in all cell shape changes such as those during endocytosis, exocytosis, and cell locomotion.

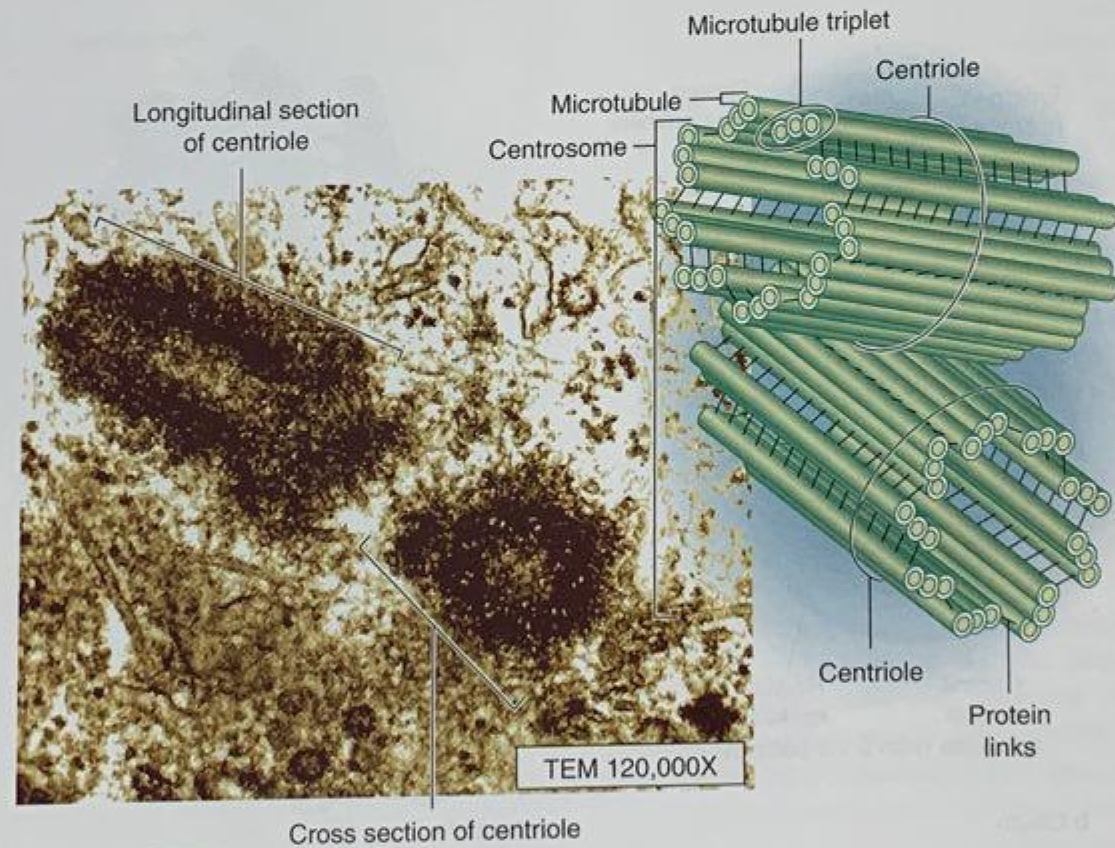
3. Microfilaments are intimately associated with several cytoplasmic organelles, vesicles, and granules and play a role in moving or shifting cytoplasmic components (cytoplasmic streaming).
4. Microfilaments are associated with myosin and form a "purse-string" ring of filaments whose constriction results in the cleavage of mitotic cells.
5. In crawling cells actin filaments are organized into parallel contractile bundles called **stress fibers** (Figure 2–20C).

Although actin filaments in muscle cells are structurally stable, in nonmuscle cells they readily dissociate and reassemble. Actin filament polymerization appears to be under the direct control of minute changes in Ca^{2+} and cyclic AMP levels. A large number of **actin-binding proteins** with different activities have been demonstrated in various cells and include:

- actin motor proteins such as the *myosins,* which carry other molecules or vesicles along microfilaments,
- actin-capping proteins such as *tropomyosin,* which bind the free end and stabilize microfilaments,
- actin filament-severing proteins such as *gelsolin,* which break microfilaments into short pieces,
- actin-bundling proteins such as *fimbrin, villin,* and *α-actinin,* which crosslink microfilaments, and
- actin-branching proteins such as *formin,* which produce branch points along a microfilament.

Intermediate Filaments

In addition to microtubules and the thin actin filaments, eukaryotic cells contain a class of filaments intermediate in size between the other two cytoskeletal components and with a more variable



Functions of Centrosomes and Centrioles

1. **Microtubule support:** Organizes microtubules and supports their growth in nondividing cells
2. **Cell division:** Directs formation of mitotic spindle in dividing cells

Figure 2–32. Centrosome. The **centrosome** is the microtubule-organizing center for the mitotic spindle and consists of paired centrioles. The TEM reveals that the two centrioles in a centrosome exist at right angles to one another in a dense matrix of free tubulin subunits and other proteins. Each centriole consists of **nine microtubular triplets**. In a poorly understood process, the centrosome duplicates itself and is divided equally during a cell's interphase, each half having a duplicated centriole pair. At the onset of mitosis, the two daughter centrosomes move to opposite sides of the nucleus and become the two poles of the mitotic spindle of microtubules attaching to chromosomes.

diameter averaging 10–12 nm (Figure 2–34). In comparison with microtubules and actin filaments, **intermediate filaments** are much more stable and vary in their protein subunit structure in different cell types. A dozen or more heterogeneous protein classes that form such intermediate filaments have been identified and localized immunocytochemically, some of which are listed in Table 2–3. The size of these intermediate filament subunits ranges from 40 to 240 kDa. All are essentially rod-like rather than globular proteins that form coiled tetramers which self-assemble into large cable-like arrays stabilized by further interactions laterally.

Intermediate filament proteins have been organized chemically and genetically into four major groups:

- **Keratins** (Gr. *keras,* horn) or cytokeratins are a diverse family of more than 20 proteins found in all epithelial cells and in the hard structures produced by epidermal cells (eg, nails, horns, feathers and scales). They are encoded by related genes but have different chemical and immunologic properties and play various roles. In epidermal cells (Figure 2–35) keratins strengthen the tissue and provide protection against abrasion and water loss.

Figure 2–33. Actin filament treadmilling. Actin filaments or microfilaments are helical two-stranded polymers assembled from **globular actin subunits**. The filaments are flexible structures, with diameters in various cells of 5-9 nm, depending on associated proteins. Assembly of actin filaments (F-actin) results in their polarity, with actin subunits (G-actin) added to the plus (+) end and removed at the minus (−) end. Even actin filaments of a constant length are highly dynamic structures, balancing G-actin assembly and disassembly at the opposite ends, with a net movement or flow along the polymer known as treadmilling.

Table 2–3. Examples of intermediate filaments found in eukaryotic cells.

Filament Type	Cell Type	Examples
Cytokeratins	Epithelium	Both keratinizing and nonkeratinizing epithelia
Vimentin	Mesenchymal cells	Fibroblasts, chondroblasts, macrophages, endothelial cells, vascular smooth muscle
Desmin	Muscle	Striated and smooth muscle (except vascular smooth muscle)
Glial fibrillary acidic proteins	Glial cells	Astrocytes
Neurofilaments	Neurons	Nerve cell body and processes

Figure 2–34. Intermediate filaments of keratin. **Intermediate filaments** display an average diameter of 10-12 nm, between that of actin filaments and microtubules, and serve to provide mechanical strength or stability to cells. Unlike the other two cytoskeletal polymers, intermediate filaments are composed of various protein subunits in different types of cells. All such subunits appear to be rodlike rather than globular and undergo step-wise assembly into a structure resembling a cable with many strands. A large and important class of intermediate filaments is composed of **keratin** subunits, which are prominent in epithelial cells. Bundles of keratin filaments associate with certain classes of intercellular junctions common in epithelial cells and are easily seen with the TEM, as shown here in two extensions in an epidermal cell bound to a neighboring cell.

- **Vimentin** is a single protein (56–58 kDa) and is the most common intermediate filament protein in mesenchymal cells derived from the middle layer of the early embryo. Important vimentin-like proteins are **desmin** found in almost all muscle cells and **glial fibrillar acidic protein (GFAP)** found in astrocytes, supporting cells of the central nervous system tissues. The desmin filaments of a cultured cell are shown after immunocytochemistry in Figure 1–13.
- **Neurofilaments** consist of at least three high-molecular-weight polypeptides (68, 140, and 210 kDa) with different chemical structures and different roles. All are restricted to neurons.
- **Lamins** consist of three proteins averaging about 70 kDa in size present in the nucleus of animal cells. They form a structural framework just inside the nuclear envelope.

MEDICAL APPLICATION

The presence of a specific type of intermediate filament in tumors can reveal which cell originated the tumor, information important for diagnosis and treatment of the cancer. Identification of intermediate filament proteins by means of immunocytochemical methods is a routine procedure.

INCLUSIONS

Unlike organelles, cytoplasmic **inclusions** are composed mainly of accumulated metabolites or other substances and are often transitory components of the cytoplasm. Nonmotile and with little or no metabolic activity, inclusions are not considered organelles. Important and commonly seen inclusions include:

- **Fat droplets**, accumulations of lipid molecules that are prominent in adipocytes (fat cells), adrenal cortex cells, liver and other cells (Figure 2–35).
- **Glycogen granules**, aggregates of a carbohydrate polymer in which glucose is stored and are also visible in several cell types, mainly liver cells, in the form of irregular clumps of PAS-positive or electron-dense material (Figure 2–35). They are not enclosed with membrane.
- **Lipofuscin granules**, small pigmented (golden-brown) bodies present in many cells, but which accumulate with age in stable nondividing cells (eg, neurons, cardiac muscle). Lipofuscin granules contain a complex mixture of material derived from residual bodies after lysosomal digestion.