MORPHOLOGY

The distinctive morphologic changes in gout are (1) acute arthritis, (2) chronic tophaceous arthritis, (3) tophi in various sites, and (4) gouty nephropathy.

Acute arthritis is characterized by a dense neutrophilic infiltrate that permeates the synovium and synovial fluid. MSU crystals are frequently found in the cytoplasm of the neutrophils and are arranged in small clusters in the synovium. They are long, slender, and needle-shaped, and are negatively birefringent. The synovium is edematous and congested, and also contains scattered lymphocytes, plasma cells, and macrophages. When the episode of crystallization abates and the crystals are resolubilized, the acute attack remits.

Chronic tophaceous arthritis evolves from the repetitive precipitation of urate crystals during acute attacks. The MSU encrusts the articular surface and forms visible deposits in the synovium (Fig. 26-47*A*). The synovium becomes hyperplastic, fibrotic, and thickened by inflammatory cells and forms a pannus that destroys the underlying cartilage and lead to juxta-articular bone erosions. In severe cases, fibrous or bony ankylosis ensues, resulting in loss of joint function.

Tophi are the pathognomonic hallmark of gout. They are formed by large aggregations of urate crystals surrounded by an intense inflammatory reaction of foreign body giant cells. (Fig. 26-47*B,C*). Tophi may appear in the articular cartilage, ligaments, tendons, and bursae. Less frequently they may occur in soft tissues (earlobes, fingertips) or kidneys. Superficial tophi can ulcerate through the overlying skin.

Gouty nephropathy (Chapter 20) refers to the renal complications caused by MSU crystals or tophi in the renal medullary interstitium or tubules. Complications include uric acid nephrolithiasis and pyelonephritis, particularly when the urates induce urinary obstruction.

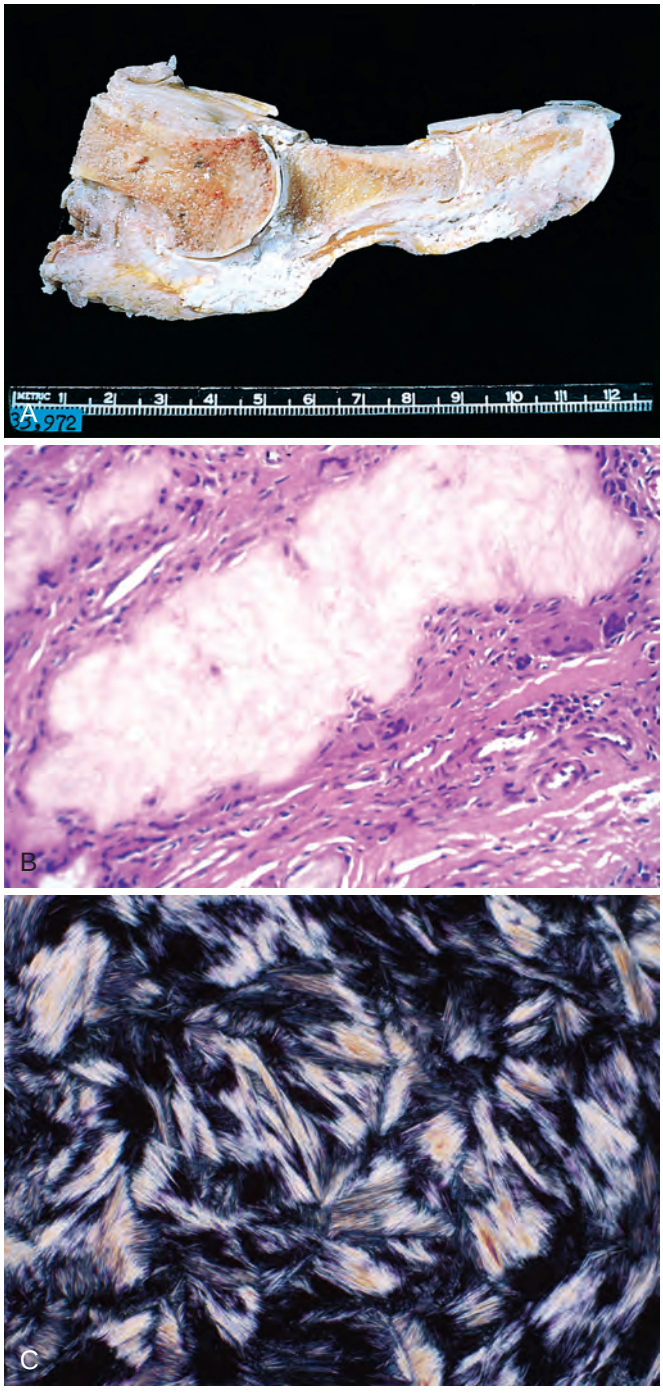

Figure 26-47 Gout. **A,** Amputated great toe with white tophi involving the joint and soft tissues. **B,** Gouty tophus—an aggregate of dissolved urate crystals is surrounded by reactive fibroblasts, mononuclear inflammatory cells, and giant cells. **C,** Urate crystals are needle shaped and negatively birefringent under polarized light.

Clinical Course. Gout is more common in men and after the age of 30. Patients with obesity, metabolic syndrome, excess alcohol intake and renal failure are at increased risk.

Four clinical stages are recognized:

- *Asymptomatic hyperuricemia* appears around puberty in males and after menopause in females.
- *Acute arthritis* presents after several years as sudden onset of excruciating joint pain associated with localized hyperemia, warmth. Constitutional symptoms are uncommon except for occasional mild fever. Most first attacks are monoarticular; 50% occur in the first metatarsophalangeal joint. Eventually, about 90% of affected individuals experience acute attacks in the following locations (in descending order of frequency): insteps, ankles, heels, knees, wrists, fingers, and elbows. Untreated, acute gouty arthritis may last for hours to weeks, but gradually there is complete resolution.
- *Asymptomatic intercritical period*: Resolution of the acute arthritis leads to a symptom free interval. Although some patients never have another attack, most experience a second acute episode within months to a few years. In the absence of appropriate therapy, the attacks recur at shorter intervals and frequently become polyarticular.
- *Chronic tophaceous gout* develops on average about 12 years after the initial acute attack and the appearance of chronic tophaceous arthritis. At this stage, radiographs show characteristic juxta-articular bone erosion caused by osteoclastic bone resorption and loss of the joint space. Progression leads to severe crippling disease.

Renal manifestations sometimes appear in the form of renal colic associated with the passage of gravel and stones and may proceed to chronic gouty nephropathy. About 20% of those with chronic gout die of renal failure.