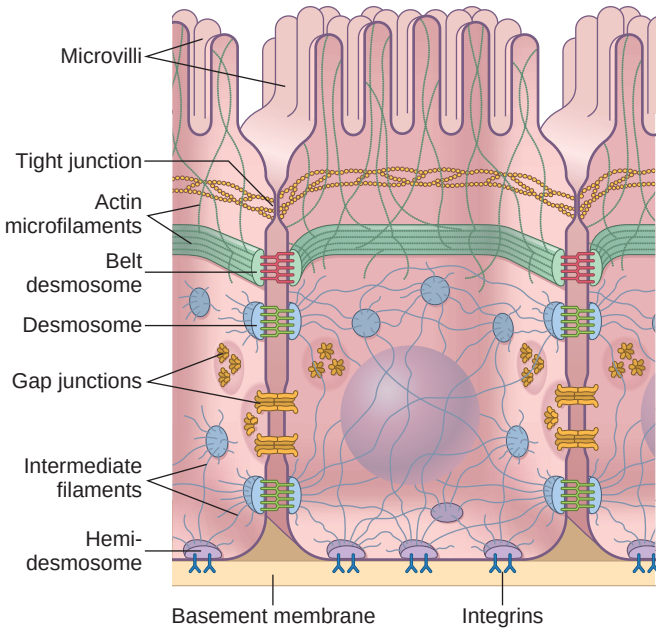

Figure 1-8 Cytoskeletal elements and cell-cell interactions. Interepithelial adhesion involves several different surface protein interactions, including through *tight junctions* and *desmosomes*; adhesion to the extracellular matrix involves cellular integrins (and associated proteins) within *hemidesmosomes*. See text for details.

- *Actin microfilaments* are 5- to 9-nm diameter fibrils formed from the **g**lobular protein actin (**G**-actin), the most abundant cytosolic protein in cells. The G-actin monomers noncovalently polymerize into long **f**ilaments (**F**-actin) that intertwine to form double-stranded helices with a defined polarity; new globular subunits are added (or lost) at the "positive" end of the strand. In muscle cells, the filamentous protein *myosin* binds to actin, and moves along it, driven by ATP hydrolysis (the basis of muscle contraction). In non-muscle cells, F-actin assembles via an assortment of actin-binding proteins into well-organized bundles and networks that control cell shape and movement.
- *Intermediate filaments* are 10-nm diameter fibrils that comprise a large and heterogeneous family. Individual types have characteristic tissue-specific patterns of expression that can be useful for assigning a cell of origin for poorly differentiated tumors.
  - *Lamin A, B, and C:* nuclear lamina of all cells
  - *Vimentin:* mesenchymal cells (fibroblasts, endothelium)
  - *Desmin:* muscle cells, forming the scaffold on which actin and myosin contract
  - *Neurofilaments:* axons of neurons, imparting strength and rigidity
  - *Glial fibrillary acidic protein:* glial cells around neurons
  - *Cytokeratins:* at least 30 distinct varieties, subdivided into acidic (type I) and neutral/basic (type II); different types present in different cells, hence can be used as cell markers

    These ropelike *intermediate filament* fibers are found predominantly in a polymerized form within cells and do not usually actively reorganize like actin and microtubules. They impart tensile strength and allow cells to bear mechanical stress. The nuclear membrane lamins are important not only for maintaining nuclear morphology but also for regulating normal nuclear transcription. The importance of lamins is seen in rare but fascinating disorders caused by lamin mutations, which range from certain froms of muscular dystrophy to progeria, a disease of premature aging. Intermediate filaments also form the major structural proteins of skin and hair.
- *Microtubules* are 25-nm-thick fibrils composed of noncovalently polymerized dimers of α- and β-tubulin arrayed in constantly elongating or shrinking hollow tubes with a defined polarity; the ends are designated "+" or "–". The "–" end is typically embedded in a *microtubule organizing center (MTOC or centrosome)* near the nucleus where it is associated with paired *centrioles*; the "+" end elongates or recedes in response to various stimuli by the addition or subtraction of tubulin dimers. Within cells, microtubules can serve as connecting cables for "molecular motor" proteins that use ATP to move vesicles, organelles, or other molecules around cells along microtubules. There are two varieties of these motor proteins: *kinesins*, for anterograde (– to +) transport, and *dyneins*, for retrograde (+ to –) transport; they also participate in sister chromatid separation during mitosis. Notably, microtubules (and their associated motors) have been adapted to form motile cilia (e.g., in bronchial epithelium) or flagella (in sperm).

Cell-Cell Interactions. **Cells interact and communicate with one another by forming junctions that provide mechanical links and enable surface receptors to recognize ligands on other cells.** *Cell junctions* are organized into three basic types (Fig. 1-8):

- *Occluding junctions (tight junctions)* seal adjacent cells together to create a continuous barrier that restricts the paracellular (between cells) movement of ions and other molecules. Viewed en face, occluding junctions form a tight meshlike network of macromolecular contacts between neighboring cells. The complexes that mediate the cell-cell interactions are composed of multiple transmembrane proteins, including *occludin, claudin, zonulin,* and *catenin*. Besides forming a high-resistance barrier to solute movement, this zone also represents the boundary that allows the segregation of apical and basolateral domains of cells, helping to maintain cellular polarity. Nevertheless, these junctions (as well as the desmosomes described later) are dynamic structures that can dissociate and reform as required to facilitate epithelial proliferation or inflammatory cell migration.
- *Anchoring junctions (desmosomes)* mechanically attach cells—and their intracellular cytoskeletons—to other cells or to the extracellular matrix (ECM). When the adhesion focus is between cells, and is small and rivet-like, it is designated a *spot desmosome* or *macula adherens*. When such a focus attaches the cell to the ECM, it is called a *hemidesmosome*. Similar adhesion domains can also occur as broad bands between cells, where they are denoted as *belt desmosomes*.