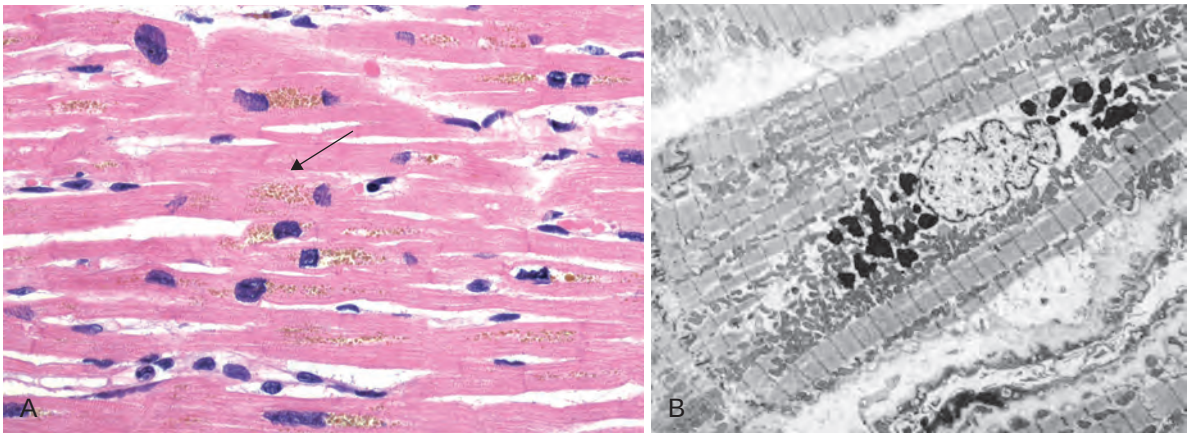

Figure 2-33 Lipofuscin granules in a cardiac myocyte shown by **(A)** light microscopy (deposits indicated by *arrows*), and **(B)** electron microscopy (note the perinuclear, intralysosomal location).

in renal tubular epithelial cells, as well as within liver cells, β cells of the islets of Langerhans, and heart muscle cells.

Glycogen accumulates within the cells in a group of related genetic disorders that are collectively referred to as the *glycogen storage diseases*, or *glycogenoses* (Chapter 5). In these diseases enzymatic defects in the synthesis or breakdown of glycogen result in massive accumulation, causing cell injury and cell death.

Pigments

Pigments are colored substances, some of which are normal constituents of cells (e.g., melanin), whereas others are abnormal and accumulate in cells only under special circumstances. Pigments can be exogenous, coming from outside the body, or endogenous, synthesized within the body itself.

Exogenous Pigments

The most common exogenous pigment is carbon (coal dust), a ubiquitous air pollutant in urban areas. When inhaled it is picked up by macrophages within the alveoli and is then transported through lymphatic channels to the regional lymph nodes in the tracheobronchial region. Accumulations of this pigment blacken the tissues of the lungs *(anthracosis)* and the involved lymph nodes. In coal miners the aggregates of carbon dust may induce a fibroblastic reaction or even emphysema and thus cause a serious lung disease known as *coal worker's pneumoconiosis* (Chapter 15). *Tattooing* is a form of localized, exogenous pigmentation of the skin. The pigments inoculated are phagocytosed by dermal macrophages, in which they reside for the remainder of the life of the embellished (sometimes with embarrassing consequences for the bearer of the tattoo when proposing to Mary while the tattoo says Valerie!). The pigments do not usually evoke any inflammatory response.

Endogenous Pigments

Lipofuscin is an insoluble pigment, also known as lipochrome or wear-and-tear pigment. Lipofuscin is composed of polymers of lipids and phospholipids in complex with protein, suggesting that it is derived through lipid peroxidation of polyunsaturated lipids of subcellular membranes. Lipofuscin is not injurious to the cell or its functions. Its importance lies in its being a telltale sign of free radical injury and lipid peroxidation. The term is derived from the Latin (*fuscus*, brown), referring to brown lipid. In tissue sections it appears as a yellow-brown, finely granular cytoplasmic, often perinuclear, pigment (Fig. 2-33). It is seen in cells undergoing slow, regressive changes and is particularly prominent in the liver and heart of aging patients or patients with severe malnutrition and cancer cachexia.

Melanin, derived from the Greek (*melas*, black), is an endogenous, brown-black, pigment formed when the enzyme tyrosinase catalyzes the oxidation of tyrosine to dihydroxyphenylalanine in melanocytes. It is discussed further in Chapter 25. For practical purposes melanin is the *only endogenous brown-black pigment*. The only other that could be considered in this category is homogentisic acid, a black pigment that occurs in patients with *alkaptonuria*, a rare metabolic disease. Here the pigment is deposited in the skin, connective tissue, and cartilage, and the pigmentation is known as *ochronosis.*

Hemosiderin, a hemoglobin-derived, golden yellow-to-brown, granular or crystalline pigment is one of the major storage forms of iron. Iron metabolism and hemosiderin are considered in detail in Chapters 14 and 18. Iron is normally carried by specific transport protein called transferrin. In cells, it is stored in association with a protein, apoferritin, to form ferritin micelles. Ferritin is a constituent of most cell types. *When there is a local or systemic excess of iron, ferritin forms hemosiderin granules*, which are easily seen with the light microscope. Hemosiderin pigment represents aggregates of ferritin micelles. Under normal conditions small amounts of hemosiderin can be seen in the mononuclear phagocytes of the bone marrow, spleen, and liver, which are actively engaged in red cell breakdown.

Local or systemic excesses of iron cause hemosiderin to accumulate within cells. *Local excesses* result from hemorrhages in tissues. The best example of localized hemosiderosis is the common bruise. Extravasated red cells at the site of injury are phagocytosed over several days by macrophages, which break down the hemoglobin and recover the iron. After removal of iron, the heme moiety is converted first to biliverdin ("green bile") and then to bilirubin ("red bile"). In parallel, the iron released from heme is incorporated into ferritin and eventually hemosiderin.