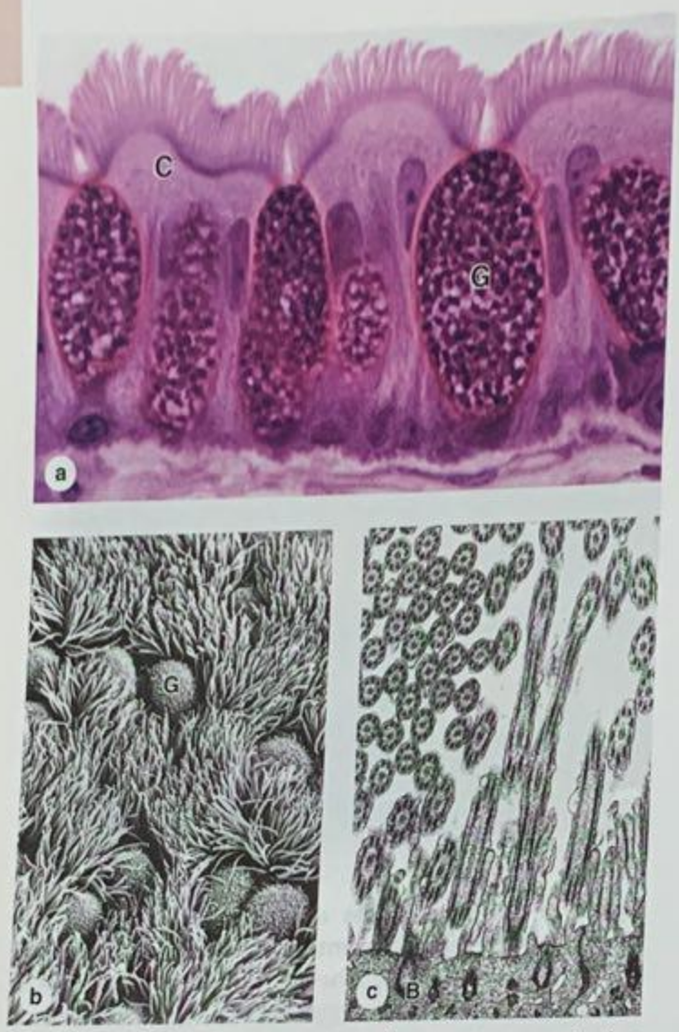


Figure 2–30. **Cilia. Cilia** are motile structures projecting from a cell, typically the apical end of epithelial cells. Each cilium is covered by the cell membrane and contains cytoplasm dominated by a specialized assembly of unusually stable microtubules, the **axoneme.** Shifting movements between microtubules of an axoneme produce whip-like motions of the cilia. Most epithelial cells lining the respiratory tract, such as those shown in the three micrographs here, have numerous cilia which move to propel mucus along the tract toward the pharynx. Between the ciliated cells are mucus-producing, non-ciliated goblet cells (G) with basal nuclei and apical cytoplasm filled with mucus granules. The relative size and spacing of the ciliated cells and goblet cells is seen in micrographs. **(a):** Light micrograph. X400. Pararosaniline-toluidine blue, PT. **(b):** SEM. X300. **(c):** TEM shows the axonemes of cilia cut in different orientations and their basal bodies in the apical cytoplasm. X9200. (Figure 2–30b reproduced, with permission from P. Andrews: *Am J Anat* 1974; 139:421. Copyright ©1974 by Wiley-Liss, Inc., a subsidiary of John Wiley & Sons, Inc.)

In addition to the numerous cilia on specialized cells such as these, many (perhaps most) other cell types have a single, short *primary cilium* with similar axoneme structure. Primary cilia lack dynein and are nonmobile, but serve as sensory structures receiving mechanical and chemical signals which are transduced by the cell to generate an appropriate response. Many signaling proteins, including those of developmentally important pathways, are concentrated in primary cilia which have various functions, including specific cell interactions during embryonic development.

In each pair the long axes of the centrioles are at right angles to each other. Before cell division, more specifically during the S period of the interphase, each centrosome duplicates itself so that now each centrosome has two pairs of centrioles. During mitosis, the centrosome divide into halves, which move to opposite poles of the cell, and become organizing centers for the microtubules of the mitotic spindle.

Cilia and **flagella** (singular: cilium, flagellum) are motile processes, covered by cell membrane, with a highly organized microtubule core. Ciliated cells typically possess a large number of cilia, each about 2–3 μm in length. The main function of cilia is to sweep fluid along the surface of cell sheets. In humans, the spermatozoa are the only cell type with a flagellum, with a length close to 100 μm, used for motility.

Both cilia and flagella possess the same core structure, consisting of nine peripheral microtubular doublets surrounding two central microtubules. This assembly of microtubules with the **9 + 2 pattern** is called an **axoneme** (Gr. *axon,* axis, + *nema,* thread). Microtubules of the nine peripheral doublets each share a few protofilaments (Figure 2–31b). The microtubules of the peripheral doublets are identified as A (complete with 13 protofilaments), and B (with only 10 protofilaments). Adjacent peripheral doublets are linked to each other by protein bridges called **nexins** and each doublet has a **radial spoke** projecting toward the center. Extending from the surface of microtubule A are inner and outer arms of **axonemal dynein,** which project toward the B microtubule of the next doublet. ATP-dependent interactions of the dyneins with the neighboring microtubule cause repetitive conformational changes that are coordinated to produce a repeated beating motion of the entire axoneme. At the base of each cilium or flagellum is a **basal body,** essentially similar to a centriole, which controls the assembly of the axoneme.

MEDICAL APPLICATION

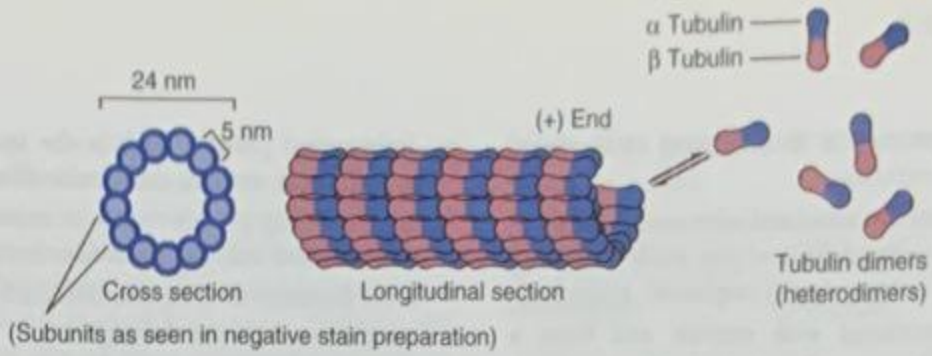
Several mutations have been described in the proteins of the cilia and flagella. They are responsible for the immotile cilia syndrome, the symptoms of which are immotile spermatozoa, male infertility, and chronic respiratory infections caused by the lack of the cleansing action of cilia in the respiratory tract.

Microfilaments (Actin Filaments)

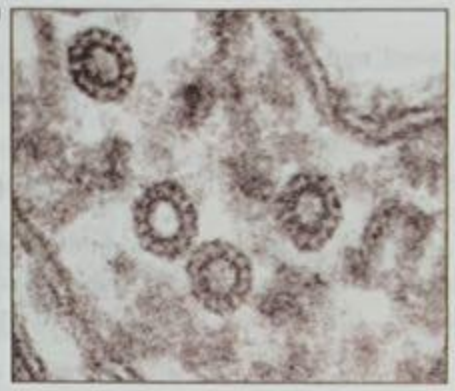
Contractile activity in cells results primarily from an interaction between **actin** and its associated protein, **myosin.** Actin is present as thin (5–7 nm diameter) polarized **microfilaments** composed of globular subunits organized into a double-stranded helix (Figures 2–33 and 2–29). There are several types of actin and this protein is present in all cells. Actin is usually found in cells as polymerized filaments of F-actin mingled with free globular G-actin subunits.

Within cells, actin microfilaments (F-actin) can be organized in several forms.

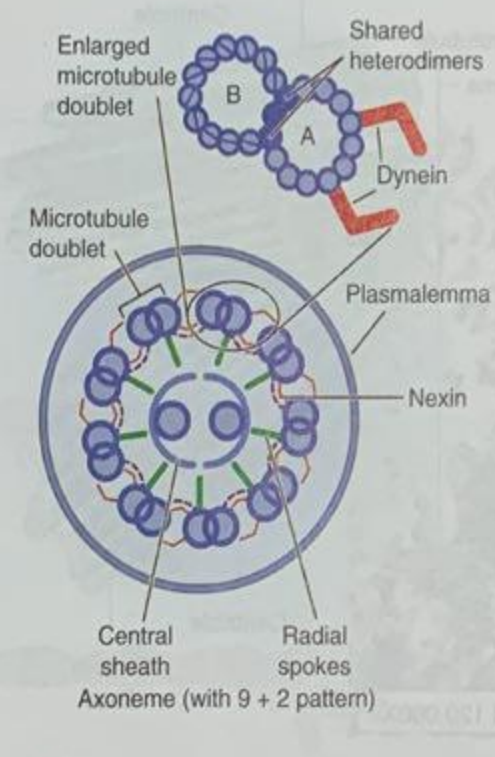
1. In skeletal muscle, they assume a stable array integrated with thick (16-nm) myosin filaments.
2. In most cells, microfilaments form a thin sheath or network just beneath the plasmalemma. These filaments are involved



Electron micrograph of microtubules showing above structural features



a Microtubule



b Cilium

c Centriole

Figure 2–31. **Microtubules, cilia, and centrioles.** Microtubules are seen (a): cross-section by TEM after fixation with tannic acid in glutaraldehyde, which leaves the unstained tubulin subunits delineated by the dense tannic acid. Cross sections of tubules reveal the ring of 13 subunits of dimeric tubulin which are arranged lengthwise as protofilaments. Changes in microtubule length are caused by the addition or loss of individual tubulin subunits from protofilaments. **(b):** A diagrammatic cross-section through a cilium reveals a cytoplasmic core of microtubules called an **axoneme**. The axoneme consists of **two central microtubules** surrounded by **nine peripheral microtubular doublets** associated with several other proteins. In the doublets, microtubule A is complete, consisting of 13 protofilaments, whereas microtubule B shares some of A's protofilament heterodimers. A series of protein complexes containing ciliary dynein, the **inner and outer dynein arms**, are bound to microtubule A along its length. When activated by ATP, the dynein arms briefly link microtubule B of the adjacent doublet and provide for slight sliding of the doublets against each other, which is then immediately reversed. This rapid back-and-forth shift between adjacent doublets, produced by the ciliary dynein motors, causes the rhythmic changes of axonemal shape that bring about the flailing motion of the entire cilium.

Each axoneme is continuous with a **basal body** located at the base of the cilium. Basal bodies are structurally very similar to centrioles, which nucleate and organize the growth of microtubules during formation of the mitotic spindle. **(c):** Each centriole consists of nine relatively short **microtubular triplets** linked together in a pinwheel-like arrangement. In the triplets, microtubule A is complete and consists of 13 protofilaments, whereas microtubules B and C share protofilaments. Under normal circumstances, these organelles are found in pairs and are oriented at right angles to one another. The *pair* of centrioles is called a **centrosome**.

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

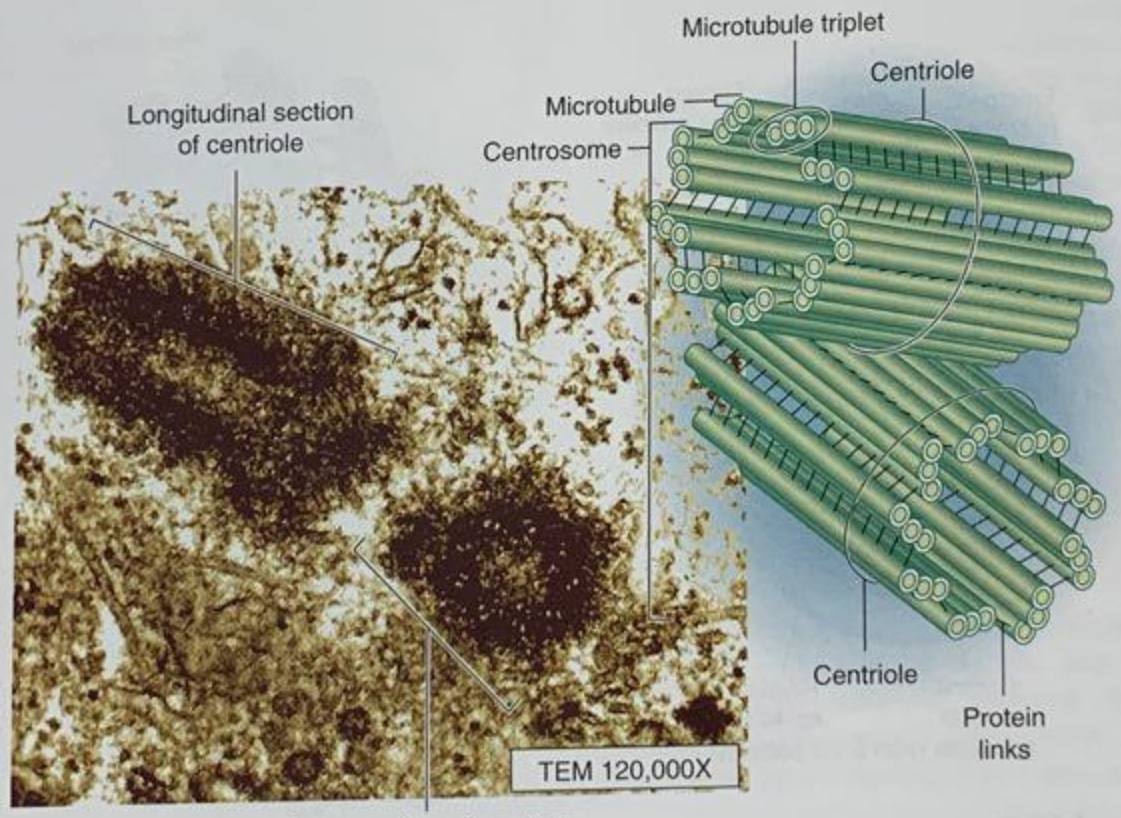
3. Microfilaments are intimately associated with several cytoplasmic organelles, vesicles, and granules and play a role in moving or shifting cytoplasmic components (cytoplasmic streaming).
4. Microfilaments are associated with myosin and form a "purse-string" ring of filaments whose constriction results 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.