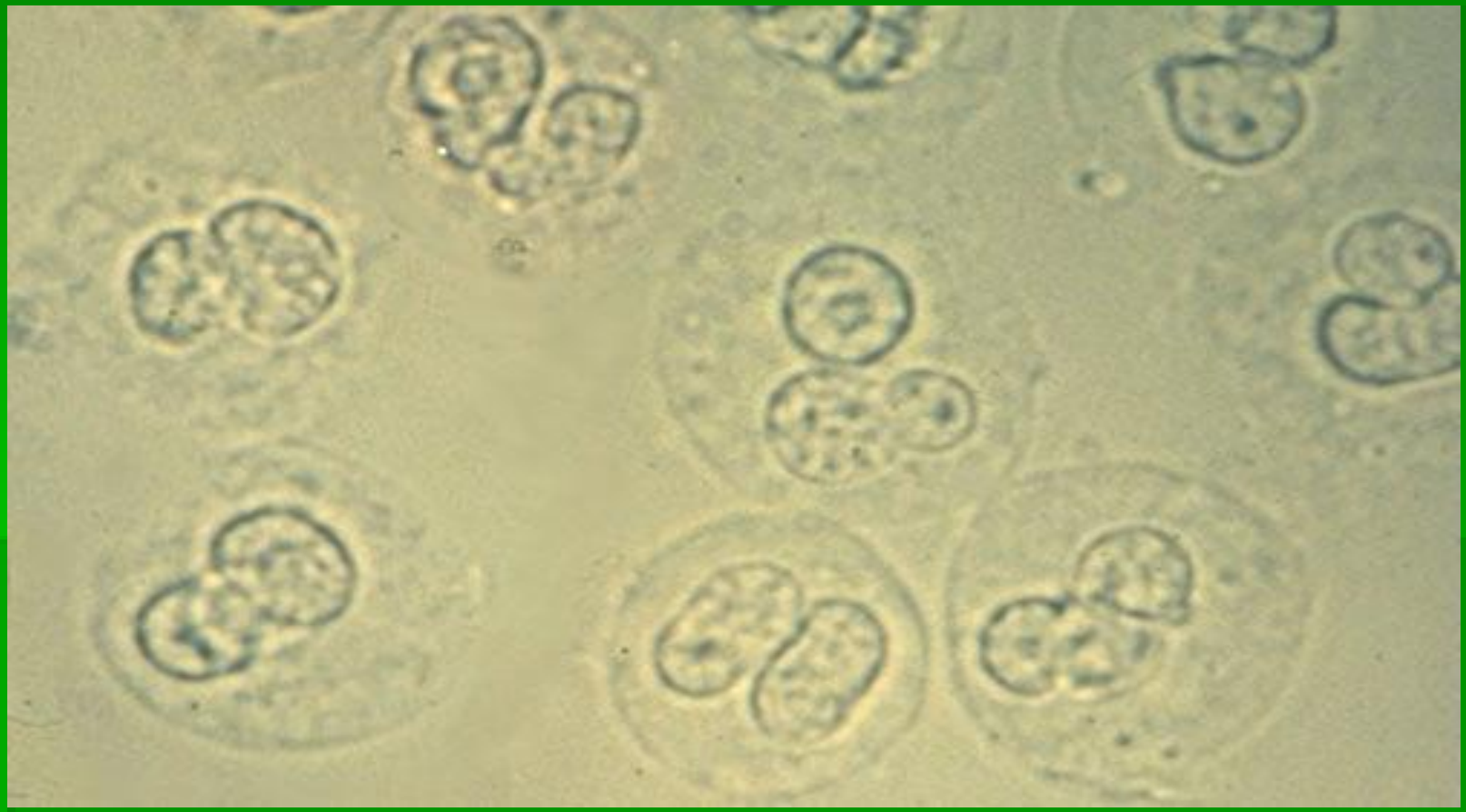
Glomerular diseases: Chronic Glomerulonephritis



Chronic Glomerulonephritis:



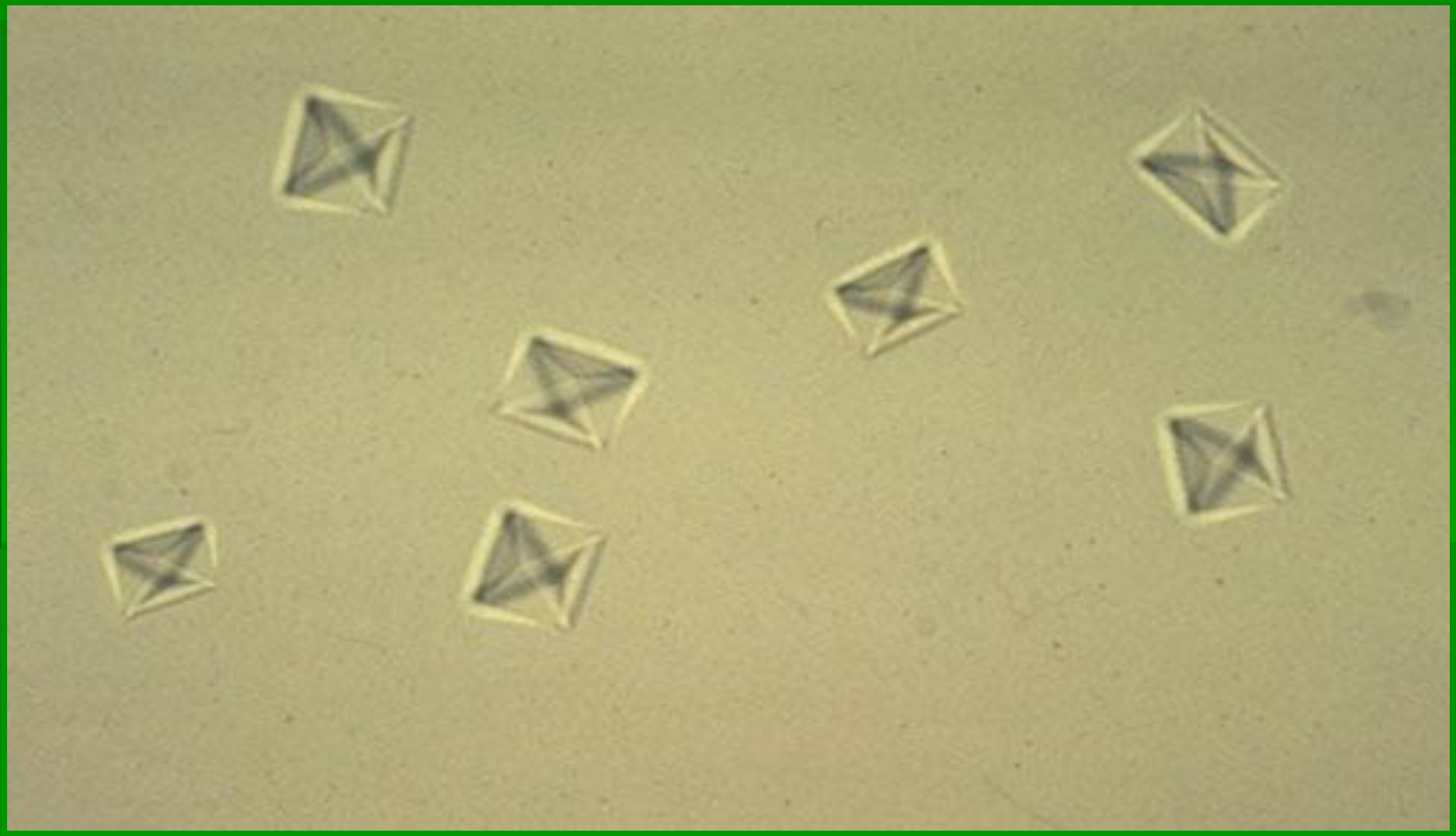
WBC in Urine :



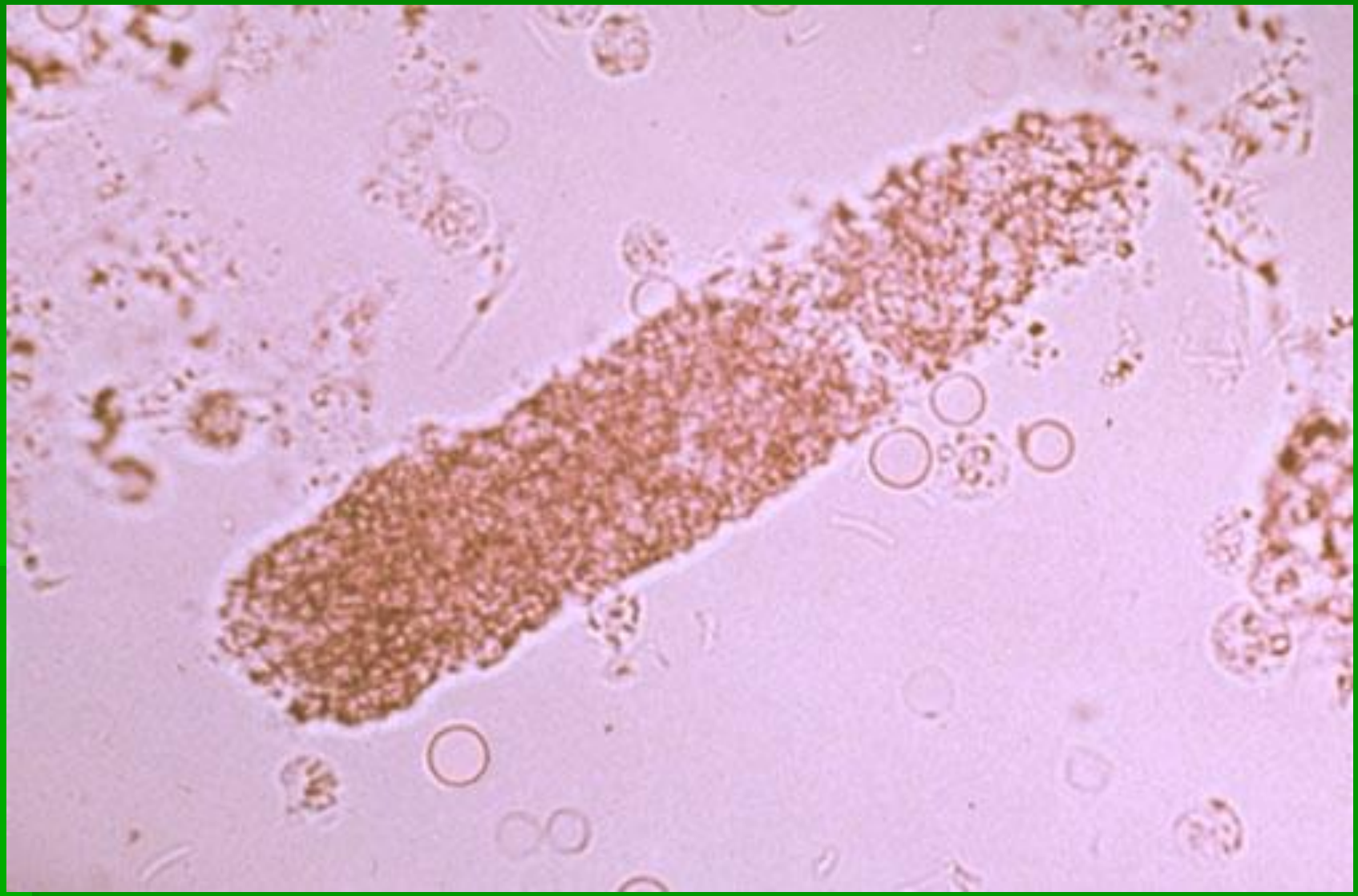
Urine Microscopy :

- Cells Casts Crystals.
- Cells - epithelial, inflammatory, malignant.
- Casts – Protein cast of nephron –
  - Suggest Kidney pathology – not URT.
  - Protein, lipid, cells or mixed.
- Crystals suggest high concentration or altered solubility.

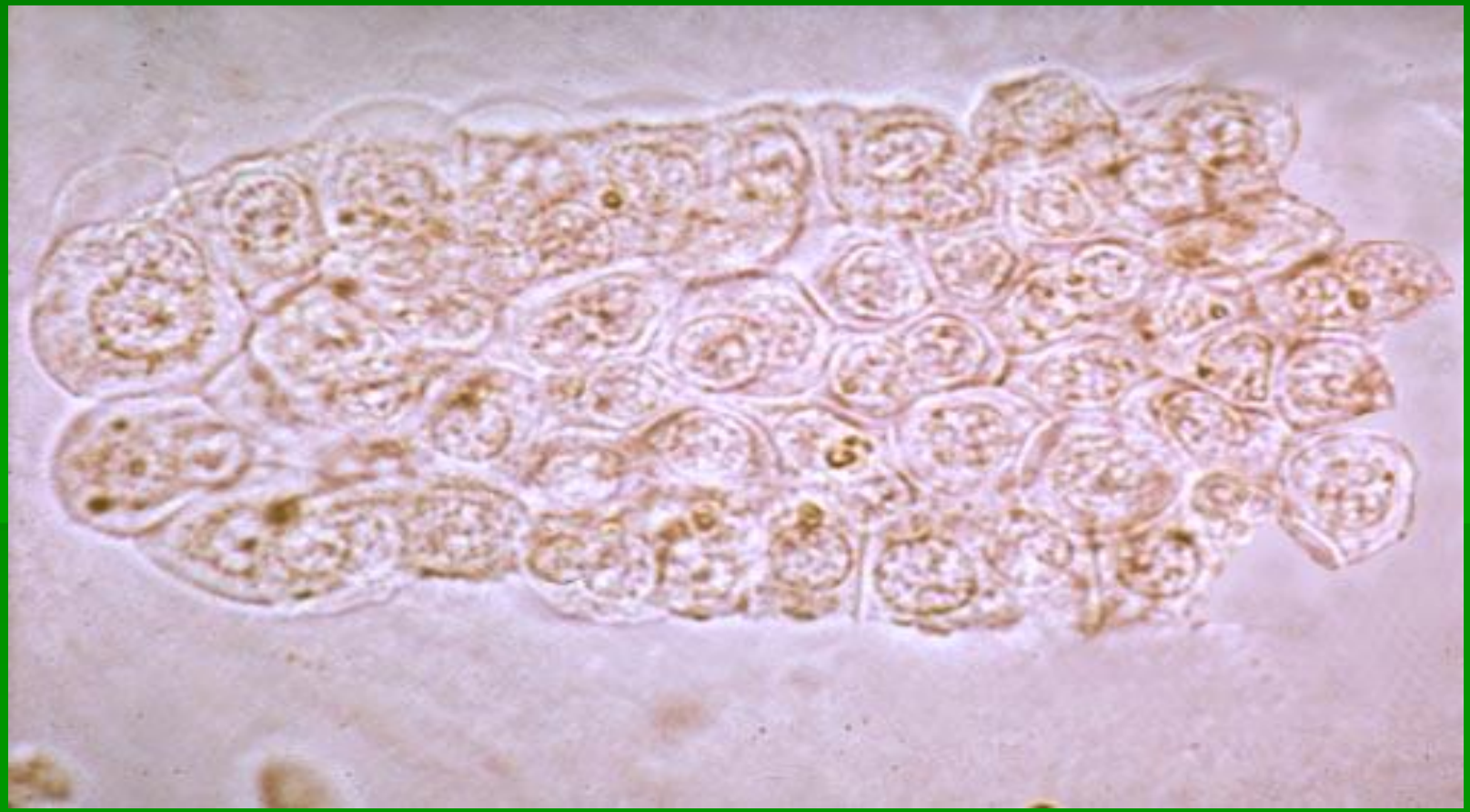
Urine Oxalate Crystals:



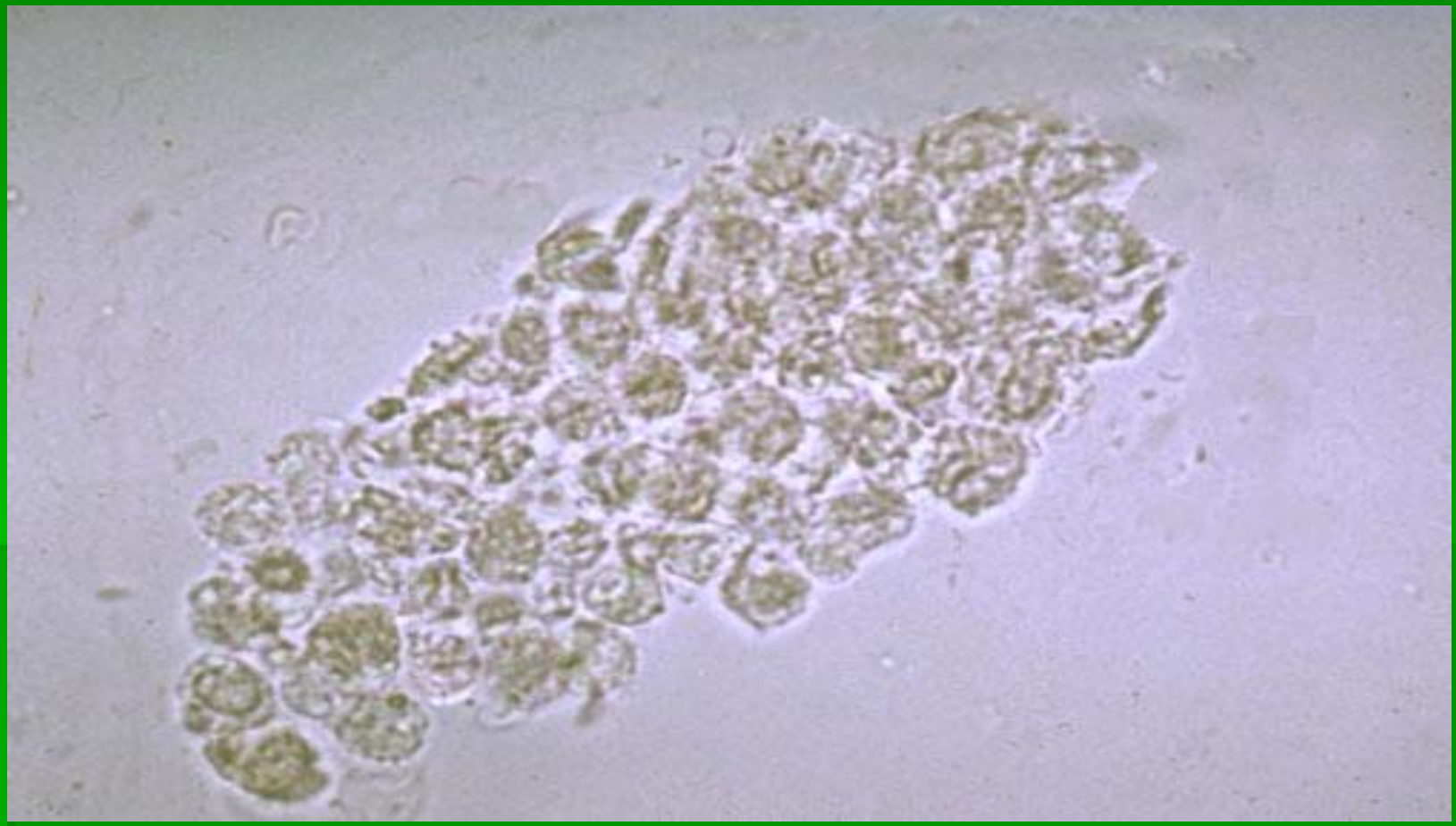
Granular Cast:



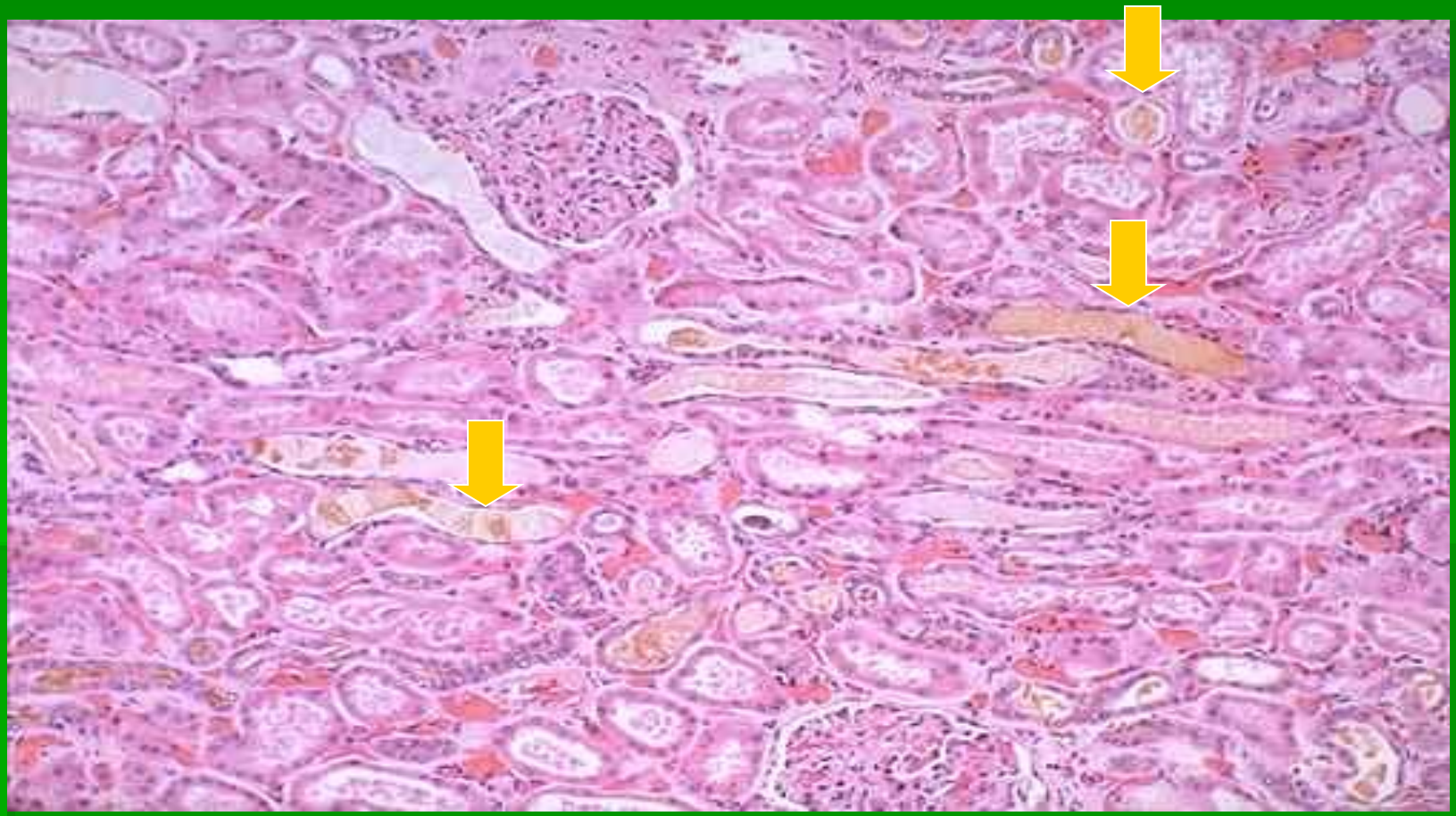
Epithelial Casts in Urine:



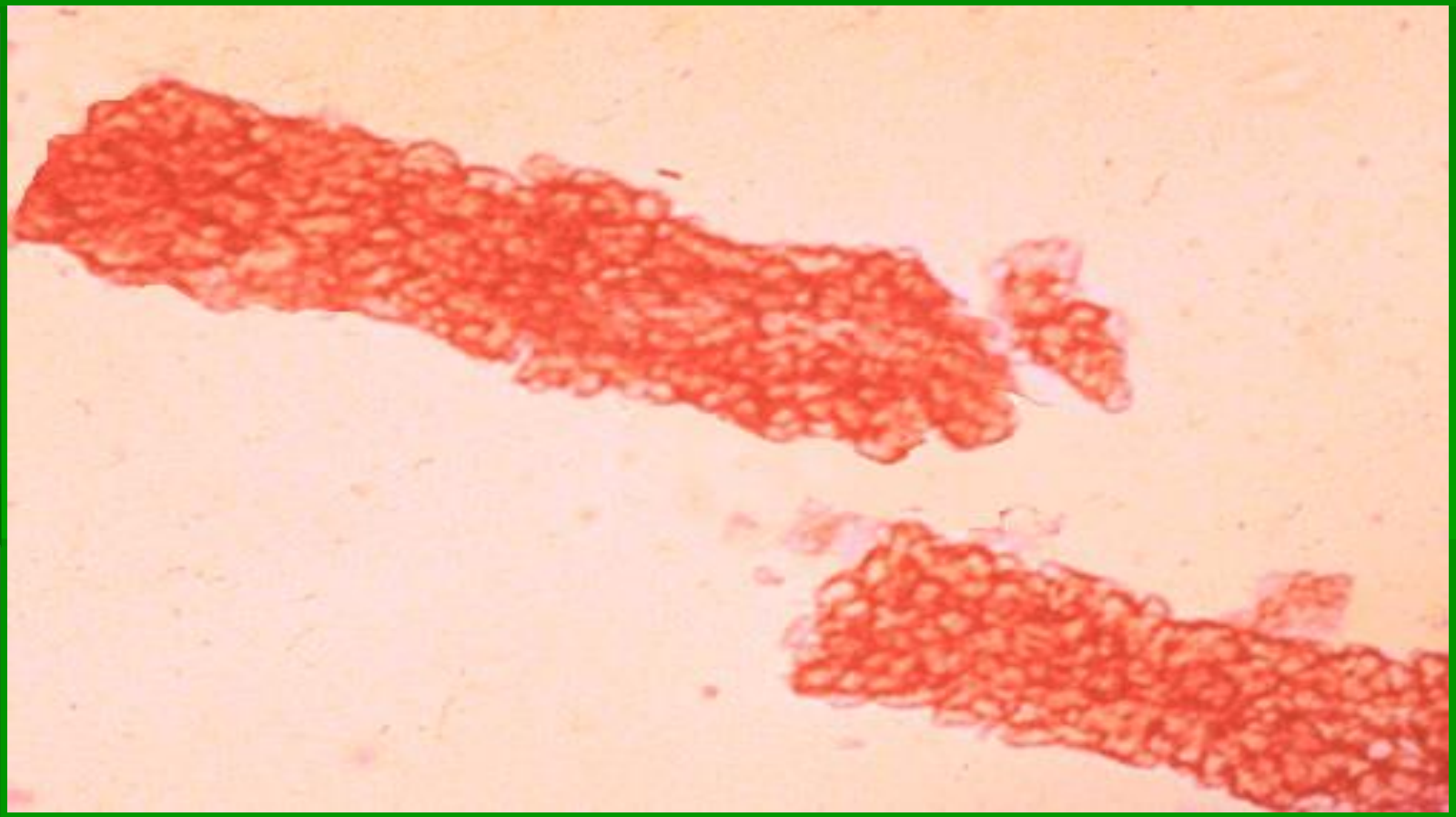
WBC Cast Urine:



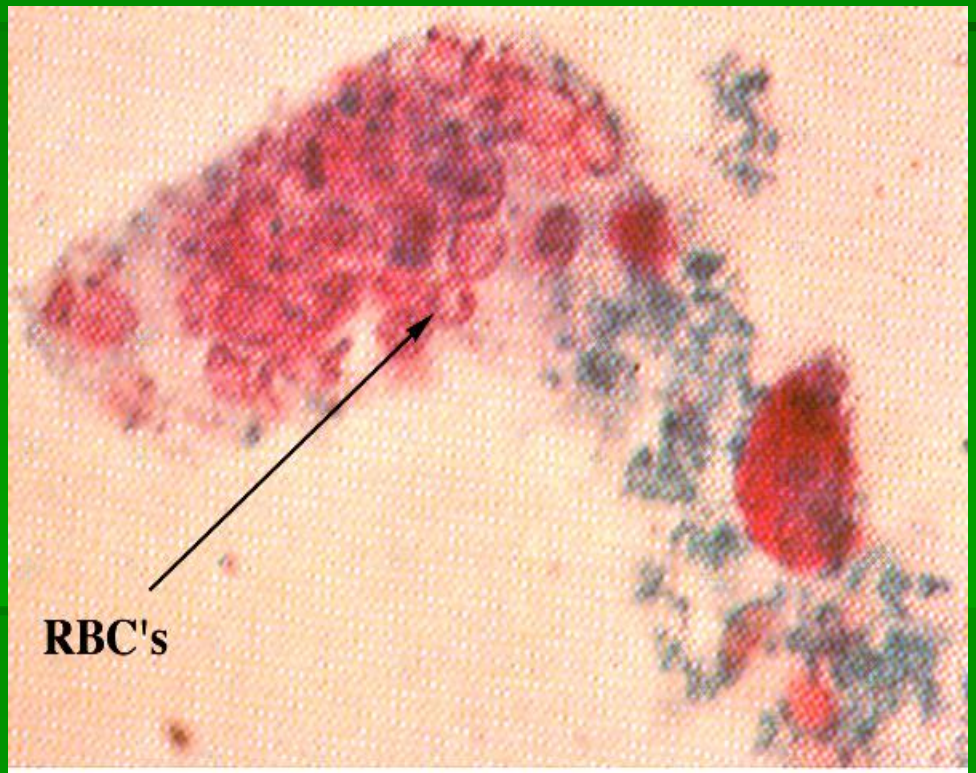
Formation of Casts:



Red cell Casts in Urine:



What is an RBC cast?



The Kidney. 5th ed. Brenner, BM (ed), WB Saunders Co., 1996, p 1160

TUBULOINTERSTITIAL DISEASE

- Most tubular diseases involve the interstitium
- 2 distinct types of diseases
  - a) inflammatory diseases
    - i) *"tubulointerstitial nephritis"*
  - b) ischemic or toxic tubular injury →
    - i) ATN
    - ii) acute renal failure

Tubulointerstitial Nephritis (TIN)

- Inflammatory disease of Interstitium/tubules
- Glomerulus not involved at all or only late in disease
- Infections induced TIN – "pyelonephritis"
- Non infection – interstitial nephritis
  a) Caused by:
    i) drugs
    ii) metabolic disorders (hypokalemia)
    iii radiation injury
    iv) immune reactions

- TIN divided into 2 categories, regardless of etiology
    a) - acute
    b) - chronic

Acute Pyelonephritis

- Kidney/renal pelvis (distal to collecting ducts)
- Caused by bacterial infections
  - (lower UTI) – cystitis, urethritis and prostatitis
  - upper UTI – (pyelonephritis)
  - both tracts
- Principle causative bacteria are gram - rods

a) E. coli (most common), Proteus, enterobacter, Klebsiella

Acute Pyelonephritis

- 2 routes bacteria can reach kidney

  a) blood stream (not very common)

  b) lower urinary tract (ascending infections)
     i) - catheterization
     ii) - cystoscopy

Acute Pyelonephritis

- Most commonly affect females (in absence of instrumentation)

  a) close proximity to rectum

  b) shorter urethra

  Urine sterile, flushing keeps bladder sterile

- Obstruction increased incidence of UTI

  i) prostate hypertrophy

  ii) uterine prolapse

  iii) UT obstructions

- Incompetent vesicoureteral orifice
  a) one way valve (at level of bladder)

  b) incompetence – reflux of urine into ureters – vesicoureteral reflux (VUR)

  c) –usually congenital defect – 30-50% of young children with UTI

- spinal cord injury can produce a flaccid bladder (residual volume remain in urinary tract) – favors bacterial growth

- Diabetes increases risk of serious complications
  - i) septicemia
  - ii) recurrence of infection
  - iii) diabetic neuropathy – dysfunction of bladder
- pregnancy
  - i) 6% develop pyuria; 40- 60% develop UTI if not treated

FACTORS

- OBSTRUCTION: Congenital or Acquired
- INSTRUMENTATION
- VESICOURETERAL REFLUX
- PREGNANCY
- AGE, SEX, why sex? F>>>M
- PREVIOUS LESIONS
- IMMUNOSUPPRESION or IMMUNODEFICIENCY

Chronic pyelonephritis and reflux nephropathy

- Interstitial inflammation with scarring of renal parenchyma
- Important cause of chronic renal failure

- Two forms:

  a) - Chronic obstructive pyelonephritis

  b) - Chronic reflux-associated pyelonephritis

Chronic obstructive pyelonephritis

•Can be bilateral (congenital disease)
• Obstruction predisposes kidney to infection
• recurrent infections on obstructive foci causes
scarring – chronic pyelonephritis!

chronic reflux-associated pyelonephritis (reflux nephropathy)

- More common form of chronic pyelonephritis

reflux nephropathy

Occurs from superimposed of a UTI on vesiculouretheral and intrarenal reflux

a) reflux may be bi- or unilateral

i) unilateral causes atrophy

ii) bilateral can cause chronic renal insufficiency

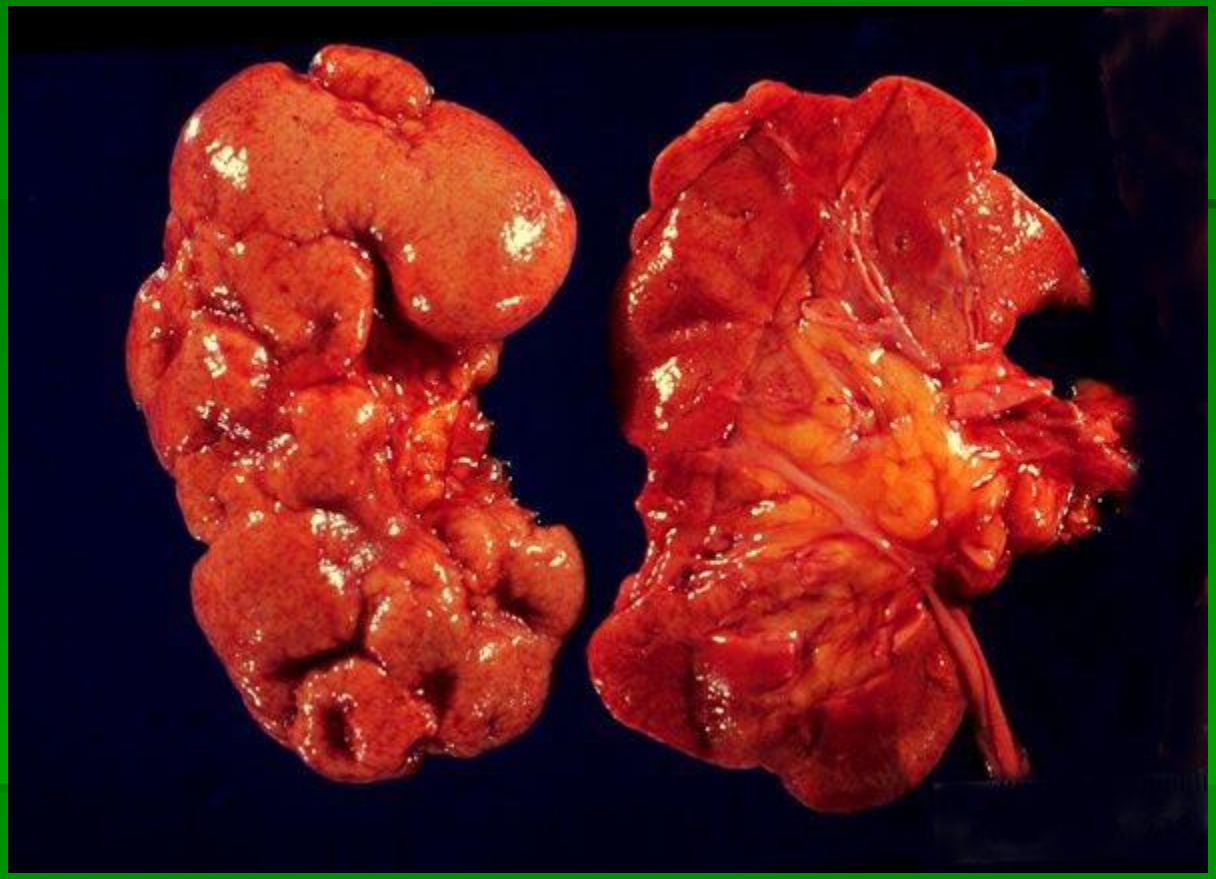
iii) diffuse or patchy

- - Unclear if sterile vesiculouretheral disease causes renal damage

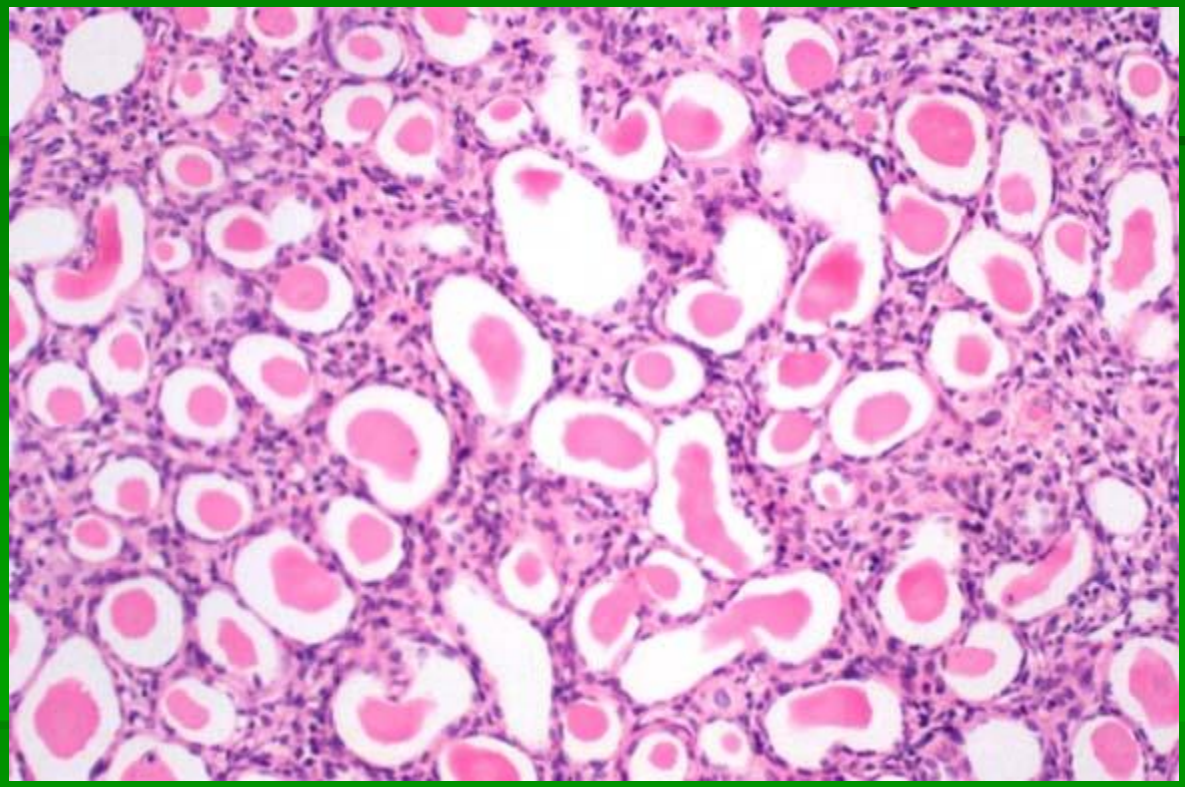
reflux nephropathy

Hallmark is scarring involving pelvis/calyces, leading to papillary blunting and deformities

- Renal papillae – area of kidney where opening from collecting ducts enters renal pelvis
- Kidneys are asymmetrically contracted



CHRONIC PYELONEPHRITIS



CHRONIC PYELONEPHRITIS

Signs and Symptoms:

a) hypertension

b) seen following normal physical exam

c) slowly progressive $\rightarrow$ late in disease

d) can cause loss of concentrating mechanisms (if bilateral and progressive)

- i) - polyuria
- ii) - nocturia

Drug-induced interstitial nephritis

- Acute TIN – seen with synthetic penicillins, diuretics (thiazides), NSAID

a) disease begins ~15 days (2-40 range)
   i) fever
   ii) rash (25% cases)
   iii) renal findings: hematuria, leukouria
   iv) increased serum creatinine or acute renal failure with oliguria (50% of cases)

Drug-induced interstitial nephritis

- Immune mechanism is indicated (suggested)

  a) IgE increased (hypersensitivity – Type I)

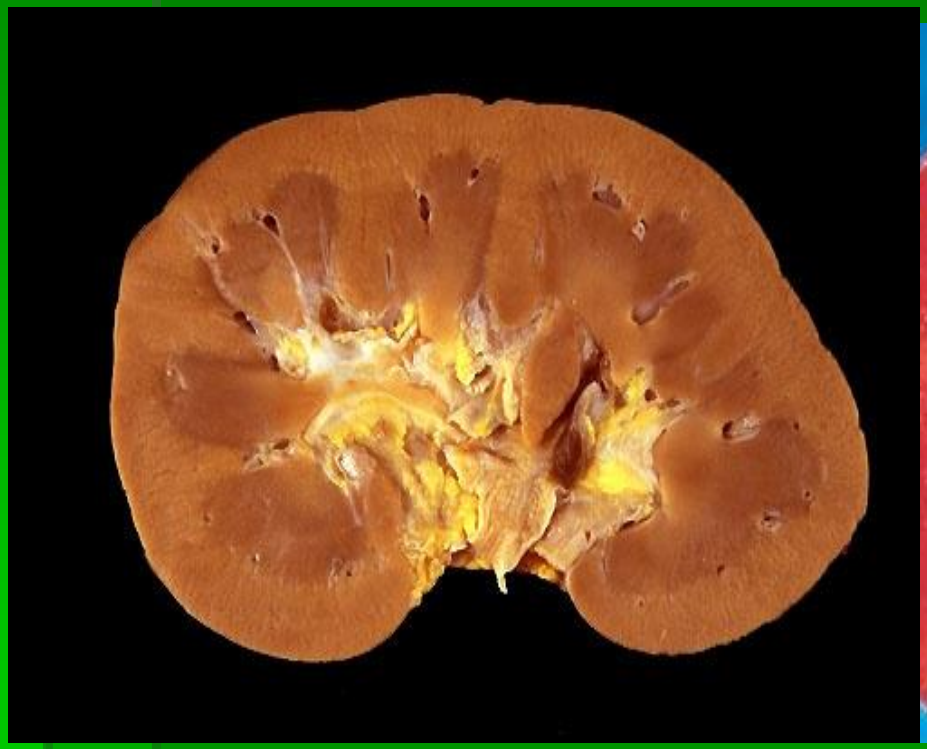
  Injury produced by IgE and cell-mediated immune reactions

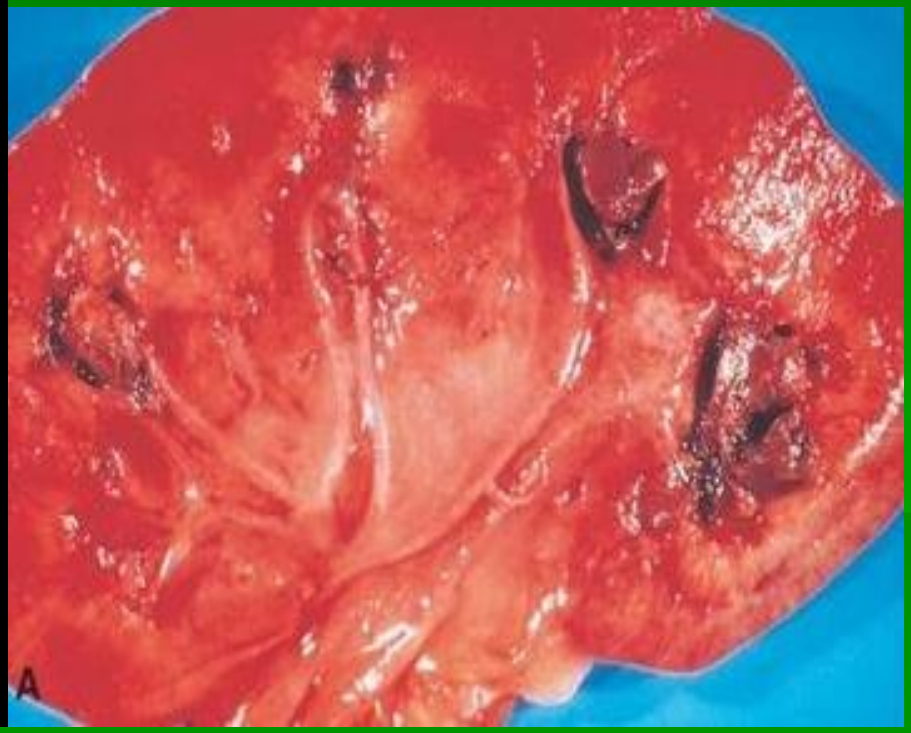
Analgesic Nephropathy

- Patients who consume large quantities of analgesics may develop chronic interstitial nephritis, often associated with renal papillary necrosis
- Usually result from consumption of a mixture for long periods of time:
  a) - aspirin
  b) - caffeine
  c) - acetaminophen
  d) - codeine
  e) - phenacetin

- Primary pathogenesis is
  a) papillary necrosis followed by
  b) interstitial nephritis is secondary
  c) acetaminophen – oxidative damage
  d) aspirin inhibits prostaglandins – vasoconstriction
  e) all the above leads to papillary ischemia
- Chronic renal failure, hypertension and anemia
- Complications may be incidence of "transitional cell carcinoma" of renal pelvis or bladder.

ANALGESIC NEPHROPATHY





ATN (Clinical entity)

- Destruction of tubular epithelial cells
- Acute suppression of renal function
- Most common cause of acute renal failure(ARF):

  Acute suppression of renal function , oliguria (400 ml/day)

Other causes of ARF

b) severe glomerular disease (RPGN
c) diffuse vascular disease (Polyarteritis nodosa)
d) diffuse cortical necrosis
e) interstitial nephritis (acute drug-induced)
f) acute papillary necrosis

- Is reversible and arise from:
  a) severe trauma
  b) septicemia (shock and hypotension)
  c) ATN associated with shock – "ischemic" -
  d) mismatched blood transfusion and other hemodynamic problems as well as myoglobinuria → all reversible ischemic ATN
  e) nephrotoxic ATN – variety of poisons
    i) - heavy metals (Hg)
    ii) - CCl_4
    iii) - etc.

- Occurs frequently

  a) since it is reversible, proper management means difference between recovery and death

- 2 major problems are:

  a) - tubular injuries

  b) - blood flow disturbances

- Major disturbances:

a) Change charge in tubules (mainly -)
i) Na+ - K+ - ATPase cause
less Na+ reabsorption and traps Na+, within tubule with more distal tube delivery of Na+ which causes vasoconstriction (feedback)

Treatment protocol

- 1) - initiating phase
- 2) - maintenance phase
- 3) - recovery phase

Initiating phase

- Last about 36 hours. Incited by:
  a) medical, surgical, obstetric event
     i) slight oliguria (transient decrease in blood flow)
     ii) rise in BUN

Maintenance phase

Anywhere from 2-6 days

a) sharp decline in urine output (50-400 ml/day)

i) may last few days to 3 weeks

b) fluid overload, uremia

c) may die from poor management

Recovery phase

- Steady increase in urine output (up to 3L/day)
- Electrolyte imbalances may continue
- Increased vulnerability to infection
- Because of these, about 25% patients die in this phase

Diseases of Blood Vessels

- Nearly all diseases of kidney involve blood vessels.
- Kidneys involved in pathogenesis of essential and secondary hypertension
- Systemic vascular disease (i.e. arteritis) also involve kidney

Benign nephrosclerosis

- Renal changes associated with benign hypertension
  a) always associated with hyaline arteriosclerosis
- Kidneys are atrophic
- Many renal diseases cause hypertension which in turn may lead to benign nephrosclerosis.
- Therefore this disease seen simultaneously with other diseases of kidney

- This disease by itself usually does not cause severe damage
  a) mild oliguria
  b) loss (slight) of concentrating mechanism
  c) decreases GFR
  d) mild degree of proteinuria is a constant finding
- These patients usually die from hypertensive heart disease or cerebrovascular disease rather than from renal disease

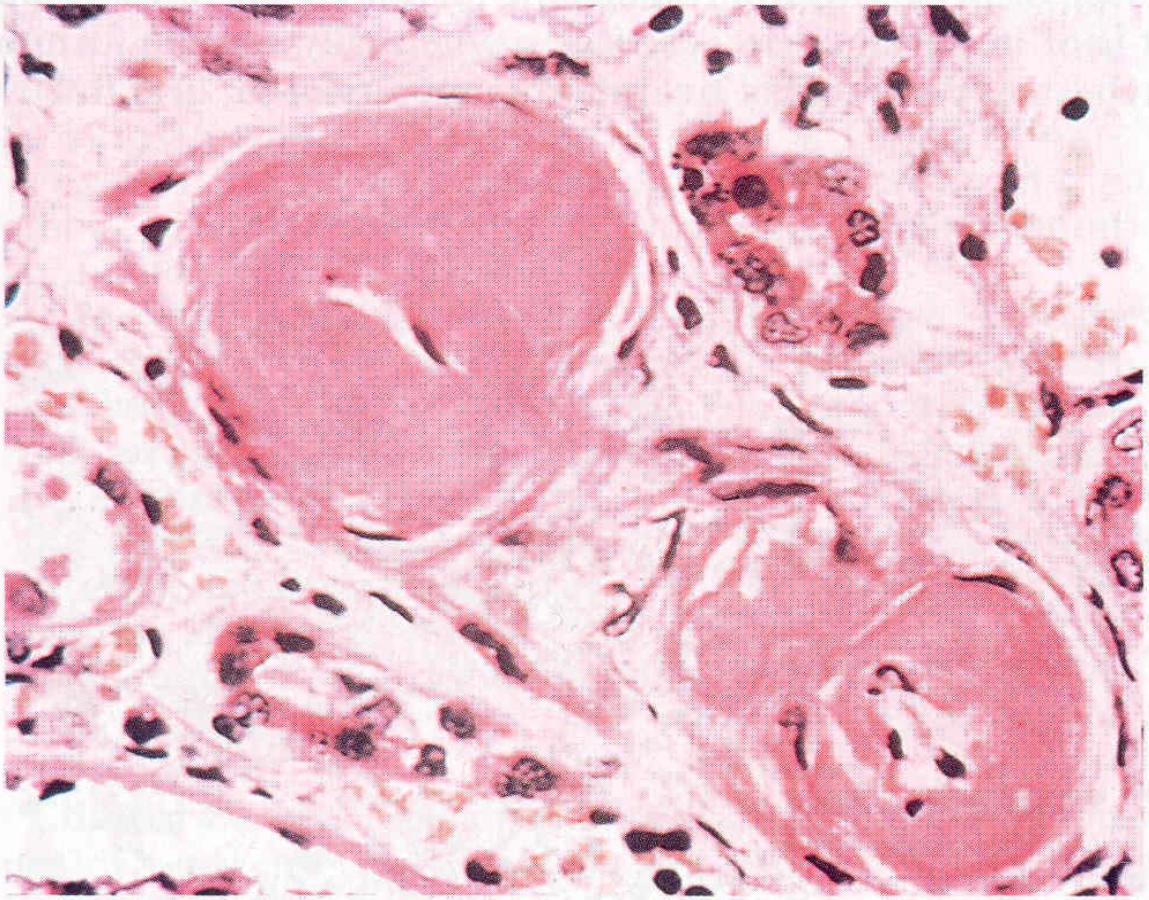
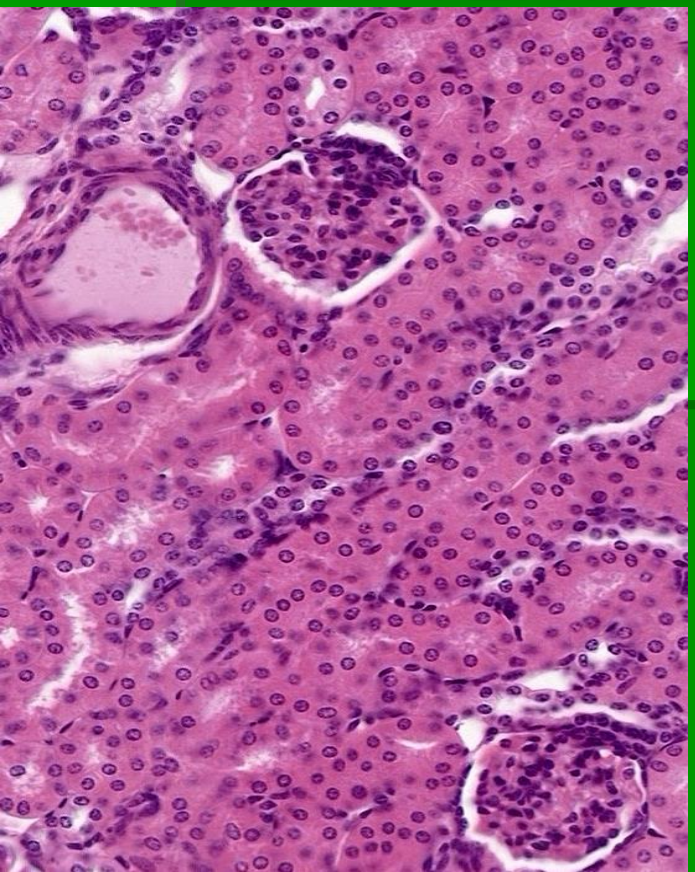
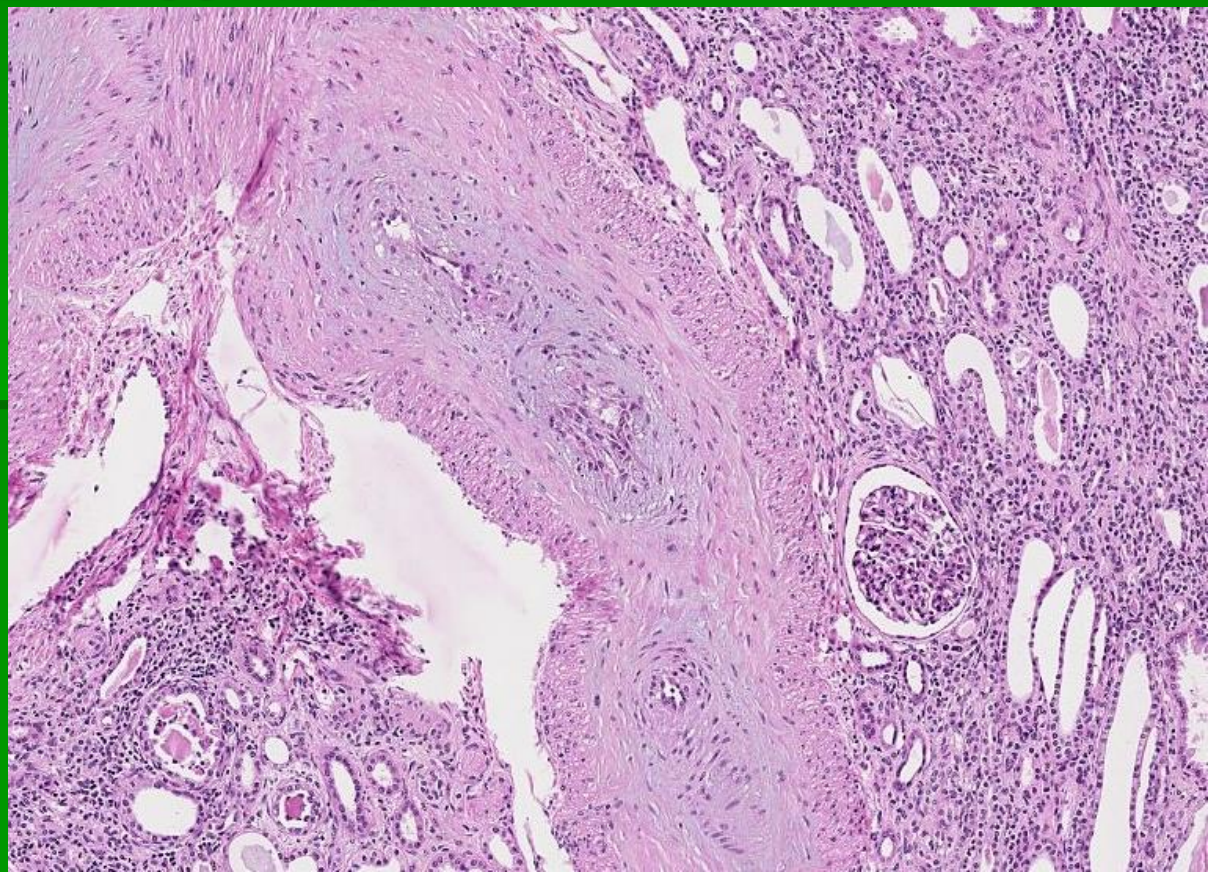


FIGURE 20–49 Hyaline arteriolosclerosis. High-power view of two arterioles with hyaline deposition, marked thickening of the walls, and a narrowed lumen. (Courtesy of Dr. M.A. Venkatachalam, Department of Pathology, University of Texas Health Sciences Center, San Antonio, TX.)

BENIGN NEPHROSCLEROSIS

- Sclerosis, i.e., “hyalinization” of arterioles and small arteries, i.e., arterio-, arteriolo-
- Is this part of “routine” atherosclerosis????
- VERY VERY VERY common





Malignant hypertension

- Less common than benign
- May arise de novo (without preexisting hypertension) or may arise suddenly in patient with mild hypertension

Factors:

- a) initial event – some form of vascular damage to kidney
- b) result is increased permeability of small blood vessels to fibrinogen and other plasma proteins, endothelial injury and platelet deposits
- c) This leads to appearance of fibroid necrosis in small arteries and arterioles and intravascular thrombosis

d) platelets (platelet derived growth factors) and plasma cause intimal hyperplasia of vessels resulting in hyperplastic arteriosclerosis, which is typical of malignant hypertension
e) narrowing of renal afferent arteriole stimulates angiotensin II production (ischemic-induced) with aldosterone secretion increases

- Diastolic pressure > 130 mmHg, papilledema, encephalopathy, CV disorders, renal failure
- 90% deaths due to uremia
- 10% deaths due to CV or cerebral disorders (hemorrhage)

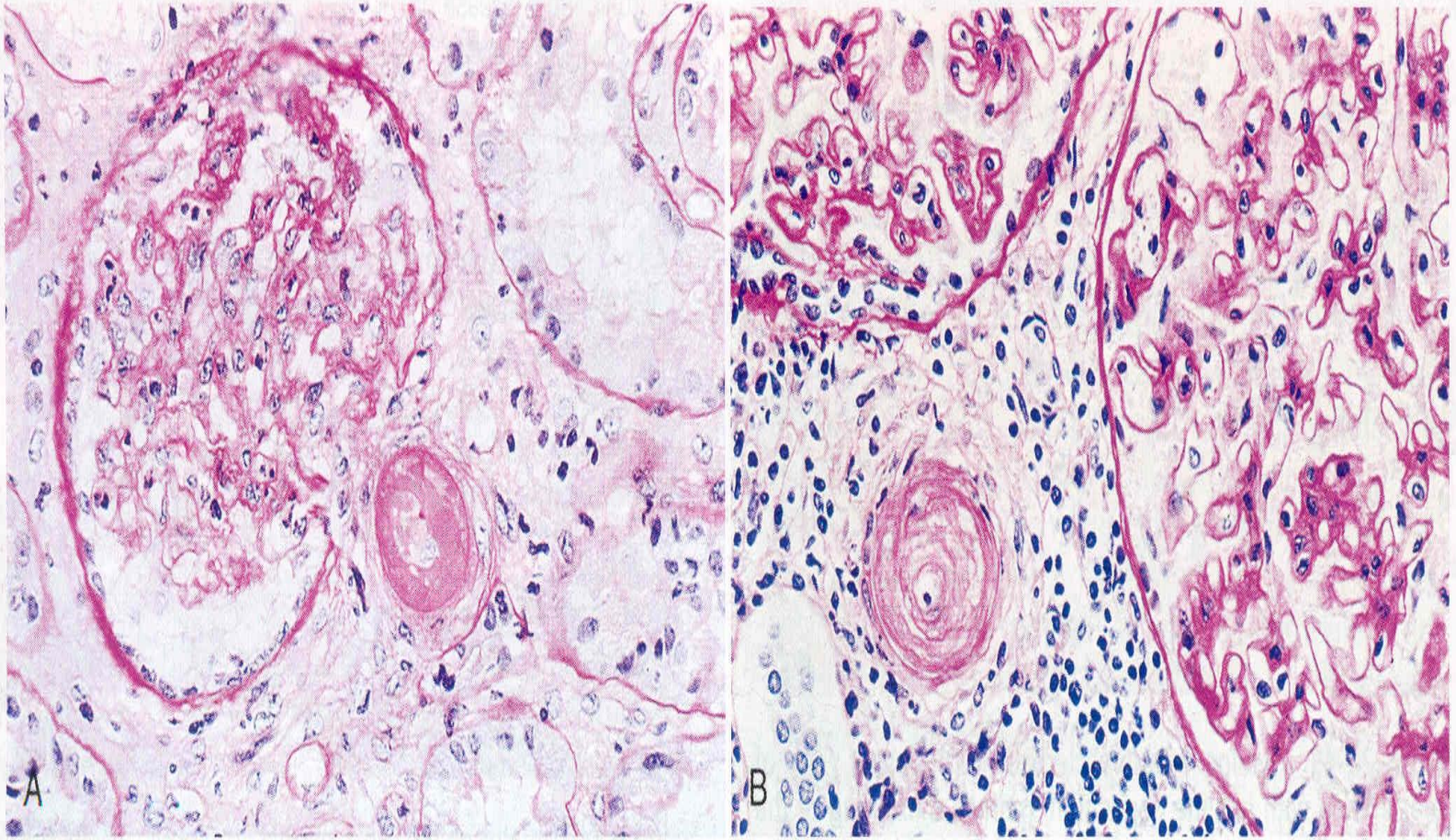
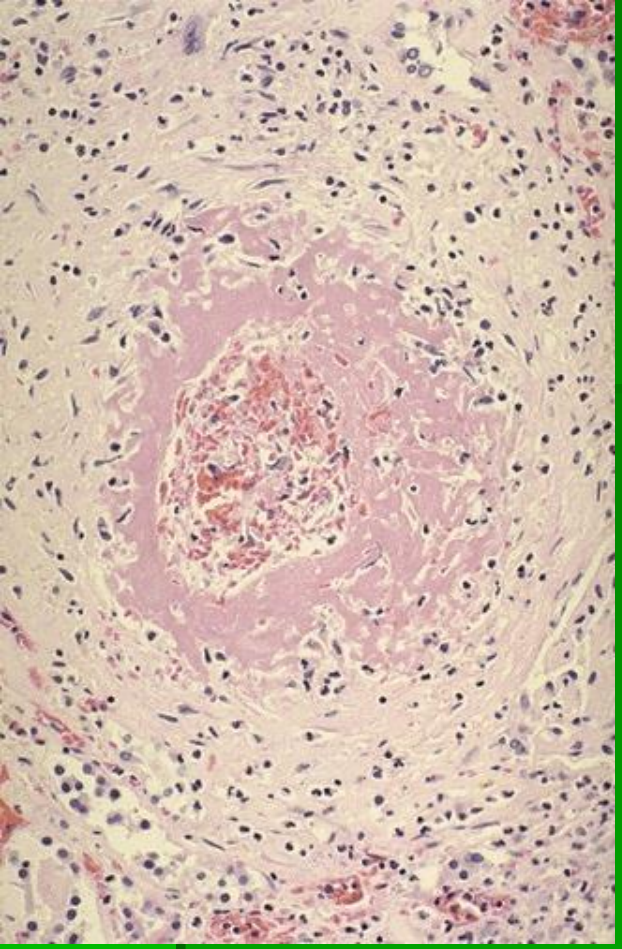
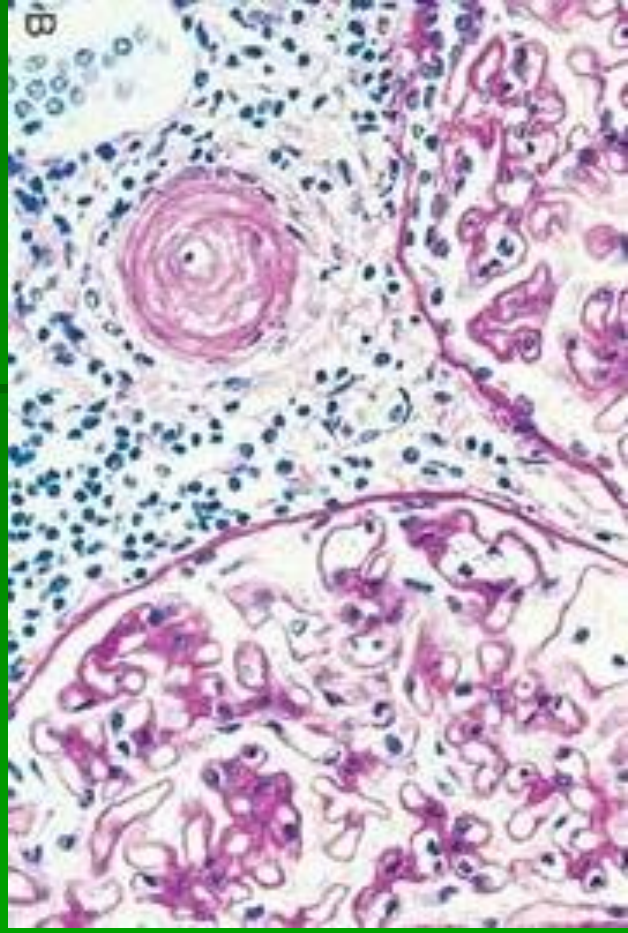


FIGURE 20–50 Malignant hypertension. *A*, Fibrinoid necrosis of afferent arteriole (PAS stain). *B*, Hyperplastic arteriolitis (onion-skin lesion). (Courtesy of Dr. H. Rennke, Brigham and Women's Hospital, Boston, MA.)





What is “onion-skinning”?

What is an onion?

What is “fibrinoid” necrosis?