Structure and function of the kidneys and their clinical assessment

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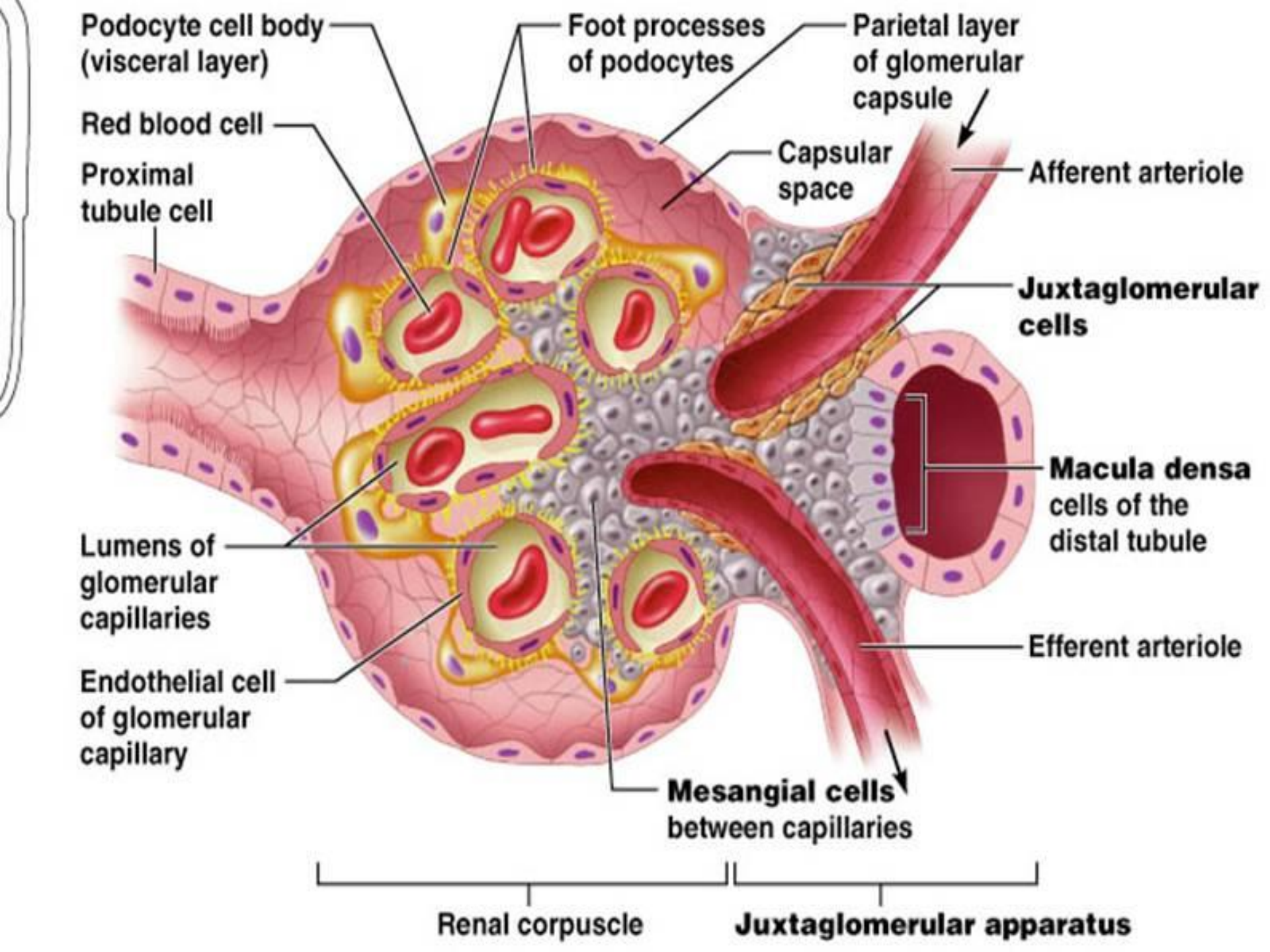
Kidney Structure

- The kidneys are two bean-shaped organs that lie in the retroperitoneal space, each weighing about 150 g.
- The functional unit of the kidney is the *nephron;* each nephron consists of a glomerulus and a long tubule, which is composed of a single layer of epithelial cells. There are approximately one million nephrons in one human kidney.
- The nephron is segmented into distinct parts—proximal tubule, loop of Henle, distal tubule, and collecting duct.


Podocyte cell body (visceral layer)
Foot processes of podocytes
Parietal layer of glomerular capsule
Red blood cell
Capsular space
Afferent arteriole
Proximal tubule cell
Juxtaglomerular cells
Macula densa
cells of the distal tubule
Lumens of glomerular capillaries
Efferent arteriole
Endothelial cell of glomerular capillary
Mesangial cells
between capillaries
Renal corpuscle
Juxtaglomerular apparatus

Renal circulation

The renal artery carries about one fifth of the cardiac output; this represents the highest tissue-specific blood flow of all larger organs in the body (about 350 mL/min per 100 g tissue).

- The renal circulation is unusual in that it breaks into two separate capillary beds: the glomerular bed and the peritubular bed. As blood leaves the glomerulus, the capillaries coalesce into the efferent arteriole. Pressure in the first capillary bed, that of the glomerulus, is rather high (40 to 50 mm Hg), whereas pressure in the peritubular capillaries is similar to that in capillary beds elsewhere in the body (5 to 10 mm Hg).

Functions of the kidney

1. Maintenance of body composition… The volume of fluid in the body; its osmolarity, electrolyte content, and concentration; and its acidity.

2. Excretion of metabolic end products and foreign substances: The kidney excretes a number of products of metabolism, most notably urea, and a number of toxins and drugs

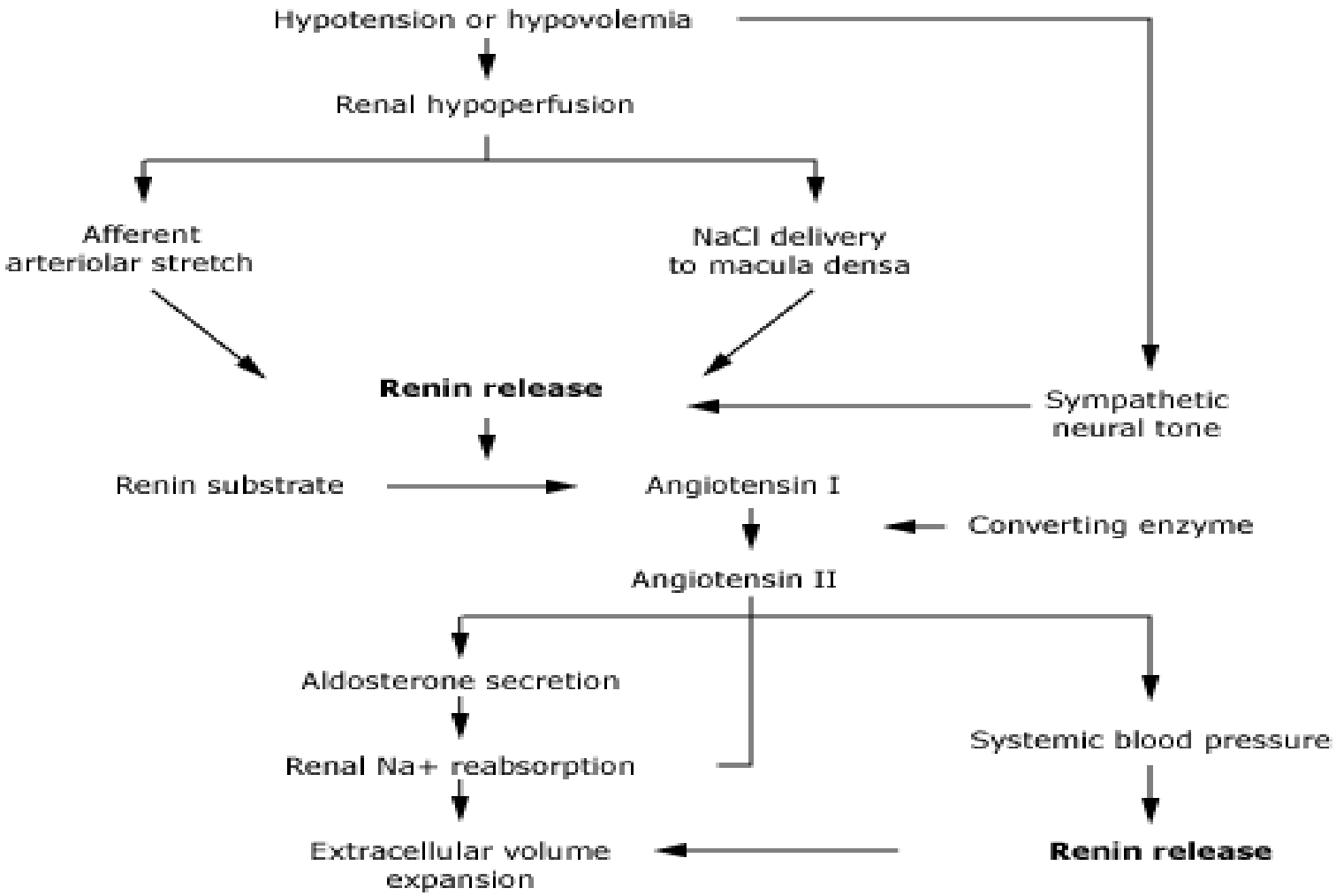
3. Production and secretion of enzymes and hormones:

a. Renin is an enzyme produced by the granular cells of the juxtaglomerular apparatus that catalyzes the formation of angiotensin from angiotensinogen. Angiotensin is a potent vasoconstrictor.

b. Erythropoietin, is produced by renal cortical interstitial cells, stimulates the maturation of erythrocytes in the bone marrow.

c. 1,25-Dihydroxyvitamin D_3, is formed by proximal tubule cells.

Regulation of renin release



The renin-angiotensin-aldosterone system and the maintenance of sodium and volume balance.

Assessment of renal function

- H&PE
- RFP… Including BUN and Cr… Cr-GFR
- UA with microscopy
- Imaging

- Others, if indicated based on the above lab findings.
- Kidney biopsy.

Assessment of Glomerular Filtration Rate

- Normal average GFR values are approximately 130 and 120 mL/min/1.73 m^2 for young men and women, respectively
- GFR is often estimated from the serum concentration of endogenous filtration markers.
- Creatinine is the most commonly used endogenous filtration marker in clinical practice.

- The most common methods utilized to estimate the GFR are:
  1. Measurement of the 24 hour urine creatinine clearance.
  2. Estimation equations based upon serum creatinine such as the Cockcroft-Gault equation, the Modification of Diet in Renal Disease (MDRD) study equations, and the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.

Urinalysis

- In conjunction with the history, physical examination, and serum chemistries, the urinalysis plays a central role in evaluating acute and chronic kidney disease. In addition, abnormal findings on a routine urinalysis, often in an otherwise asymptomatic patient, may be the first evidence of underlying kidney disease.
- A complete urinalysis consists of three components: gross evaluation, dipstick analysis, and microscopic examination of the urine sediment.

- Normal urine is clear and light yellow in color.
- The urine dipstick provides a rapid semiquantitative assessment of urinary characteristics on a series of test pads embedded on a reagent strip. Most dipsticks permit the analysis of the following core urine parameters: heme, leukocyte esterase, nitrite, albumin, hydrogen ions, specific gravity, and glucose.

- Microscopic examination of the urine sediment is an essential part of the urinalysis, as it enables confirmation and clarification of urine dipstick findings and also the identification of structures that are not evaluated by the urine dipstick (eg, epithelial cells, casts, crystals).

Crystals

- Crystals, such as uric acid crystals, calcium phosphate or calcium oxalate crystals, cystine crystals, and magnesium ammonium phosphate crystals.

Uric acid crystals in the urine

Urine sediment loaded with uric acid crystals. These crystals are pleomorphic, most often appearing as rhombic plates or rosettes. They are yellow or reddish-brown and form only in an acid urine (pH 5.5 or less).

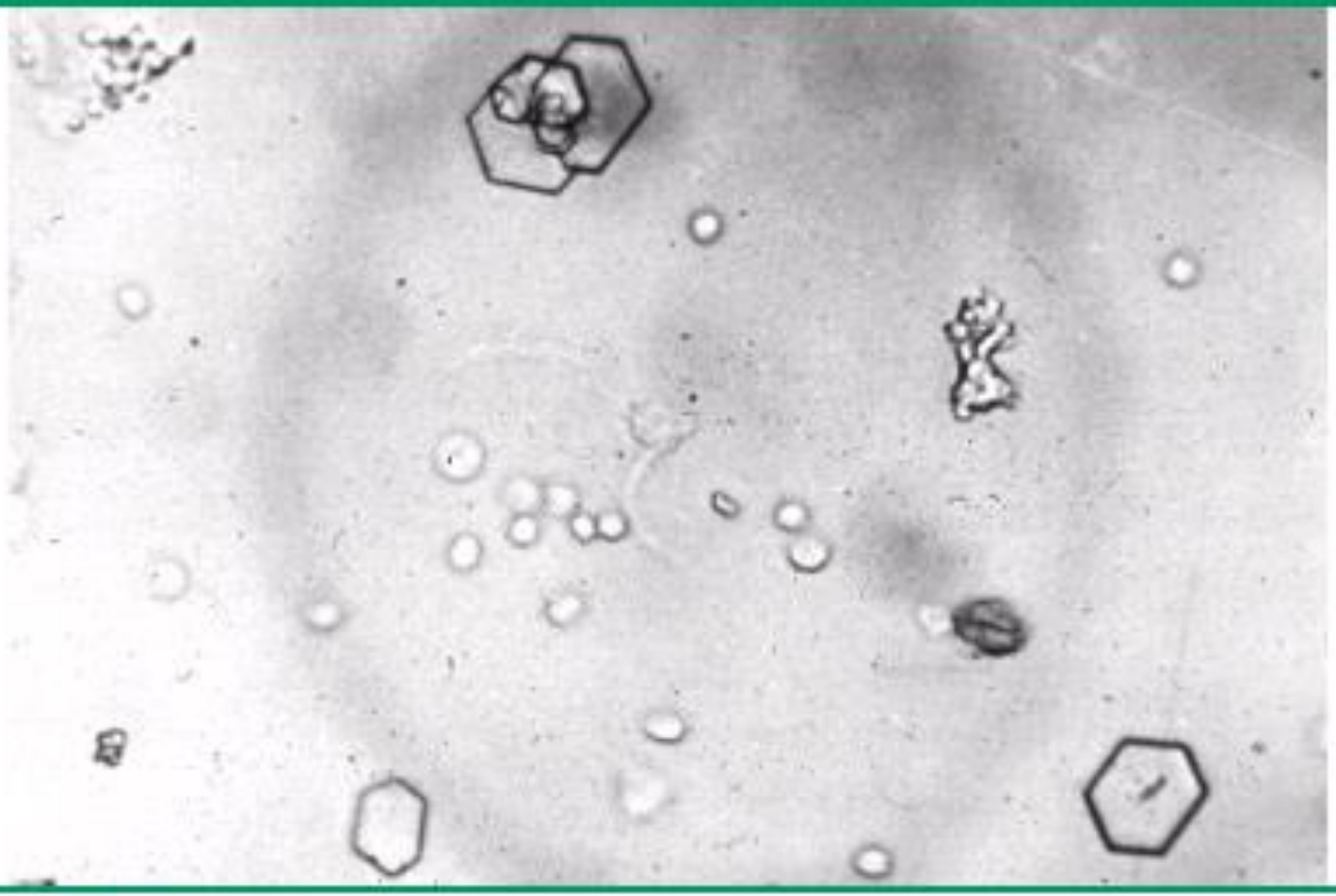
Courtesy of Harvard Medical School.

Calcium oxalate crystals in the urine

Urine sediment showing both dumbbell-shaped calcium oxalate monohydrate (long arrow) and envelope-shaped calcium oxalate dihydrate (short arrows) crystals. Although not shown, the monohydrate crystals may also have a needle-shaped appearance. The formation of calcium oxalate crystals is independent of the urine pH.

Courtesy of Frances Andrus, BA, Victoria Hospital, London, Ontario.

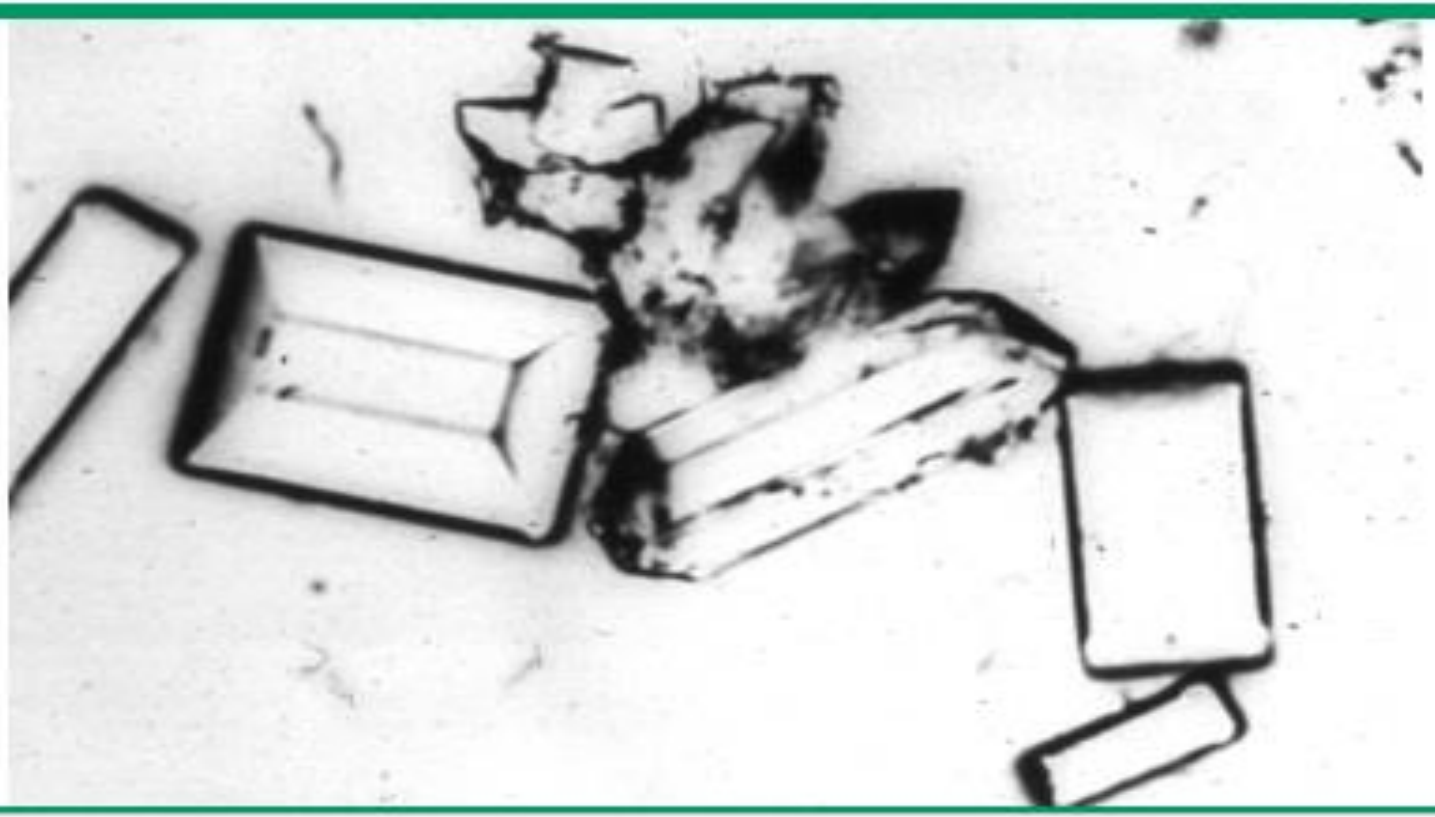
Urine sediment showing cystine crystals



Urine sediment showing hexagonal cystine crystals that are essentially pathognomonic of cystinuria.

Courtesy of Harvard Medical School.

Urine sediment showing struvite (magnesium ammonium phosphate) crystals

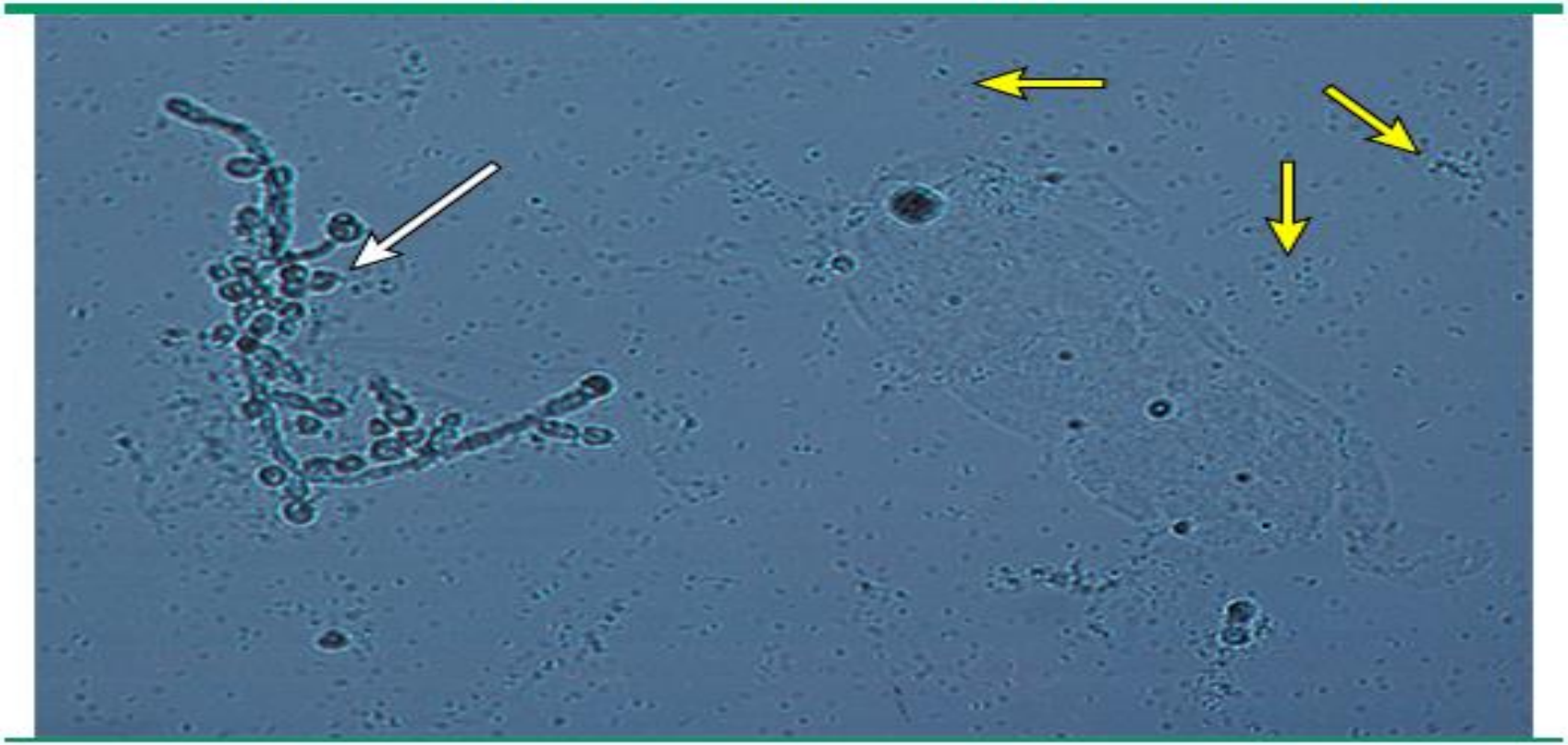


Urine sediment showing multiple "coffin lid" magnesium ammonium phosphate crystals (struvite) that form only in an alkaline urine (pH usually above 7.0) caused by an upper urinary tract infection with a urease-producing bacteria.

Courtesy of Harvard Medical School.

Bacteria or fungi

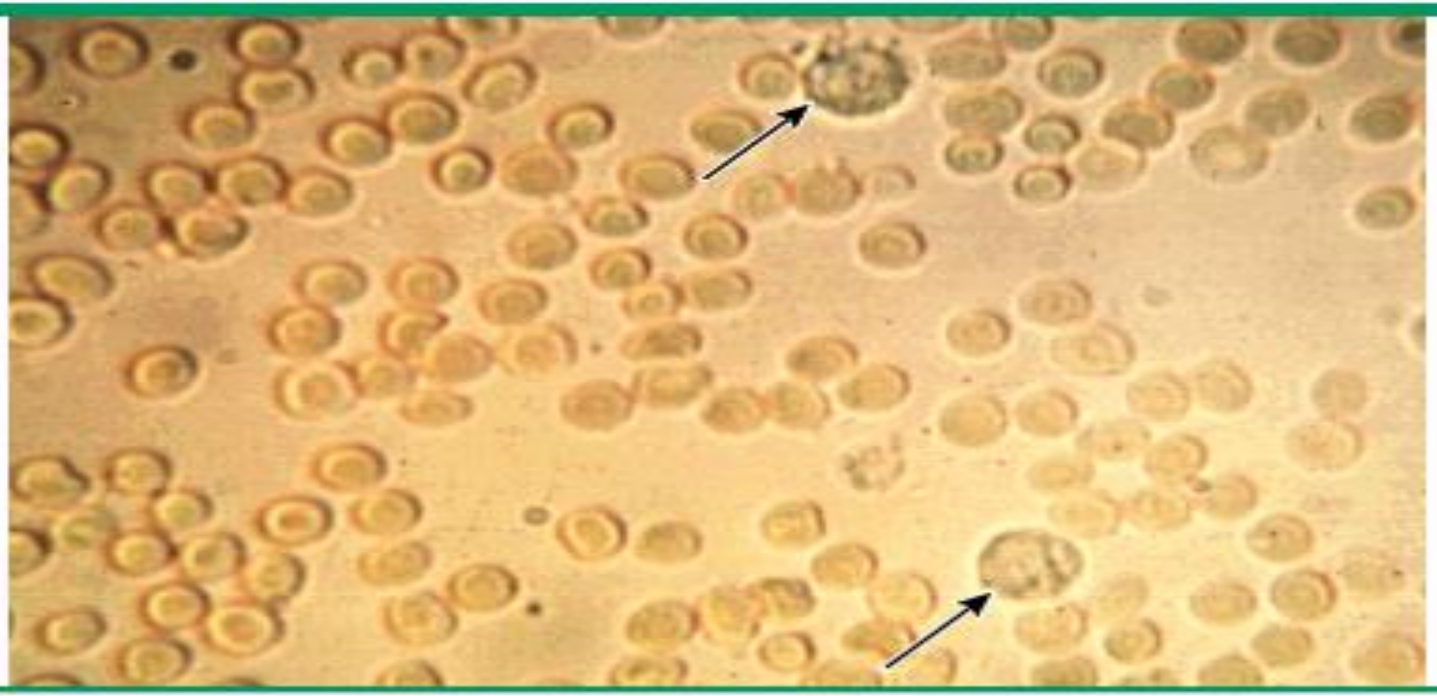
Urine sediment showing bacteria, budding yeast, and hyphae



The background contains budding yeast and hyphae (white arrow), as well as a bacteria (yellow arrows). There is also a broad hyaline cast. (Bright-field microscopy, 3100.)

Red blood cells

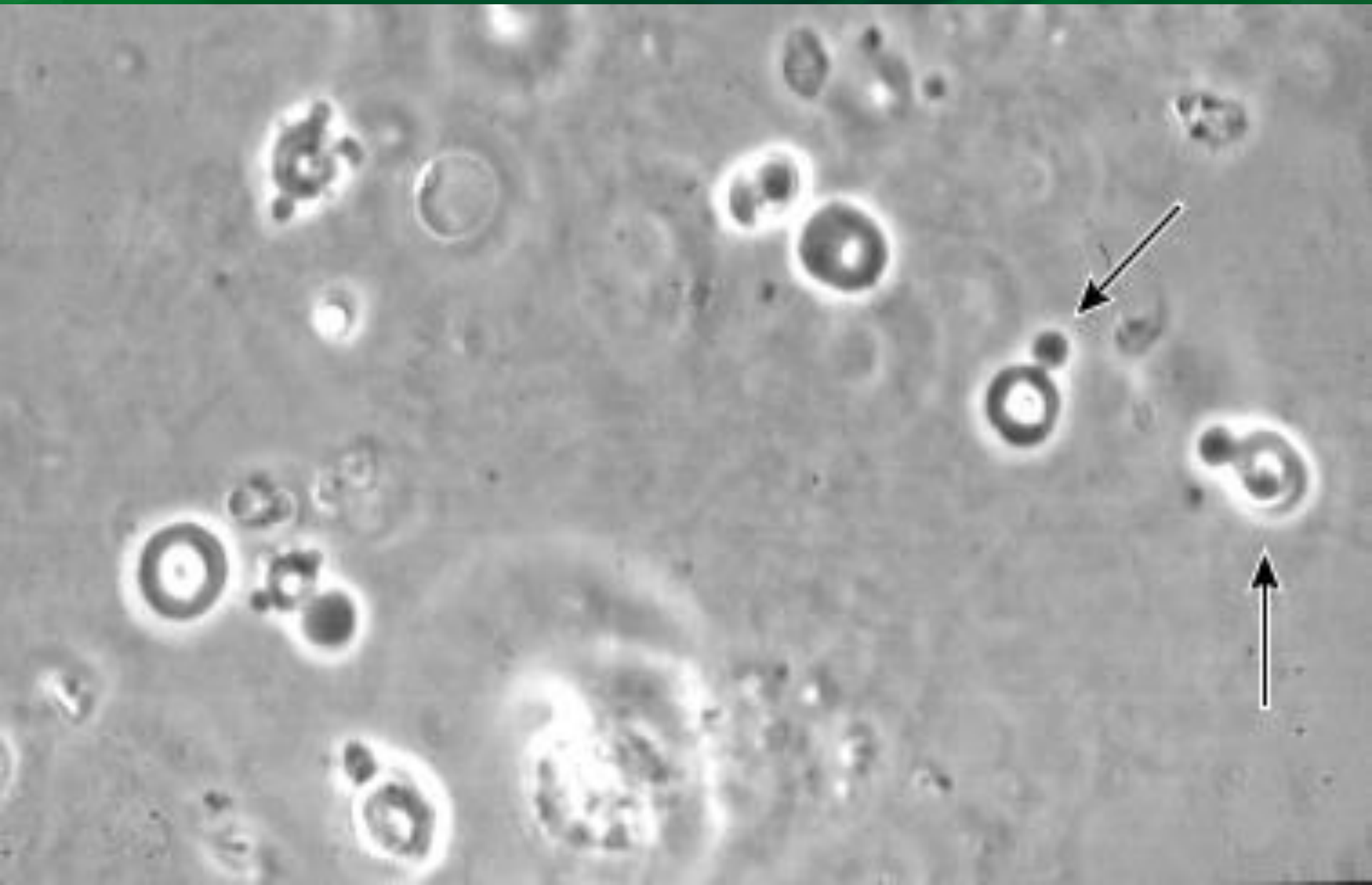
Phase-contrast micrograph showing monomorphic red cells in urine sediment



Urine sediment viewed by phase-contrast microscopy showing many red cells and an occasional larger white cell with a granular cytoplasm (arrows). The red cells have a uniform size and shape, suggesting that they are of nonglomerular origin.

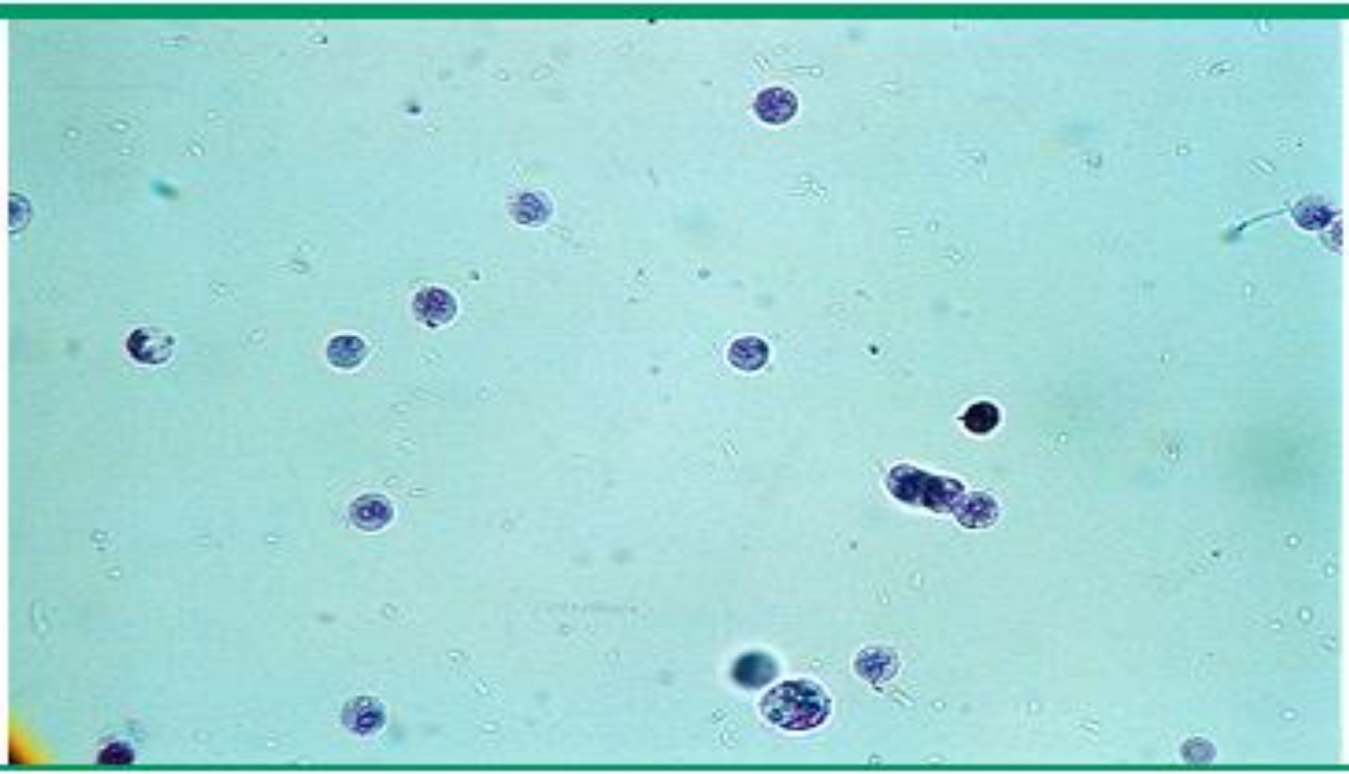
Courtesy of Harvard Medical School.

Dysmorphic RBCs



White blood cells

Photomicrograph of urine sediment with white blood cells



White blood cells in the urine sediment with nuclei and granular cytoplasm.

Courtesy of Frances Andrus, BA, Victoria Hospital, London, Ontario.

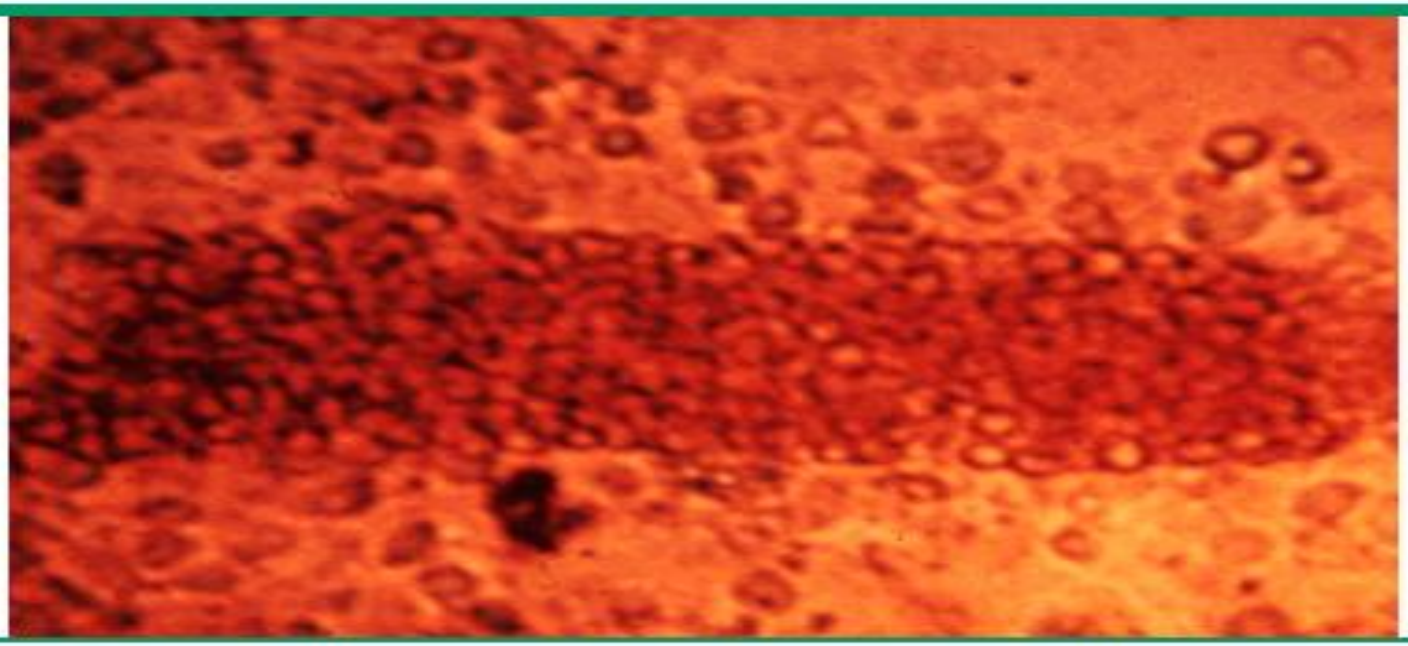
Renal tubular epithelial cells

Urine sediment showing renal tubular epithelial cells and a fragmented epithelial cell cast

This slide shows renal tubular cells (arrows) found in the urine, together with a fragment of a tubular epithelial cell cast (arrowhead). The tubular cells are characterized by one central nucleus and many cytoplasmic granules.

RBC casts, which are usually diagnostic of glomerular hematuria

Photomicrograph of urine sediment with a red cell cast

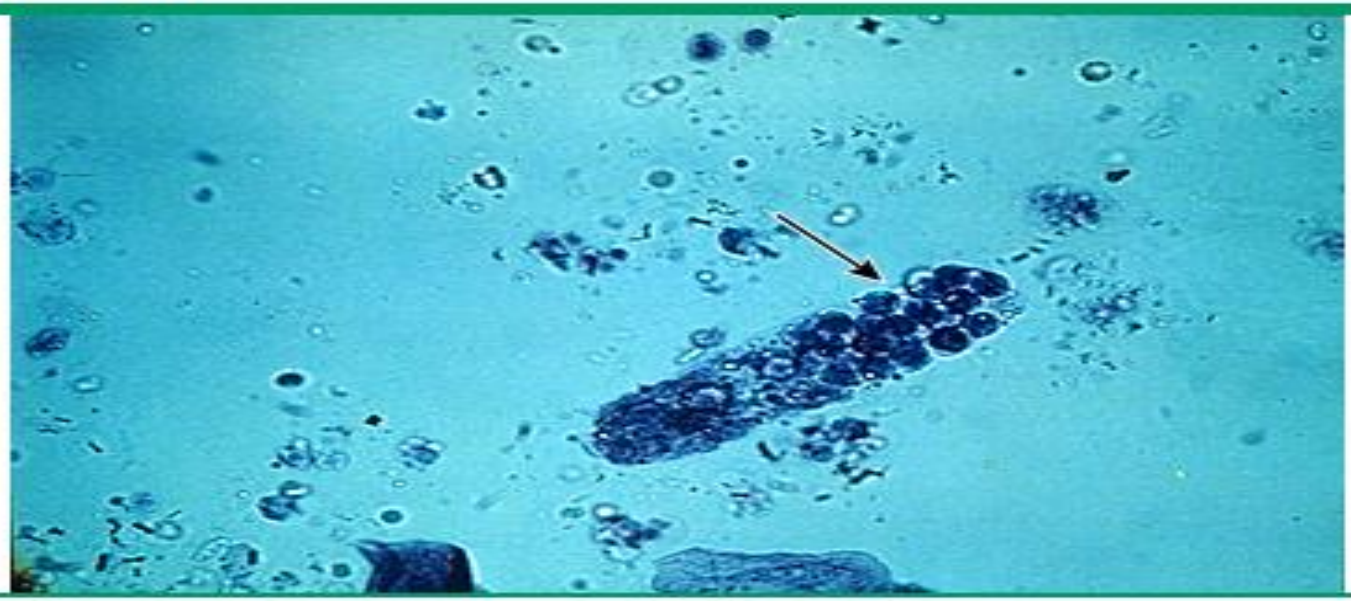


Urine sediment showing free red cells and a red cell cast that is tightly packed with red cells. It is more common for red cell casts to have fewer red cells trapped within a hyaline or granular cast. Red cell casts are virtually diagnostic of glomerulonephritis or vasculitis.

Courtesy of Harvard Medical School.

WBC casts, which are indicative of kidney inflammation,(eg, pyelonephritis, interstitial nephritis)

Photomicrograph of urine sediment with white blood cell cast (I)



White cell cast in which blue stained white cells (arrow) are contained within a granular cast.

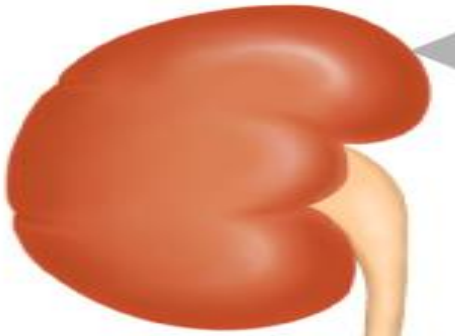
Courtesy of Frances Andrus, BA, Victoria Hospital, London, Ontario.

Muddy brown casts

Hematuria

- Generally, hematuria is defined as the presence of 5 or more red blood cells (RBCs) per high-power field in 3 of 3 consecutive centrifuged specimens obtained at least 1 week apart.
- Hematuria can be either gross (ie, overtly bloody, smoky, or tea-colored urine) or microscopic.

Causes of hematuria



RENAL

Benign renal mass (angiomyolipoma, oncocytoma, abscess)
Malignant renal mass (renal cell carcinoma, transitional cell carcinoma)
Glomerular bleeding (IgA nephropathy, thin basement membrane disease, hereditary nephritis – Alport's syndrome)
Structural disease (polycystic kidney disease, medullary sponge kidney)
Pyelonephritis
Hydronephrosis/ distension
Hypercalciuria/ hyperuricosuria
Malignant hypertension
Renal vein thrombus/ renal artery embolism
Arteriovenous malformation
Papillary necrosis (sickle-cell disease)

MIMICS OF HEMATURIA

Menstruation
Drugs (pyridium, phenytoin, rifampin, nitrofurantoin)
Pigmenturia
Beeturia

URETER

Malignancy
Stone
Stricture
Fibroepithelial polyp
Post-surgical conditions (ureteroiliac fistula)

Renal and/or upper or lower collecting system:

Infection (bacterial, fungal, viral)
Malignancy
Urolithiasis
Tuberculosis
Schistosomiasis
Trauma
Recent instrumentation including lithotripsy
Exercise-induced hematuria
Bleeding diathesis/ anticoagulation*

Upper collecting system

Lower collecting system

BLADDER

Malignancy (transitional cell carcinoma, squamous cell carcinoma)
Radiation
Cystitis

PROSTATE/URETHRA

Benign prostatic hyperplasia
Prostate cancer
Prostatic procedures (biopsy, transurethral resection of the prostate)
Traumatic catheterization
Urethritis
Urethral diverticulum

* Hematuria may not be attributed solely to alterations in coagulation or platelet function until competing causes have been ruled out.

Courtesy of Michael Kurtz, MD.

Proteinuria

- Total urinary protein excretion in the normal adult should be less than 150 mg/day.
- The normal rate of albumin excretion is less than 30 mg/day.

- Persistent albumin excretion between 30 and 300 mg/day is called moderately increased albuminuria (formerly called "microalbuminuria").
- Persistent albumin excretion above 300 mg/day is considered overt proteinuria or severely increased albuminuria (formerly called "macroalbuminuria"), the level at which the standard dipstick becomes positive.

- Two semiquantitative methods are available to screen patients for proteinuria. These are the standard urine dipstick and the precipitation of urine proteins with sulfosalicylic acid (SSA).
- In contrast to the urine dipstick, which primarily detects albumin, SSA detects **all** proteins in the urine.

- Patients with persistent proteinuria should undergo a quantitative measurement of total protein excretion.

- Most commonly, the urine protein-to-creatinine ratio (UPCR) in a spot first- or second-morning urine sample after avoiding exercise is used to estimate 24-hour proteinuria.
- Usually, the urine protein concentration in a spot sample is measured in mg/dL and is divided by the urine creatinine concentration, also measured in mg/dL (at JUH lab it is measured in gm/L (so x100 to make it mg/dl), yielding a dimensionless number that estimates the 24-hour in grams.

Classification and characterization of proteinuria types

Classification of proteinuria	Clinical setting	Typical level of proteinuria
Transient proteinuria	Fever, heavy exercise, vasopressor infusion, albumin infusion	<1 g/day
Persistent proteinuria - orthostatic proteinuria	Uncommon over age 30 years, may occur in 2 to 5 percent of adolescents	<1 to 2 g/day
Persistent proteinuria - overflow proteinuria	Myeloma (monoclonal light chains), Hemolysis (hemoglobinuria), Rhabdomyolysis (myoglobinuria)	Variable, could be nephrotic range
Persistent proteinuria - glomerular proteinuria	Primary glomerular diseases, secondary glomerular diseases, diabetic nephropathy, hypertensive nephrosclerosis	Variable, often nephrotic range
Persistent proteinuria - tubulointerstitial proteinuria	Heavy metal intoxications, autoimmune or allergic interstitial inflammation, medication-induced interstitial injury	<3 g/day
Post-renal proteinuria	Urinary tract infections, nephrolithiasis, genito-urinary tumor	<1 g/day

Kidney Imaging

- Plain KUB… Non yielding… I rarely order these days.
- Renal US. Kidney size, cortical thickness and echogenicity. Renal cysts. Rule out hydronephrosis, Renal calculi greater than 3-5 mm within the renal pelvis with relative insensitivity to ureteric calculi.
- Renal Doppler to assess patency and flow in renal vasculature

- CT scan provides the highest sensitivity for detecting fine calcifications within the kidney parenchyma and through out the collecting system, making unenhanced CT the optimal test for detecting stone disease.
- Contrast enhanced multiphase CT to evaluate kidney masses.

35 yo lady presented to the ER with bilateral LE edema and joint pain. BP was 160/100. Cr was 2.5 with eGFR around 25 ml/min. UA showed 2+ proteinuria, 2+ blood, 5-10 WBCs, +dysmorphic RBCs.

What is your provisional diagnosis?

A. Nephrotic syndrome.
B. Acute glomerulonephritis
C. Pyelonephritis
D. Nephrolithiasis
E. Renal cell carcinoma

75 yo man presented to the ER c/o hematuria. UA showed 3+ blood, 5-10 WBCs, 1+ protein. Monomorphic RBCs on microscopy. Cr was 1.2.

What is the best next step?

A. Renal imaging + cystoscopy.
B. Consult nephrology urgently.
C. D/C home and refer to nephrology clinic as outpatient.
D. D/C home and advise to drink more water.
E. No further testing.

45 yo man presented to the ER c/o bilateral LE edema. Cr was 1.4 with eGFR around 45 ml/min. UA showed 3+ protein, 0-5 RBCs, 0-5 WBCs. Urine protein/Creatinine ration UPCR was around 6.5 gm/day.

What is your provisional diagnosis?

A. Acute nephritic syndrome.
B. Acute Kidney Injury.
C. Nephrolithiasis
D. Acute pyelonephritis
E. Nephrotic syndrome.

60 yo lady presented c/o left loin pain and dysuria. UA showed trace protein, 5-10 RBCs, 40-50 WBCs.

What is your provisional diagnosis?

A. Acute GN.
B. Acute nephrotic syndrome
C. UTI
D. Musculoskeletal back pain
E. Acute appendicitis

35 yo lady prsented c/o LE edema, malar rash and dysuria. UA showed 3+ protein, numerous dysmorphic RBCs and numerous WBCs.

What is your provisional diagnosis?

A. Acute GN
B. Acute UTI
C. Nephrotic Syndrome
D. Acute GN + UTI
E. Nephrolithiasis.

Questions??