These conversions account for the often dramatic play of colors seen in a healing bruise, which typically changes from red-blue to green-blue to golden-yellow before it is resolved.

When there is *systemic overload of iron* hemosiderin may be deposited in many organs and tissues, a condition called *hemosiderosis*. The main causes of hemosiderosis are (1) increased absorption of dietary iron due to an inborn error of metabolism called hemochromatosis, (2) hemolytic anemias, in which premature lysis of red cells leads to release of abnormal quantities of iron, and (3) repeated blood transfusions, because transfused red cells constitute an exogenous load of iron. These conditions are discussed in Chapters 14 and 18.

Pathologic Calcification

Pathologic calcification is the abnormal tissue deposition of calcium salts, together with smaller amounts of iron, magnesium, and other mineral salts. There are two forms of pathologic calcification. When the deposition occurs locally in dying tissues it is known as *dystrophic calcification*; it occurs despite normal serum levels of calcium and in the absence of derangements in calcium metabolism. In contrast, the deposition of calcium salts in otherwise normal tissues is known as *metastatic calcification*, and it almost always results from hypercalcemia secondary to some disturbance in calcium metabolism.

Dystrophic Calcification

Dystrophic calcification is encountered in areas of necrosis, whether they are of coagulative, caseous, or liquefactive type, and in foci of enzymatic necrosis of fat. Calcification is almost always present in the atheromas of advanced atherosclerosis. It also commonly develops in aging or damaged heart valves, further hampering their function (Fig. 2-34). Whatever the site of deposition, the calcium salts appear macroscopically as fine, white granules or clumps, often felt as gritty deposits. Sometimes a tuberculous lymph node is virtually converted to stone.

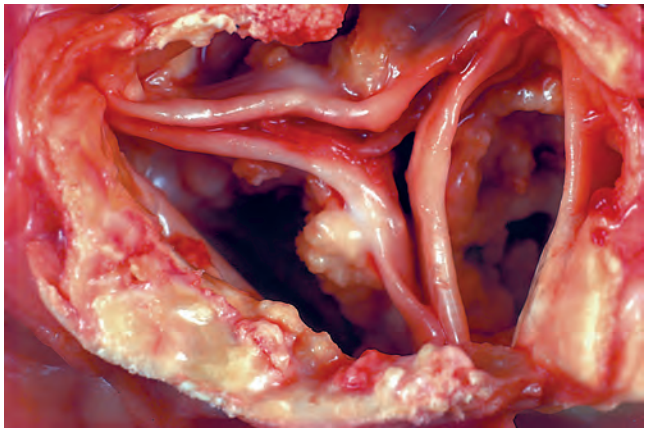

Figure 2-34 Dystrophic calcification of the aortic valve. View looking down onto the unopened aortic valve in a heart with calcific aortic stenosis. It is markedly narrowed (stenosis). The semilunar cusps are thickened and fibrotic, and behind each cusp are irregular masses of piled-up dystrophic calcification.

MORPHOLOGY

Histologically, with the usual hematoxylin and eosin stain, calcium salts have a basophilic, amorphous granular, sometimes clumped appearance. They can be intracellular, extracellular, or in both locations. In the course of time, **heterotopic** bone may be formed in the focus of calcification. On occasion single necrotic cells may constitute seed crystals that become encrusted by the mineral deposits. The progressive acquisition of outer layers may create lamellated configurations, called **psammoma bodies** because of their resemblance to grains of sand. Some types of papillary cancers (e.g., thyroid) are apt to develop psammoma bodies. In asbestosis, calcium and iron salts gather about long slender spicules of asbestos in the lung, creating exotic, beaded dumbbell forms (Chapter 15).

Although dystrophic calcification may simply be a telltale sign of previous cell injury, it is often a cause of organ dysfunction. Such is the case in calcific valvular disease and atherosclerosis, as will become clear in further discussion of these diseases. Serum calcium is normal in dystrophic calcification.

Metastatic Calcification

Metastatic calcification may occur in normal tissues whenever there is hypercalcemia. Hypercalcemia also accentuates dystrophic calcification. There are four principal causes of hypercalcemia: (1) increased secretion of parathyroid hormone (PTH) with subsequent bone resorption, as in *hyperparathyroidism* due to parathyroid tumors, and ectopic secretion of PTH-related protein by malignant tumors (Chapter 7); (2) *resorption of bone tissue*, secondary to primary tumors of bone marrow (e.g., multiple myeloma, leukemia) or diffuse skeletal metastasis (e.g., breast cancer), accelerated bone turnover (e.g., Paget disease), or immobilization; (3) *vitamin D–related disorders*, including vitamin D intoxication, sarcoidosis (in which macrophages activate a vitamin D precursor), and idiopathic hypercalcemia of infancy (Williams syndrome), characterized by abnormal sensitivity to vitamin D; and (4) *renal failure*, which causes retention of phosphate, leading to secondary hyperparathyroidism. Less common causes include aluminum intoxication, which occurs in patients on chronic renal dialysis, and milk-alkali syndrome, which is due to excessive ingestion of calcium and absorbable antacids such as milk or calcium carbonate.

Metastatic calcification may occur widely throughout the body but principally affects the interstitial tissues of the gastric mucosa, kidneys, lungs, systemic arteries, and pulmonary veins. Although quite different in location, all of these tissues excrete acid and therefore have an internal alkaline compartment that predisposes them to metastatic calcification. In all these sites, the calcium salts morphologically resemble those described in dystrophic calcification. Thus, they may occur as noncrystalline amorphous deposits or, at other times, as hydroxyapatite crystals.

Usually the mineral salts cause no clinical dysfunction, but on occasion massive involvement of the lungs produces remarkable x-ray images and respiratory compromise. Massive deposits in the kidney (nephrocalcinosis) may in time cause renal damage (Chapter 20).