Hematuria

Dr. Akram Askar
Nephrology Consultant
Department of Medicine
King Saud University

Definition

- Presence of RBC's in urine
- > 2-3 RBC/HPF(x400) of centrifugal, freshly voided urine
- DD from urine discoloration by pigments
  - Proteinaceous materials; hemoglobin/myoglobin
  - Other substances; food dyes, drugs (Rifampicin)

Initial Approach to Hematuria

Genuine erythrocyturia (i.e not hemoglobinuria/myoglobinruia)?	**Presence of erythrocytes confirmed by microscopy**
Microscopic or macroscopic?	Visible change in color of urine
Intermittent or sustained?	---
Accompanied by proteinuria?	Proteinuria>1000 mg/24 hr
Associated with menstruation or catheterization?	---
Associated with infection?	Pyuria or nitrates, or positive urine microscopy or culture for microorganisms

Types of Hematuria

TYPE	CHARACTERISTICS
Glomerular Hematuria	Microscopic or macroscopic
	Majority of erythrocytes are dysmorphic
	Proteinuria>1000 mg/24 hr
	Presence of erythrocytes casts
	Absence of symptoms, signs or other evidence of nonglomerular hematuria
Non-Glomerular Hematuria	Microscopic or macroscopic
	Majority or erythrocytes have normal morphology
	Proteinuria absent or <0.5 g/g (500 mg/24 hr)
	Symptoms, signs, or other evidence of nonglomerular urinary tract pathology
	Absence of erythrocyte casts
Intermediate hematuria	Microscopic or macroscopic hematuria
	Presence of some dysmorphic erythrocytes
	Proteinuria present but <1000 mg/24 hr
	Absence of erythrocyte casts

Causes of Hematuria

Glomerular hematuria	
Primary Glomerulo-nephritis	Mesangial proliferative glomerulonephritis (typically immunoglobulin A nephropathy)
	Membranoproliferative glomerulonephritis
	Crescentic glomerulonephritis
	Anti–glomerular basement membrane disease
	Focal, segmental glomerulosclerosis
	Membranous glomerulonephritis (<30%)
	Minimal change glomerulonephritis (<20%)
	Fibrillary glomerulopathy
Multisystem autoimmune disease	Systemic lupus erythematosus
	Vasculitis (e.g., Wegener's granulomatosis, microscopic polyangiitis, Churg-Strauss angiitis, Henoch-Schönlein purpura)
	Scleroderma glomerulopathy
	Thrombotic microangiopathy (e.g., anti-phospholipid syndrome, hemolytic uremic syndrome)
Other	Hereditary (e.g., Alport's disease, thin membrane disease, nail-patella syndrome, Fabry's disease)
	Infection-associated glomerulonephritis (e.g., HIV nephropathy, poststreptococcal glomerulonephritis, infective endocarditis, shunt nephritis)

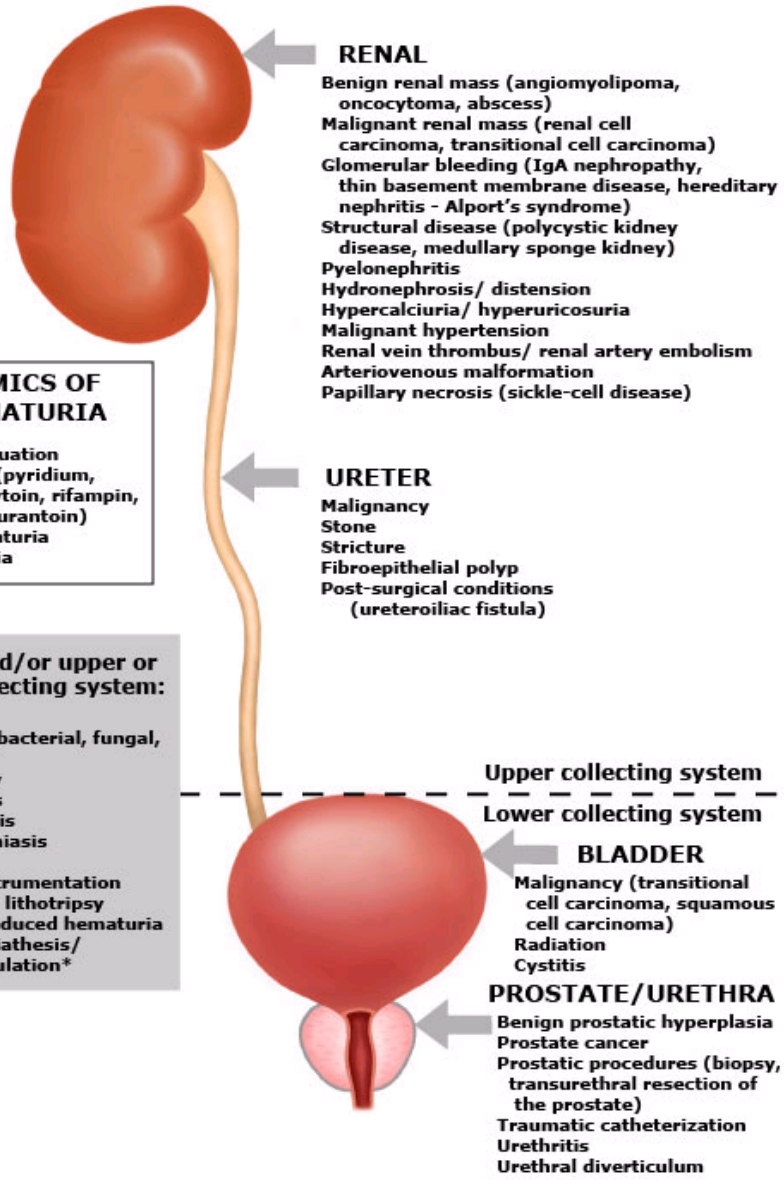
Causes of Hematuria

Nonglomerular hematuria	
Renal origin	Tubulointerstitial disorder
	Hypersensitivity tubulointerstitial nephritis
	Tubulointerstitial nephritis with uveitis
	Sjögren's syndrome
	Vascular disorder
	Malignant hypertension
	Scleroderma renal crisis
	Polyarteritis nodosa
	Renal embolism or arterial or venous thrombosis
	Arteriovenous malformation
	Neoplasia (e.g., renal cell carcinoma, Wilms' tumor, leukemia, lymphoma, metastatic disease)
	Papillary necrosis (causes include diabetes mellitus, sickle cell anemia, analgesic abuse, and obstructive uropathy)
	Infection (e.g., pyelonephritis, tuberculosis, hantavirus, BK virus in transplants)
	Hereditary (e.g., polycystic kidney disease, medullary sponge kidney)
	Trauma
	Idiopathic renal hematuria

Nonglomerular hematuria	
Urinary tract origin	Neoplasia
	Transitional cell carcinoma
	Carcinoma of bladder, prostate, or urethra
	Calculi (e.g., calcium oxalate/phosphate, uric acid, xanthine, cysteine, struvite, drugs)
	Trauma or foreign body
	Infection (e.g., periureteritis, cystitis, prostatitis, urethritis, tuberculosis, Schistosoma haematobium)
	Malformations
	Nevi
	Vascular malformations
	Hereditary hemorrhagic telangiectasia
	Inflammatory
	Retroperitoneal fibrosis/aortitis
	Endometriosis
	Diverticulitis, appendicitis, Crohn’s disease
	Hypersensitivity cystitis or urethritis
	Vasculitis (polyarteritis nodosa and Churg-Strauss angiitis)
	Drug and radiation-induced hematuria (e.g., by cyclophosphamide, nitrogen mustard)
	Urinary obstruction or relief of obstruction

Nonglomerular hematuria	
Other	Loin-pain hematuria syndrome
	Acquired cystic disease of renal failure
	Coagulation disorder (e.g., thrombocytopenia, hemophilia, anticoagulant therapy)
	Factitious (malingering)

Causes of hematuria



* 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.

Approach to the patient with Hematuria

- **History**
  - Recent symptoms
    - Fever
    - Rash
    - Weight loss
  - Previous disease
    - Diabetes Mellitus
    - Malignancy
  - Family History
  - Drug history
    - Anti-coagulant
    - Herbal medicine

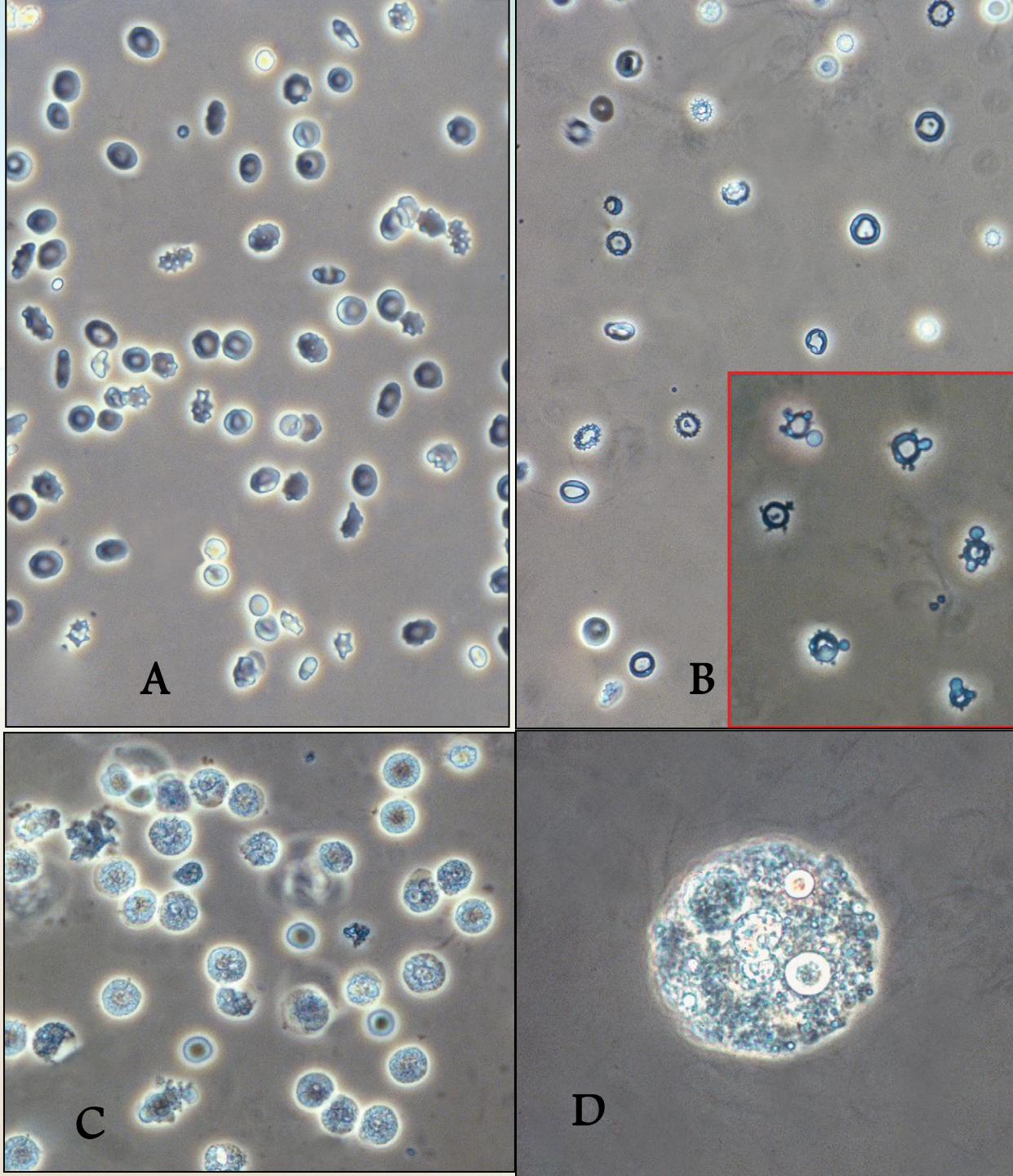
Approach to the patient with Hematuria

- **Examination**
  - Purpura in vasculitis
  - Deafness in Alport Syndrome
  - Flank mass in polycystic disease
- **Type of hematuria from urine examination**

Laboratory Investigation of Glomerular Hematuria

DIAGNOSIS	RELEVANT ABNORMAL INVESTIGATIONS
Membranoproliferative glomerulonephritis (MPGN)	C3/C4, C3 nephritic factor, cryoglobulins, hepatitis B/C
Anti–GBM disease	Anti-GBM antibodies, chest radiograph
Systemic lupus erythematosus	ANA, anti-dsDNA, ENAs, C3/C4, anticardiolipin
Vasculitis (Wegener's granulomatosis, microscopic polyangiitis, Churg-Strauss angiitis)	ANCA (C-ANCA/PR3-ANCA or PANCA/MPO-ANCA)
Thrombotic microangiopathy	Anti-cardiolipin, lupus anticoagulant
Hereditary	
Alport's disease	Audiometry
Fabry's disease	Plasma alpha-galactosidase A activity
Infection-associated glomerulonephritis	
HIV nephropathy	HIV
Poststreptococcal glomerulonephritis	ASO, anti-DNAase, C3/C4, rheumatoid factor
Infective endocarditis	Echocardiography, C3/C4, rheumatoid factor

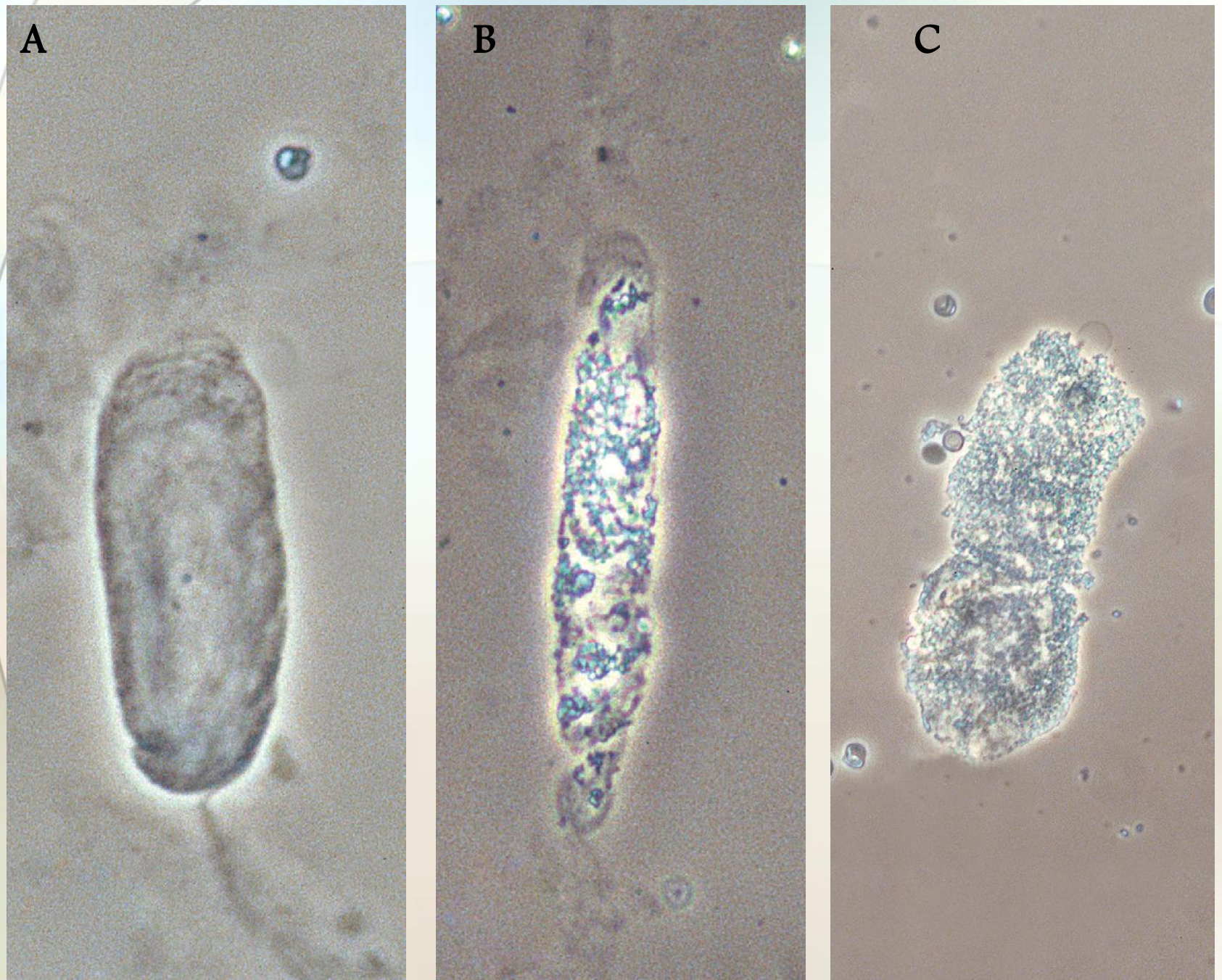
Urinary sediment cells.
A. Isomorphic nonglomerular erythrocytes. The *arrows indicate the so-called crenated erythrocytes, which are* a frequent finding in nonglomerular hematuria.
B. Dysmorphic glomerular erythrocytes. The dysmorphism consists mainly of irregularities of the cellcmembrane. *Inset, Acanthocytes with their typical ring-formed cell bodies with one or more blebs of different sizes and shapes.*
C. *Neutrophils.*
Note: their typical lobulated nucleus and granular cytoplasm.
D. A granular phagocytic macrophage (diameter about 60 μm).

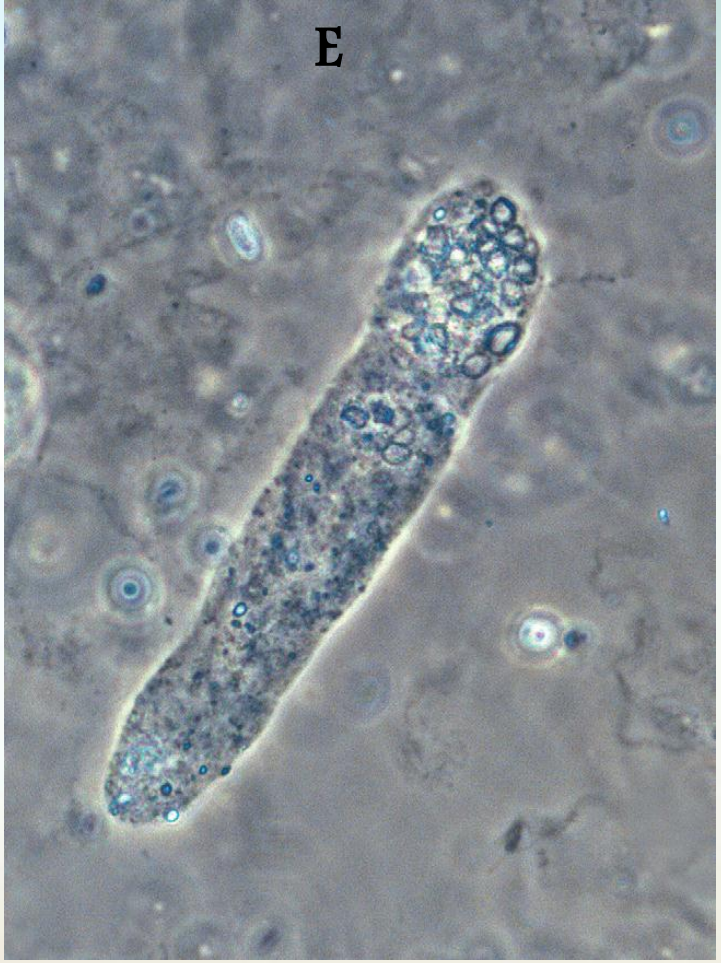


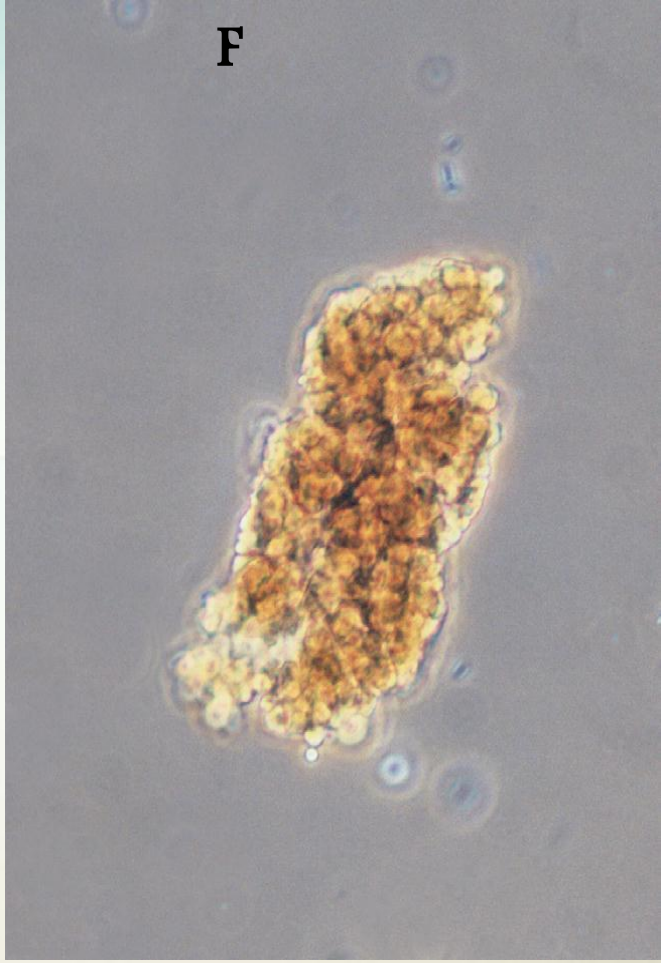
Clinical Significance of Urinary Casts

Cast	Main Clinical Associations
Hyaline	Normal subject and renal disease
Hyaline-granular	Normal subject and renal disease
Granular	Renal disease
Waxy	Renal impairment; rapidly progressive renal disease
Fatty	Marked proteinuria; nephrotic syndrome
Erythrocyte	Glomerular hematuria; proliferative or necrotizing glomerulonephritis
Hemoglobin	The same as the erythrocyte cast; hemoglobinuria due to intravascular hemolysis
Leukocyte	Acute interstitial nephritis; acute pyelonephritis; proliferative glomerulonephritis
Renal tubular epithelial cell (epithelial casts)	Acute tubular necrosis; acute interstitial nephritis; proliferative glomerulonephritis; nephrotic syndrome
Myoglobin	Rhabdomyolysis
Bacterial, fungal	Bacterial or fungal infection in the kidney

Casts. A. Hyaline cast. B. Hyaline-granular cast. C. Finely granular c





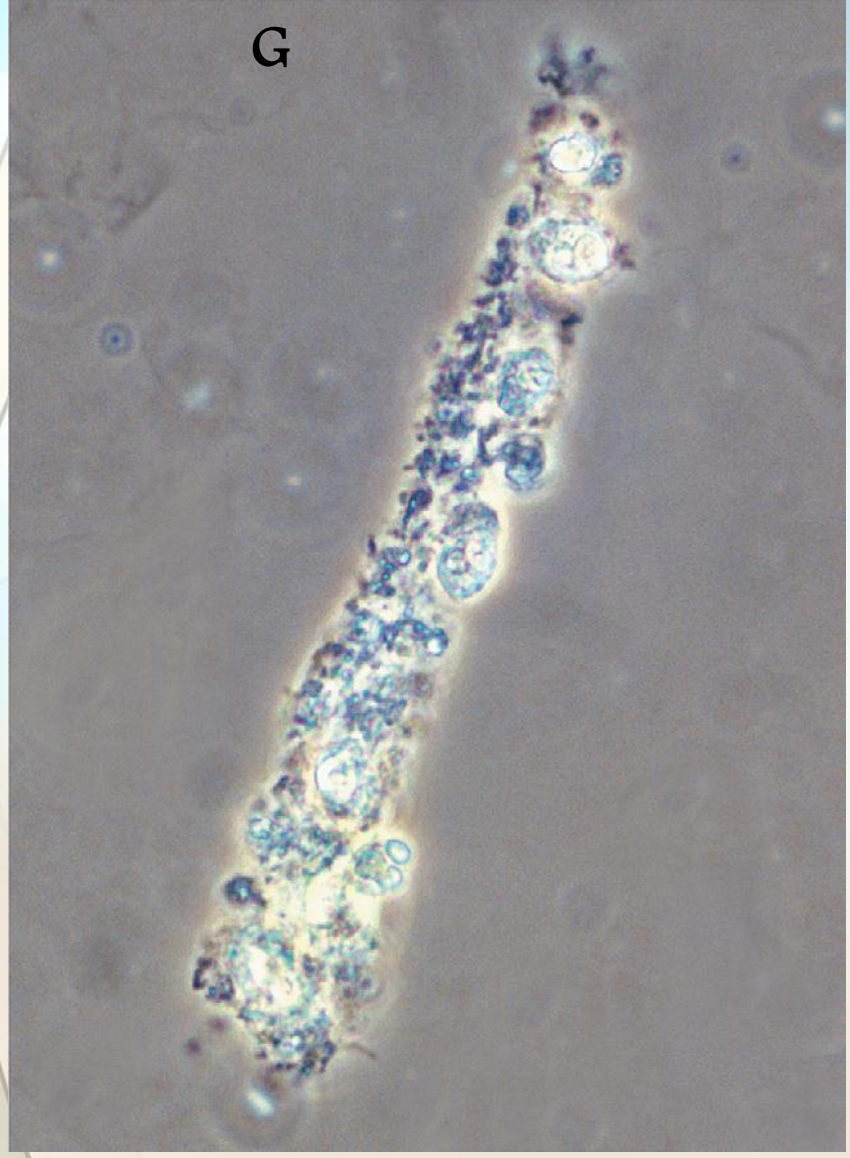


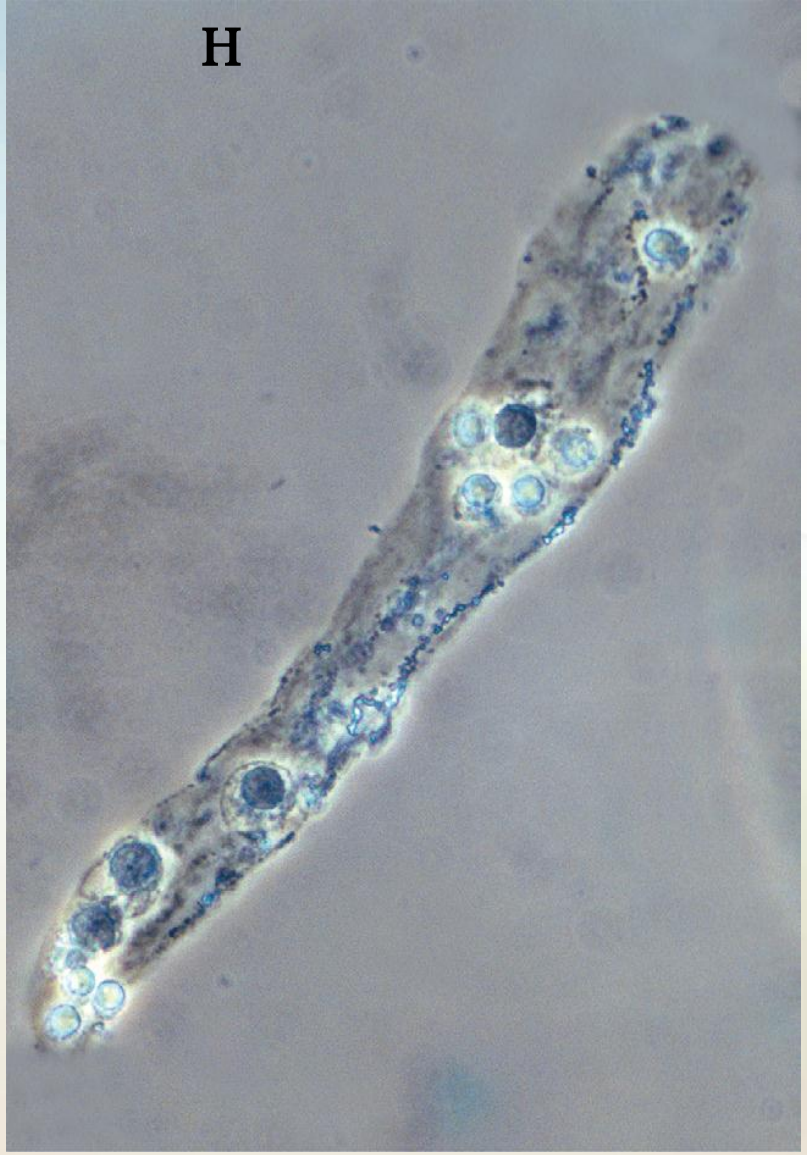
D. Waxy cast.

E. Erythrocyte casts.

F. Hemoglobin casts

(note typical brownish hue).

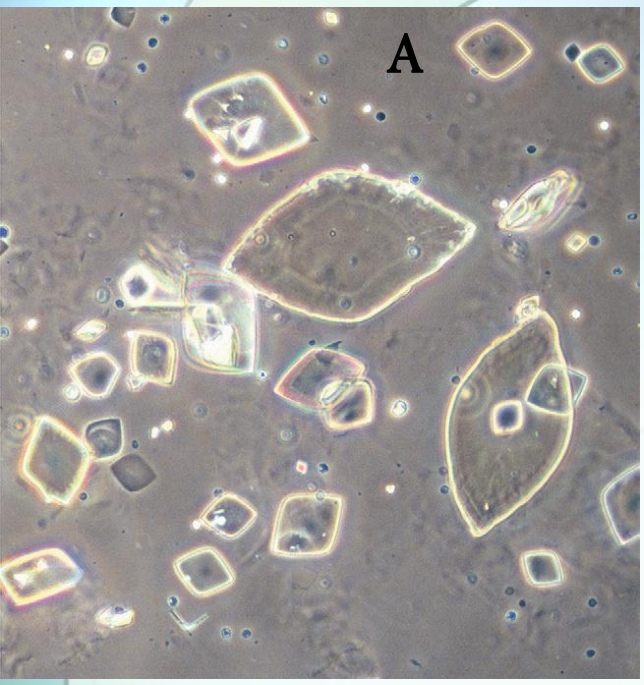


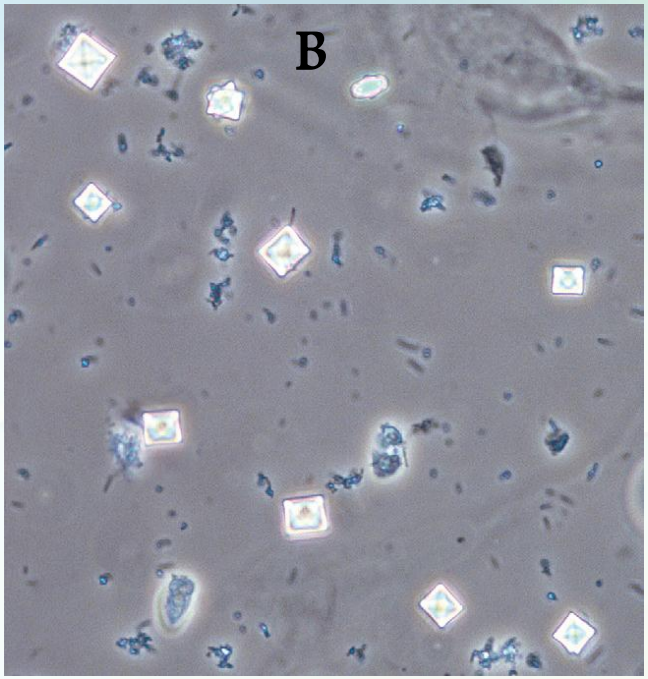


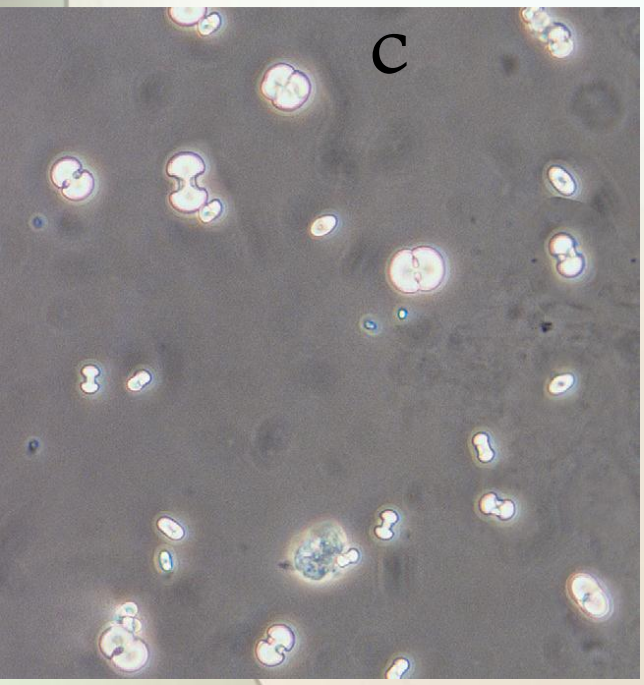
G. Leukocyte cast. The polymorphonuclear leukocytes are identifiable by their lobulated nucleus *(arrows).*

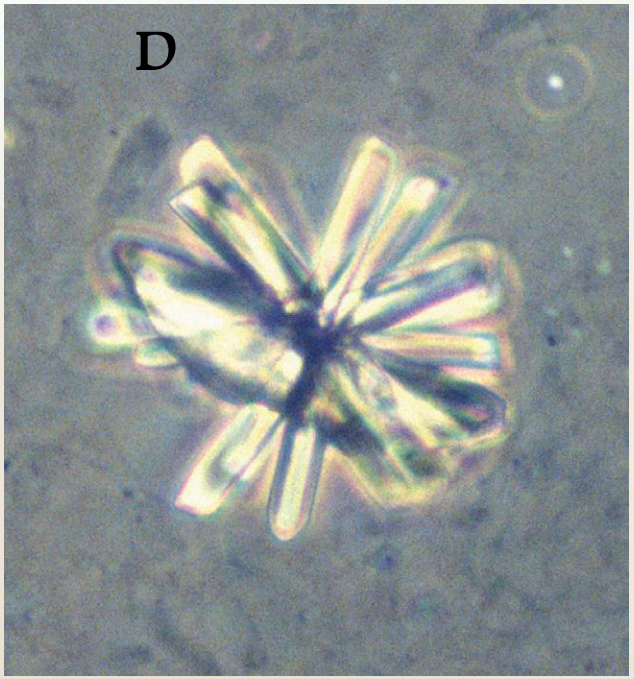
H. *Epithelial cell* casts. Renal tubular cells are identifiable by their large nucleus.

(All images by phase contrast microscopy; original magnification ×400.)









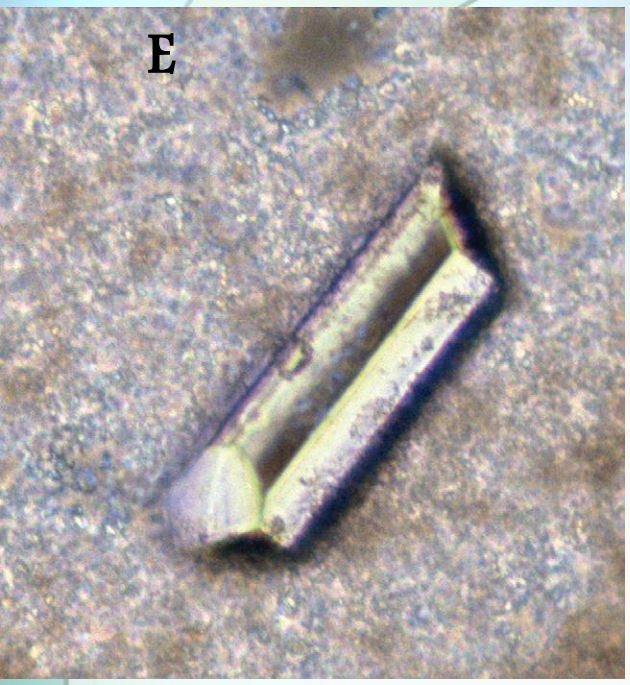
Crystals.

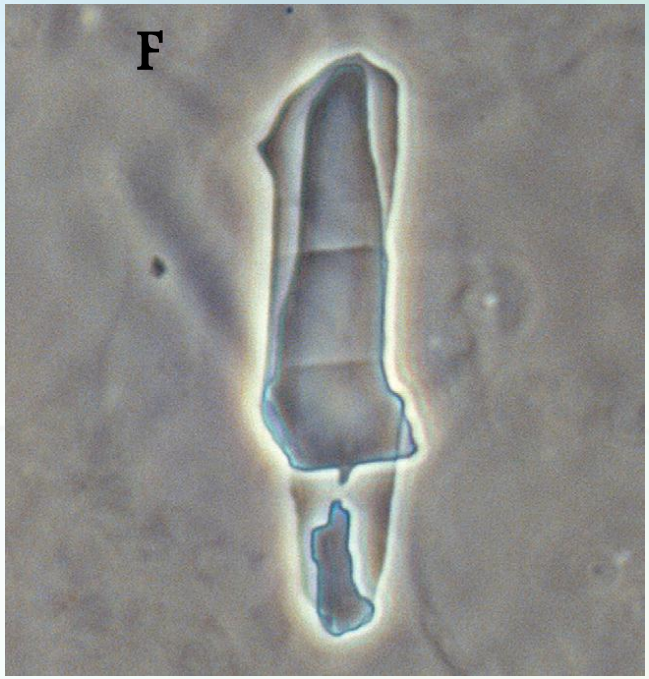
A.Uric acid crystals. This rhomboid shape is the most frequent.

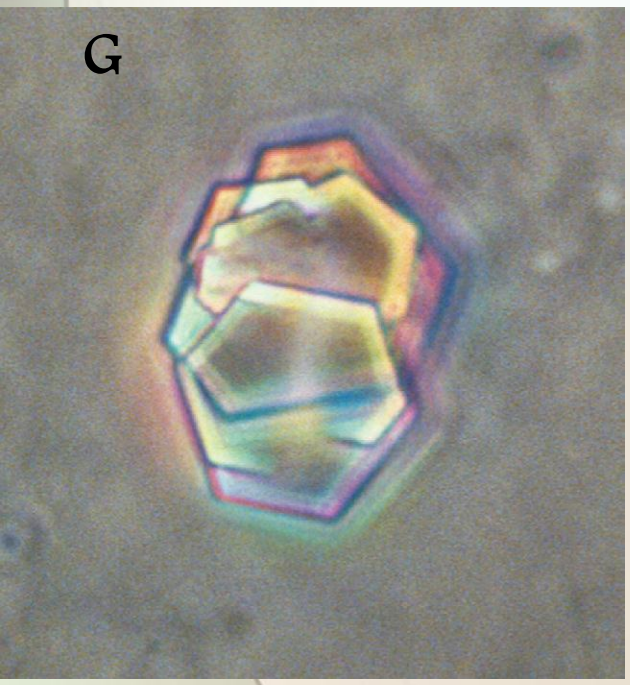
B. Bihydrated calcium oxalate crystals with their typical appearance of a “letter envelope.”

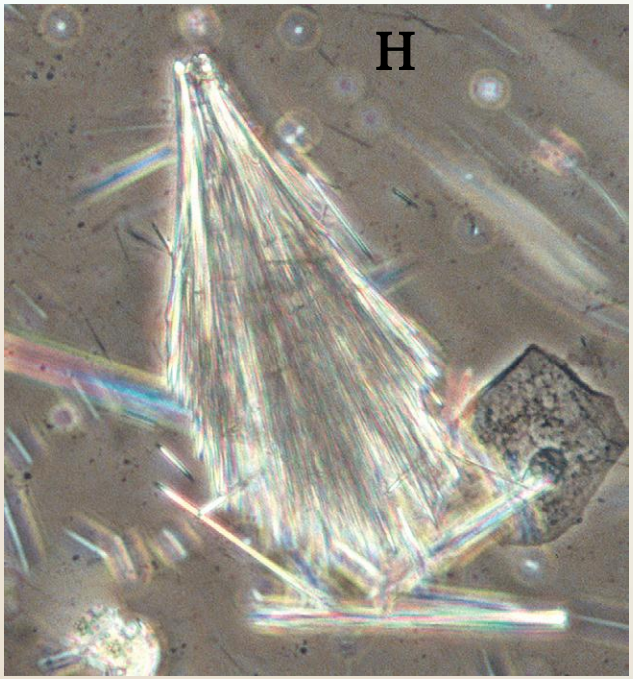
C. Different types of monohydrated calcium oxalate crystals.

D. A star-like calcium phosphate crystal.







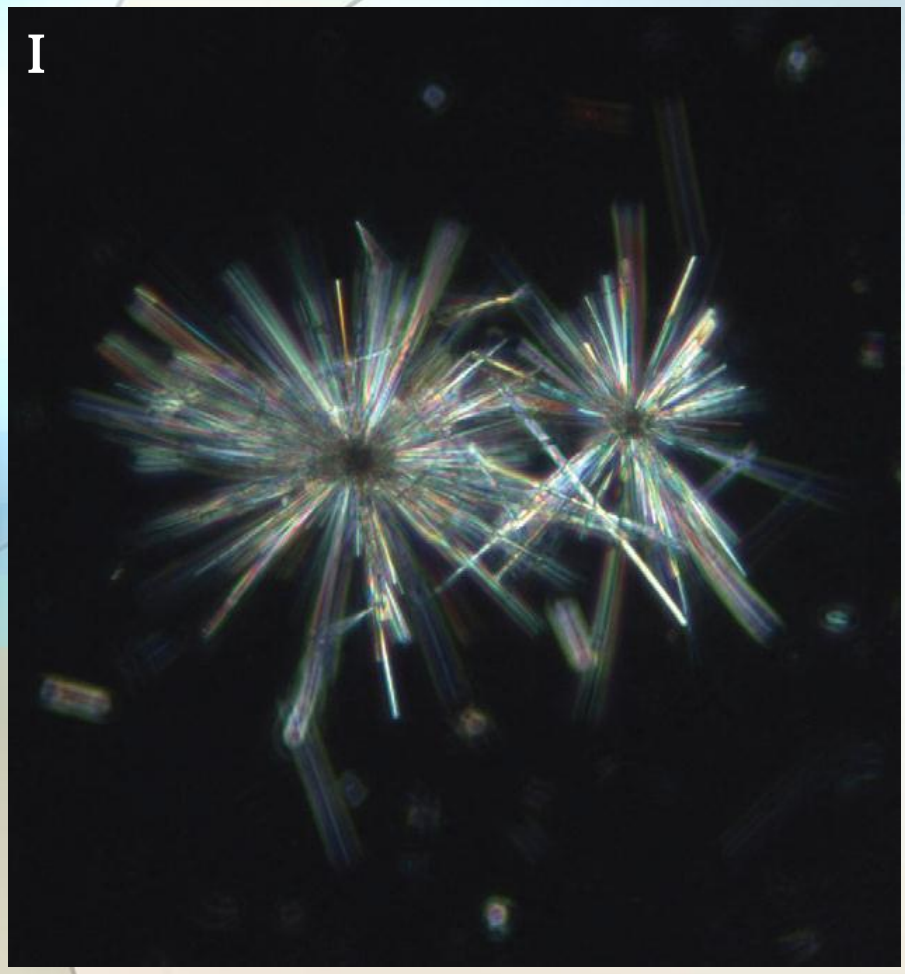


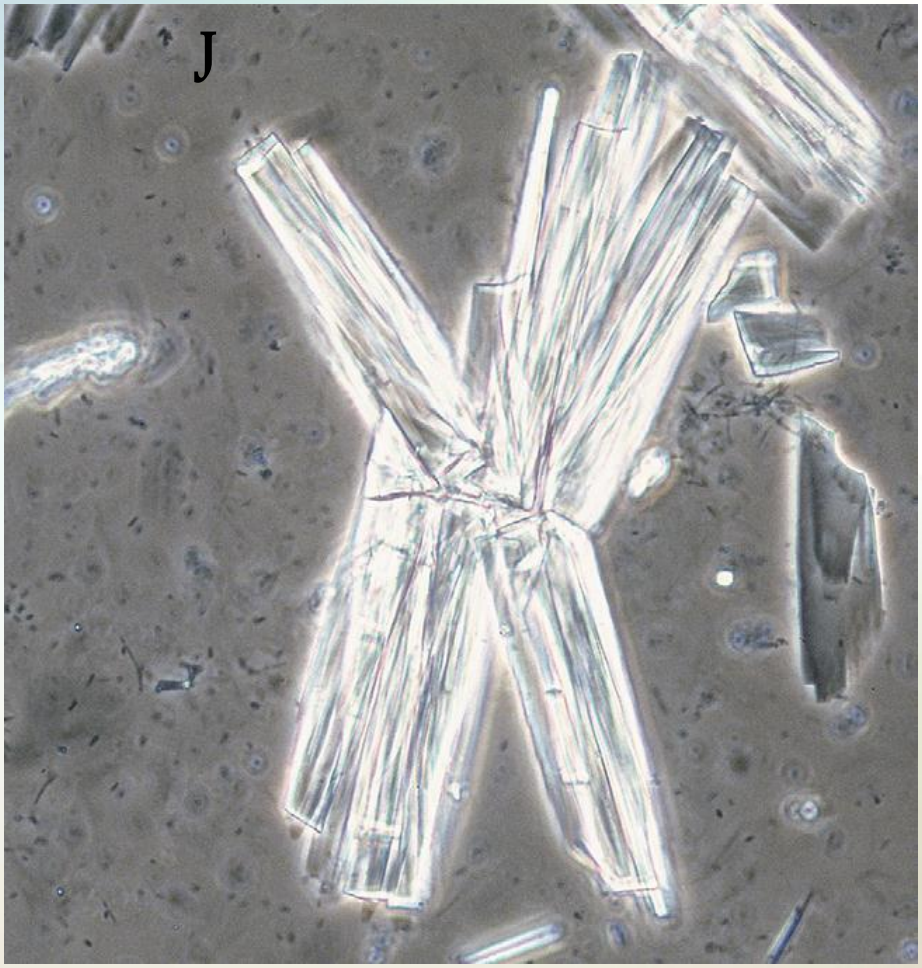
E. Triple phosphate crystal, on the background of a massive amount of amorphous phosphate particles.

F. Cholesterol crystal.

G. Cystine crystals heaped one on the other.

H. Amoxicillin crystal resembling a branch of a broom bush.





I. Star-like ciprofloxacin crystals as seen by polarized light.

J. A large crystal of indinavir.

(All images by phase contrast microscopy; original magnification ×400.)


Thank You!