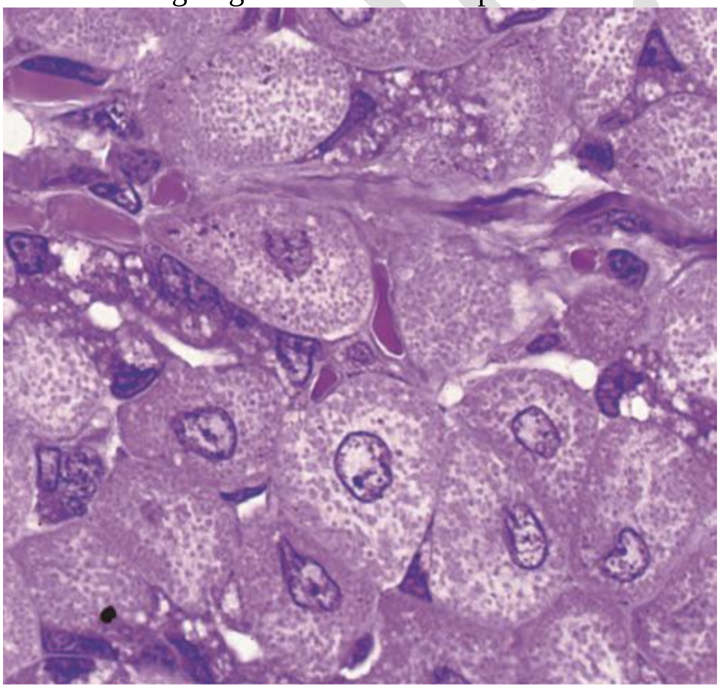
❖ Mitochondria

- Mitochondria(Gr. *mitos*, thread, + *chondros*, granule) (singular, **mitochondrion**) are membrane-bounded organelles
- They are usually elongated structures with diameters of 0.5-1 µm and lengths up to 10 times greater.
- They are highly plastic, rapidly changing shape, fusing with one another and dividing, and are moved through the cytoplasm along microtubules.
- The number of mitochondria is related to the cell's energy needs: cells with a high-energy metabolism (eg, cardiac muscle, liver cells and cells of kidney tubules) have abundant mitochondria, whereas cells with a low-energy metabolism have few mitochondria such as small lymphocyte
- Mitochondria are membrane-enclosed organelles with arrays of enzymes specialized for aerobic respiration and production of adenosine triphosphate (ATP), with high-energy phosphate bonds, which supplies energy for most cellular activities. Glycolysis converts glucose anaerobically to pyruvate in the cytoplasm, releasing some energy. The rest of the energy is captured when pyruvate is imported into mitochondria and oxidized to CO_2 and H_2O. Mitochondrial enzymes yield 15 times more ATP than is produced by glycolysis alone. Some of the energy released in mitochondria is not stored in ATP but is dissipated as heat that maintains body temperature.

LM: Mitochondria are often large enough to be visible with the light microscope as numerous discrete organelles. In certain sectioned cells stained with H&E, mitochondria appear throughout the cytoplasm as numerous eosinophilic structures. The mitochondria usually appear round or slightly elongated and are more numerous in cytoplasmic regions with higher energy demands, such as near the cell membrane in cells undergoing much active transport.



Mitochondria in the light microscope.

The structure of mitochondria under TEM: each mitochondrion consists of:

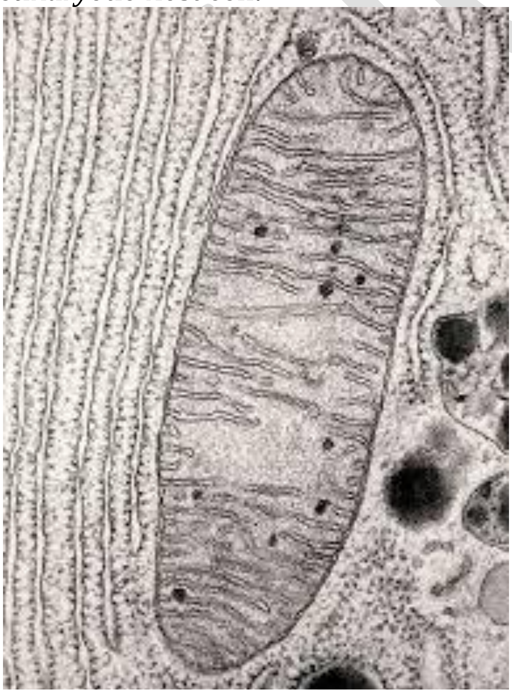
1. **Outer membrane:** is sieve-like, containing many transmembrane proteins called porins that form channels through which small molecules such as pyruvate and other metabolites readily pass from the cytoplasm to the intermembrane space.

2. **Intermembrane space:** Because of channels in the outer membrane of the mitochondria, the content of the intermembrane space is similar to that of the content of the cytoplasm.
3. **Inner membrane:** is folded to form a series of long infoldings called cristae, which project into the matrix and greatly increase this membrane's surface area. The number of cristae in mitochondria also corresponds to the energy needs of the cell. and contain most of the respiratory chain enzymes and ATP synthase which is responsible for cell respiration (oxidative phosphorylation) and production of cell ATP.

✓ Shape of cristea different according type of cells;
   1. In protein secreting cells cristea project into the interior of the organelle like shelve.
   2. In steroid secreting cells such as the adrenal cortex or interstitial cells in the testes, the mitochondria cristea are tubular.

4. **Mitochondrial matrix:** the matrix is the space within the inner membrane; contain enzymes for Krebs cycle, mitochondrial DNA **(circular DNA),** special ribosome, tRNA, mRNA and enzymes for gene expression. All with similarities to the corresponding bacterial components. Protein synthesis occurs in mitochondria, but because of the reduced amount of mitochondrial DNA, only a small subset of mitochondrial proteins is produced locally. Most are encoded by nuclear DNA and synthesized on free polyribosomes of the cytosol. These proteins have short terminal amino acid sequences that serve as signals for their uptake across the mitochondrial membranes.

   The observation that mitochondria have certain bacterial characteristics led with later work to the understanding that mitochondria evolved from an ancestral aerobic prokaryote that lived symbiotically within an ancestral eukaryotic host cell.



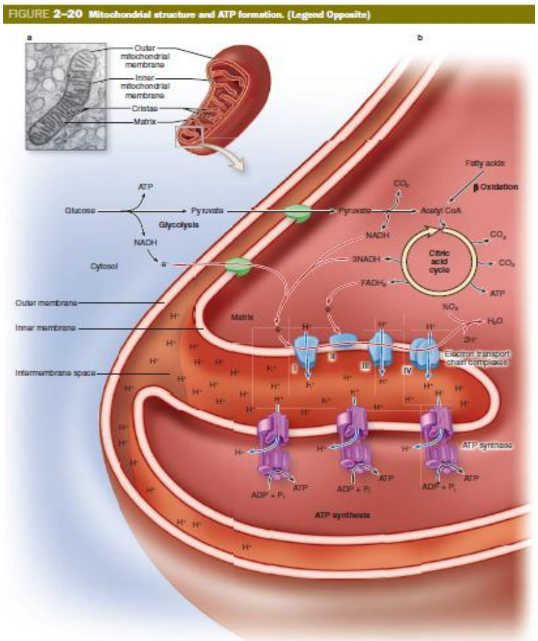


FIGURE 2–20 Mitochondrial structure and ATP formation. (Legend Opposite)

➢ **Replication of mitochondria**

Mitochondria replicate similarly to bacterial cells, when they get large, they undergo **fission**. This involves furrowing of the inner and then the outer membrane as if someone was pinching the mitochondrion. The two daughter mitochondria must first replicate the DNA.

- **Function of mitochondria**
  1. Mitochondria are primary sites for ATP synthesis (site of Krebs cycle**)** from organic material so that known as **powerhouse** of the cell.
  2. Cell respiration.
  3. Maintain body heat because some energy dissipated as heat.
  4. They have key role in apoptosis programmed cell death.
  5. Some mitochondrial functions are performed only in specific types of cells, e.g. mitochondria in liver cells contain enzymes that allow them to detoxify ammonia, a waste product of protein metabolism.
  6. Heme synthesis occurs partly in the mitochondria and partly in the cytosol, Heme is an essential prosthetic group in proteins that is necessary as a subcellular compartment to perform diverse biological functions like hemoglobin and myoglobin. The major tissues for heme synthesis are bone marrow by erythrocytes and the liver by hepatocytes.
  7. Other metabolic reactions happened in mitochondria include gluconeogenesis and ketogenesis

Medical application

Myoclonic epilepsy with ragged red fibers (MERRF) is a rare disease occurring in individuals in whom cells of specific tissues, notably regions of skeletal muscle, inherit mitochondrial DNA with a mutated gene for lysine-tRNA, leading to defective synthesis of respiratory chain proteins which can produce structural abnormal in muscle fibers and other cells.

Inclusions

The cytoplasmic inclusions are cytoplasmic structures or deposits filled with stored macromolecules and are not present in all cells that accumulate in the cytoplasm of certain cells not able to carry out any metabolic activity and are not bound by membranes. Inclusions are stored nutrients, secretory products, and pigment granules. Examples of inclusions are:

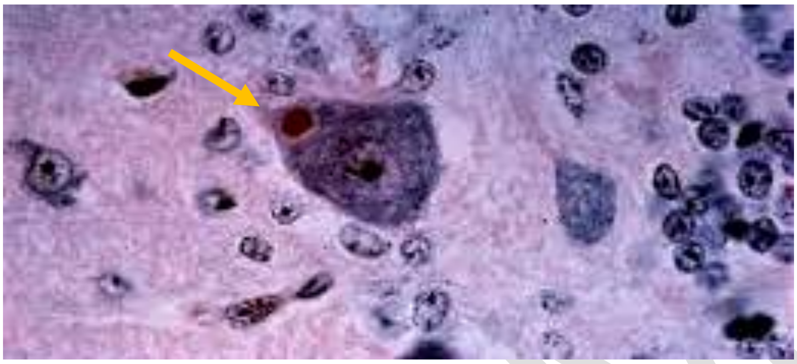
Glycogen: Glycogen granules are the most common form of glucose in animals and especially abundant in cells of muscles and liver.

Lipids: Lipids are triglycerides in storage form the common form of inclusions not only are stored in specialized cells (adipocytes) but also are located as individual's droplets in various cell type especially hepatocytes. These are fluid at body temperature and appear in living cells as refractile spherical droplets.

Crystals: Crystalline inclusions have long been recognized as normal constituents of certain cell types such as Sertoli cells and Leydig cells of the human testis, and occasionally in macrophages. It is believed that these structures are crystalline forms of certain proteins which is located everywhere in the cell such as in nucleus, mitochondria, endoplasmic reticulum, Golgi body, and free in cytoplasmic matrix.

Pigments: The most common pigment in the body, besides hemoglobin of red blood cells is melanin, manufactured by melanocytes of the skin and hair, pigments cells of the retina and specialized nerve cells in the substantia nigra of the brain. These pigments have protective functions in skin and aid in the sense of sight in the retina but their functions in neurons is not understood completely. Furthermore, cardiac tissue and central nervous system neurons shows yellow to brown pigment called lipofuscin, some believed that they have lysosomal activity.

This type of inclusion called **endogenous pigment** because is formed by the cells, while other type of inclusion come from outside called **exogenous pigment** like tattoo marks, carotene and dust the epithelial surface of lung alveoli where it inhaled particulate matter known as dust cells.

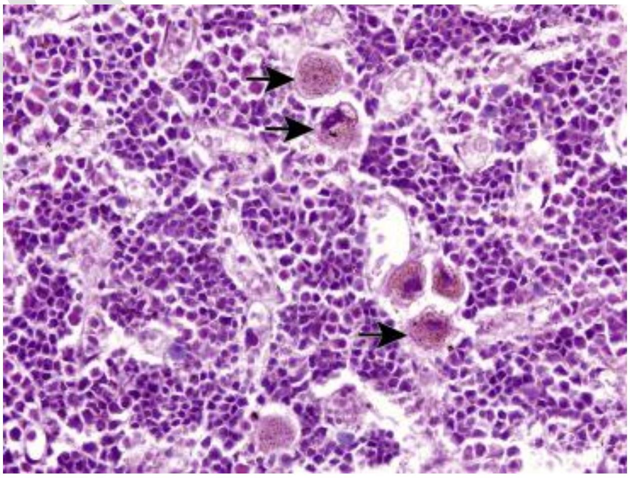


The inclusion body (lipofuscin) in neuron

Hemosiderin is a dense brown aggregate of denatured ferritin proteins with many atoms of bound iron. It occurs in phagocytic cells, especially macrophages of the liver and spleen, where it results from phagocytosis of red blood cells.

Medical application

A condition termed **hemosiderosis**, in which the iron containing inclusion hemosiderin occurs in cells of organs throughout the body, may be seen with increased uptake of dietary iron, impaired iron utilization, or with excessive lysis of red blood cells. Hemosiderosis itself does not damage cell or organ function. However, extreme accumulations of iron in cellular hemosiderin can lead to disorders such as **hemochromatosis and iron overload syndrome**, in which tissues of the liver and other organs are damaged.



Several macrophages (arrows) contain moderate amounts of brown pigment consistent with iron.