Cell Membrane Transport Processes

Bulk Transport:

Exocytosis & Endocytosis

Learning Objectives:

- Define the terms: Exocytosis, Endocytosis, Phagocytosis, Pinocytosis, Receptor-mediated endocytosis and describe **BRIEFLY** their mechanisms.

- Give examples of how human cells are using each of the above mentioned processes in the cellular life functions.

Bulk Transport (Vesicular Transport):

- In vesicular transport, fluids containing large particles and macromolecules are transported across cellular membranes inside membranous sacs called ***vesicles***.

- Like active transport, vesicular transport moves substances into the cell ***(endocytosis)*** and out of the cell ***(exocytosis).***

- Vesicles (vacuoles) are small, globular, membrane-bound structures within cells formed by ***"pinching off"*** from other membranes ***(eg. ER, Golgi body, cell membrane).***

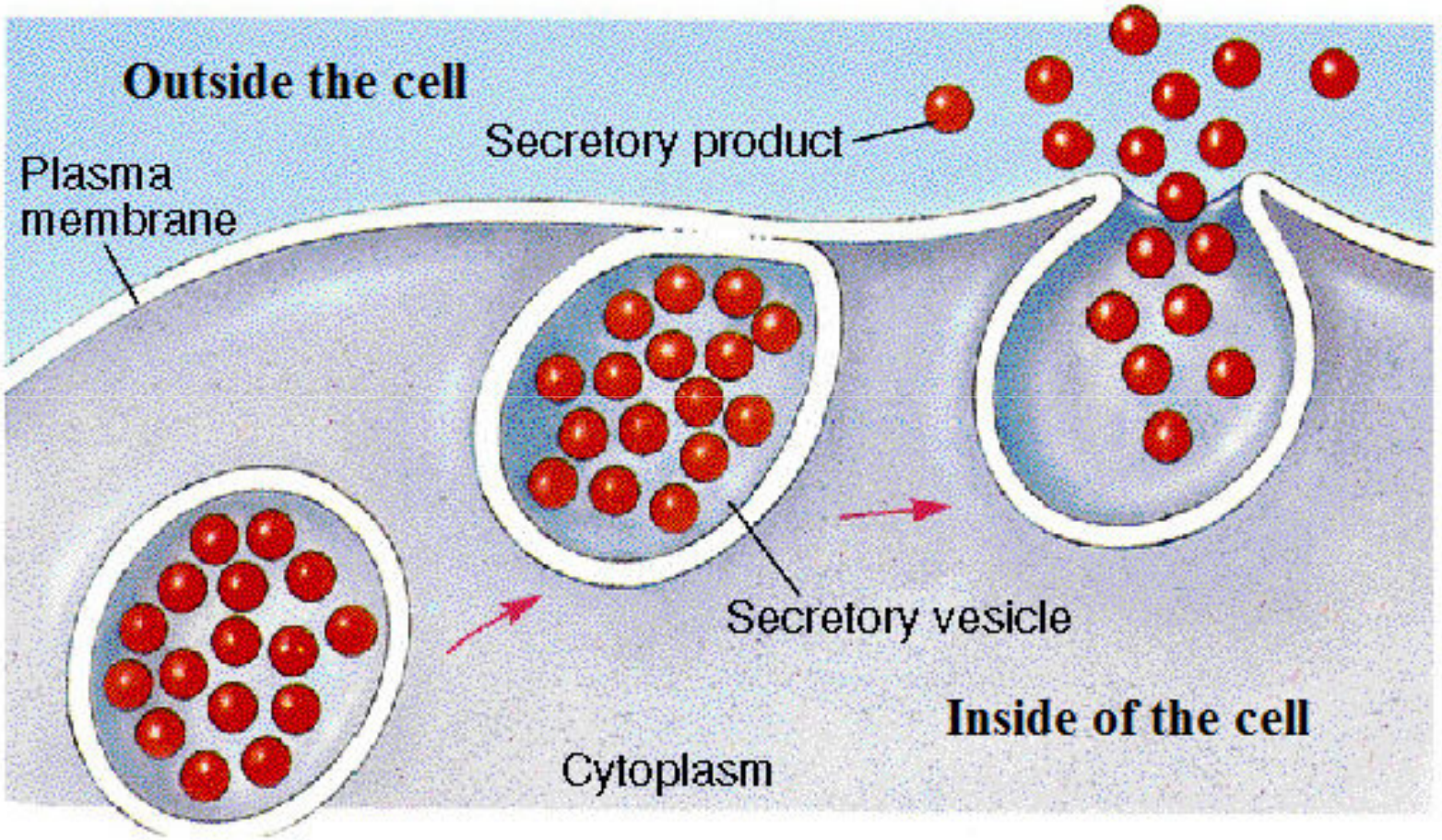
- Later, they merge with other membranes, (e.g. plasma membrane, ER, Golgi). As they pinch off, they may have material included within their membrane. They merge with another membrane, to release that material on the other side of it.

Bulk Transport – *Exocytosis:*

❖ Exocytosis is used for moving secretory materials to the outside of the cell.
Secretion of neurotransmitter substances at a synapse is a good example of this:

1. Vesicle pinches off from the ER, containing secretory material.
2. Vesicle goes to the ***Golgi complex***, where material is ***"packaged".***
3. ***"Condensing vacuoles"*** pinch off from the periphery of the Golgi complex.
4. Condensing vacuoles usually merge to form a bigger ***"secretory granule".***
5. Secretory granules move towards the outside of the cell.
6. Voltage-gated calcium channels open in response to nerve stimulus.
7. Influx of Ca^{++}causes secretory granule membrane to fuse with plasma membrane.
8. Contents of secretory granule are released to outside of cell.
9. The inside surface of the granule thus becomes the exterior surface of the cell.

Bulk Transport – *Exocytosis:*



Bulk Transport – *Endocytosis:*

- **Endocytosis:** The cell internalizes large molecules/objects from outside. Plasma membrane is infolded to form an internal cytoplasmic vesicle.

- There are 3 types of endocytosis:

  - **Phagocytosis:** Cell "eating" large particles.

  - **Pinocytosis** : Cell "drinking" large molecules in solution.

  - **Receptor-mediated endocytosis** a.k.a. ***adsorptive pinocytosis***.

Bulk Transport – *Phagocytosis:*

- In phagocytosis the cell engulfs some relatively large or solid material, such as ***a clump of bacteria, cell debris, or inanimate particles (e.g. asbestos fibers or glass,). Lower animals use this process for their nutrition, e.g. protozoa, sponges, flatworms.***

- When a particle binds to receptors on the cell's surface, cytoplasmic extensions called ***pseudopods*** form and flow around the particle.

- This forms an endocytotic vesicle called ***a phagosome "eaten body".*** In most cases, the phagosome then fuses with a ***lysosome*** and its contents are digested.

- Any indigestible contents are ejected from the cell by exocytosis. In the human body, ***only macrophages and certain white blood cells are "experts" at phagocytosis***.

- Commonly referred to as ***phagocytes***, these cells help protect the body by ingesting and disposing of ***bacteria, other foreign substances, and dead tissue cells***.

- The disposal of dying cells is crucial, because dead cell remnants trigger inflammation in the surrounding area or may stimulate an undesirable immune response.

- Most phagocytes move about by ***amoeboid motion "changing shape"***; that is, the flowing of their cytoplasm into temporary extensions allows them to creep along.

Bulk Transport – *Phagocytosis Steps:*

Step 1: Cell membrane folds around the particle to form a ***"food cup".***

Step 2: Membrane invaginates and folds extend further around the particle. Eventually the particle is completely engulfed.

Step 3: Membrane pinches off to form a free phagocytic vacuole in the cytoplasm.

Step 4: Phagocytic vacuole moves towards Golgi region.

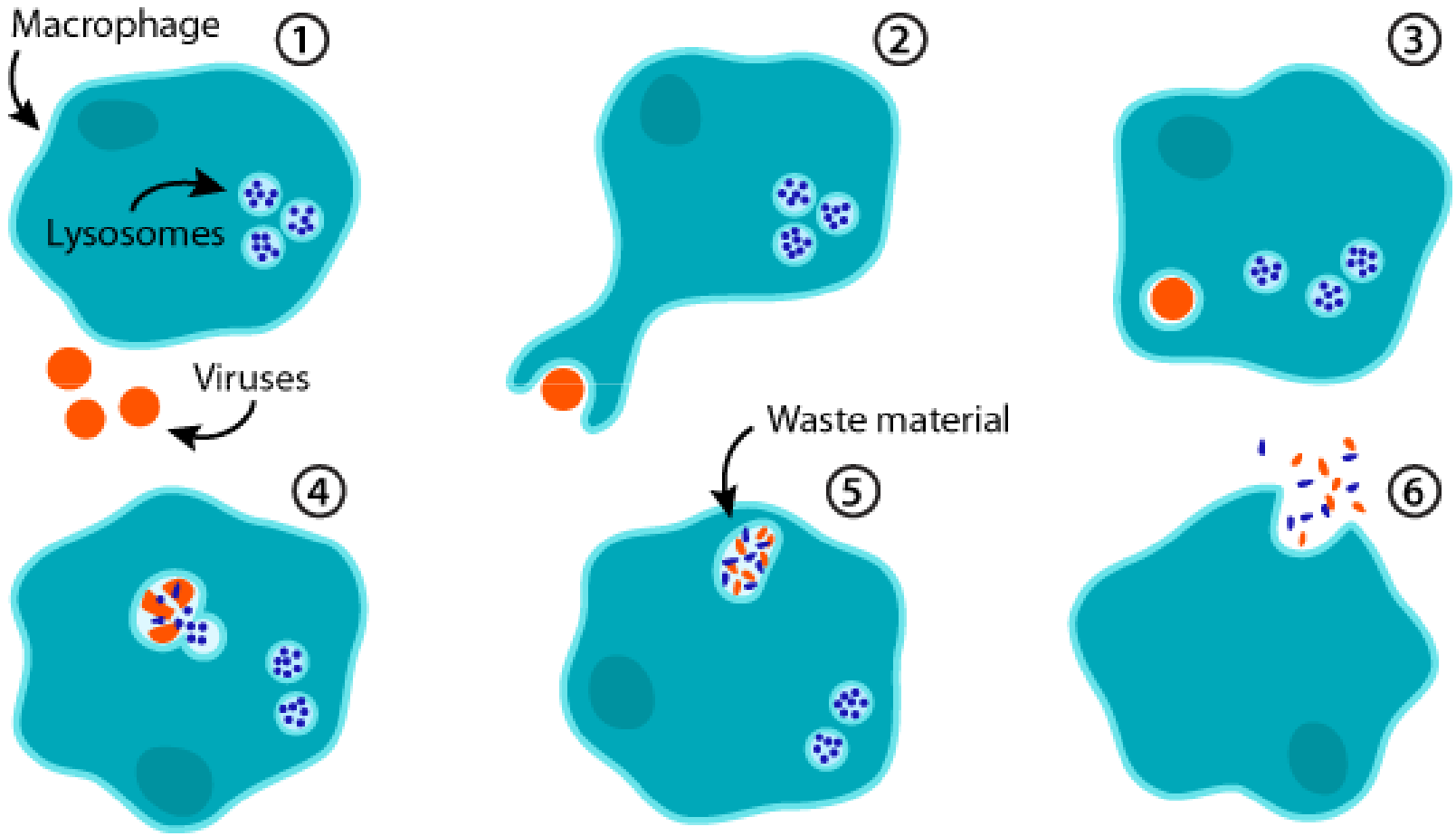
Step 5: Phagocytic vacuole merges with a primary lysosome. This causes primary lysosome to form secondary ***heterophagic lysosome***.

Step 6: Internal pH of lysosome is reduced by proton pumps in lysosomal membrane. At pH 5, lysosomal enzymes are all activated, so particle is digested.

Step 7: Undigestible waste may have either of these fates:

- *In lower organisms, it is excreted by exocytosis.*
- *In mammalian phagocytes, some stay in the cell and contributes to cell aging.*
- *Neutrophils may "eat until they burst" because they don't release old waste.*

Bulk Transport – *Phagocytosis:*



Bulk Transport – *Pinocytosis:*

- In pinocytosis ("cell drinking"), also ***called fluid-phase endocytosis***, a bit of infolding plasma membrane (which begins as a protein-coated pit) surrounds a very small volume of extracellular fluid containing dissolved molecules.

- This droplet then enters the cell. ***Unlike phagocytosis***, ***pinocytosis is a routine activity of most cells***, affording them a nonselective way of sampling the extracellular fluid.

- ***It is particularly important in cells that absorb nutrients, such as cells that line the intestines.*** As mentioned, bits of the plasma membrane are removed when the membranous sacs are internalized. However, these membranes are recycled back to the plasma membrane by exocytosis as described shortly, so the surface area of the plasma membrane remains remarkably constant.

Bulk Transport – *Pinocytosis - Steps:*

Step 1: Macromolecules bind to ***general receptors*** on plasma membrane.

Step 2: Membrane invaginates, drawing particles into a "cupped" region.
(Different from a phagocytic "food cup" because no externally projecting folds).

Step 3: Cupped region becomes completely enclosed by invagination.

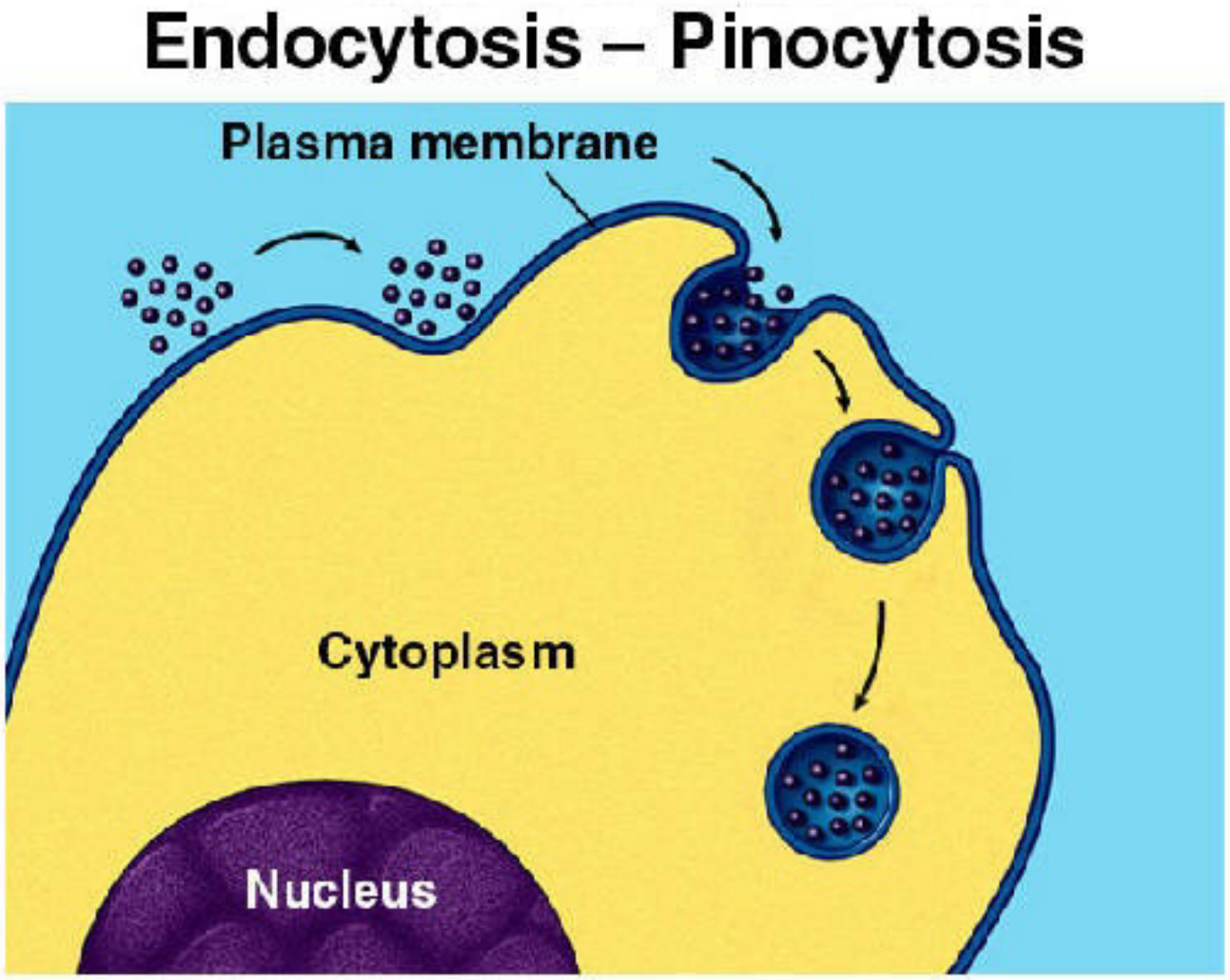
Step 4: Pinches off to form a free pinocytic vesicle within the cytoplasm.

Step 5: Two outcomes have been observed:

- Pinocytic vesicles may fragment into smaller vesicles = ***micropinocytosis.***
  Ingested molecules are transported to lysosomes by the small vesicles, which have been called ***endosomes*** in the most recent studies.

- Pinocytic vesicles may coalesce to form larger vesicles = ***macropinocytosis.***
  This usually happens during transcellular transport, e.g. GI epithelial cells.
  The final stages of pinocytosis are not understood completely.

Bulk Transport – *Pinocytosis* - *Steps:*



Bulk Transport – *Receptor-Mediated Endocytosis:*

- Also called ***"Adsorptive pinocytosis".*** This exquisitely selective mechanism allows cells to concentrate material that is present only in small amounts in the extracellular fluid.

- Since this process uses specialized membrane receptors, it has much in common with the receptor functions described earlier, but it leads to endocytosis of many identical molecules simultaneously, rather than the transport of just one at a time. Examples:

  - ***Low-density lipoprotein (LDL)*** is taken up, for the cell to obtain the cholesterol.

  - ***Transferrin*** is taken up, for the cell to obtain the iron.

  - ***Bacterial toxins*** (e.g. diphtheria toxin) subvert this process so toxin enters the cell.

- Special equipment is needed:

  - The macromolecule to be taken up, (LDL or transferrin) is called the ***ligand***.
  - ***Receptors*** are specific transmembrane proteins in the plasma membrane.
  - ***Clathrin*** (Greek for basket) is a protein that forms a coating around some vesicles.
  - ***Coated pits*** are areas of the plasma membrane with clathrin underneath it.

Bulk Transport – *Receptor-Mediated Endocytosis - Steps:*

Step 1: Ligand binds to specific receptors on the cell membrane.

Step 2: Ligand-receptor complexes move laterally in the membrane to assemble in the coated pits, which become points of collection and internalization.

Step 3: Endocytosis occurs in the region of the coated pit.

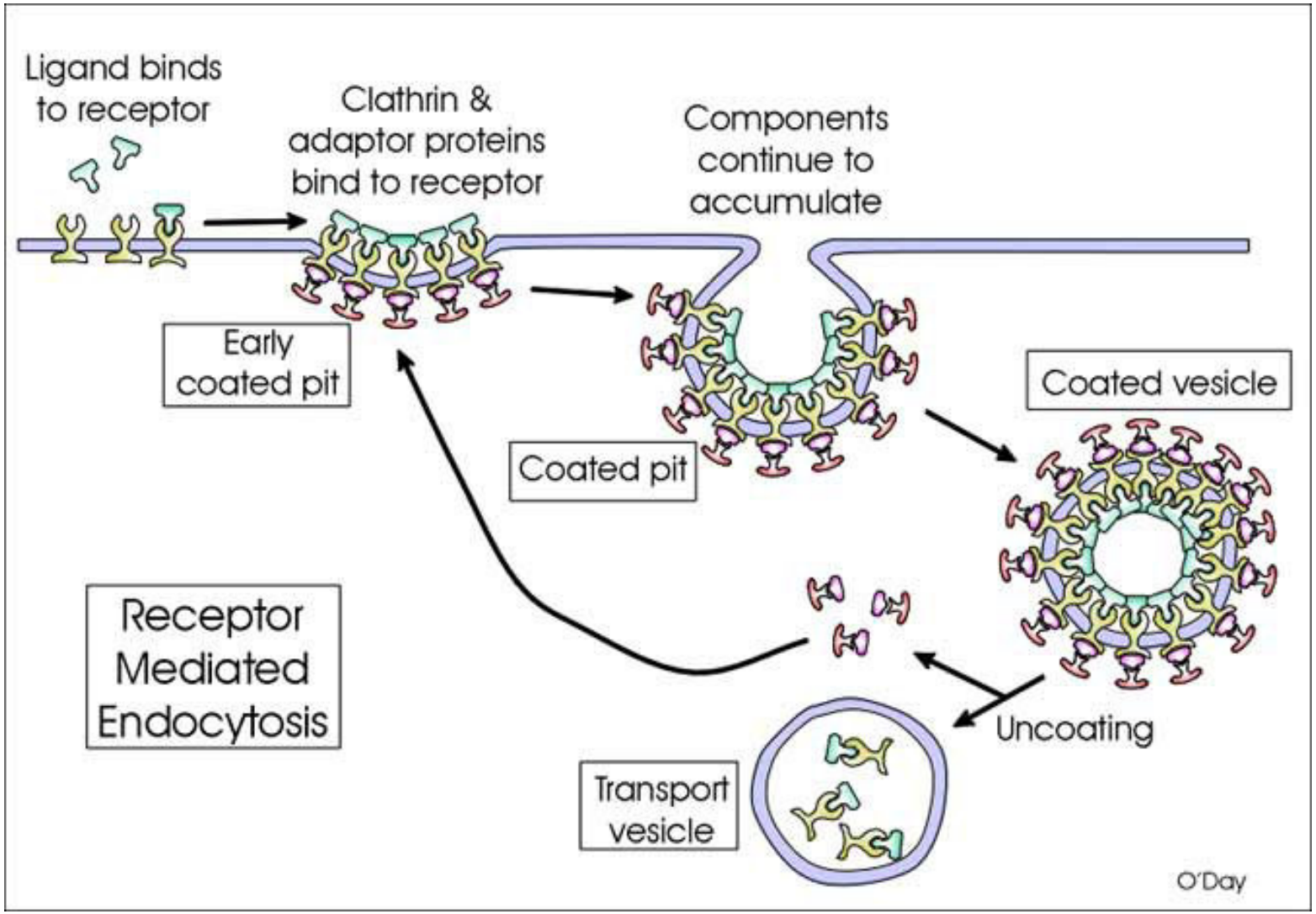
Step 4: A coated vesicle is formed in the cytoplasm.

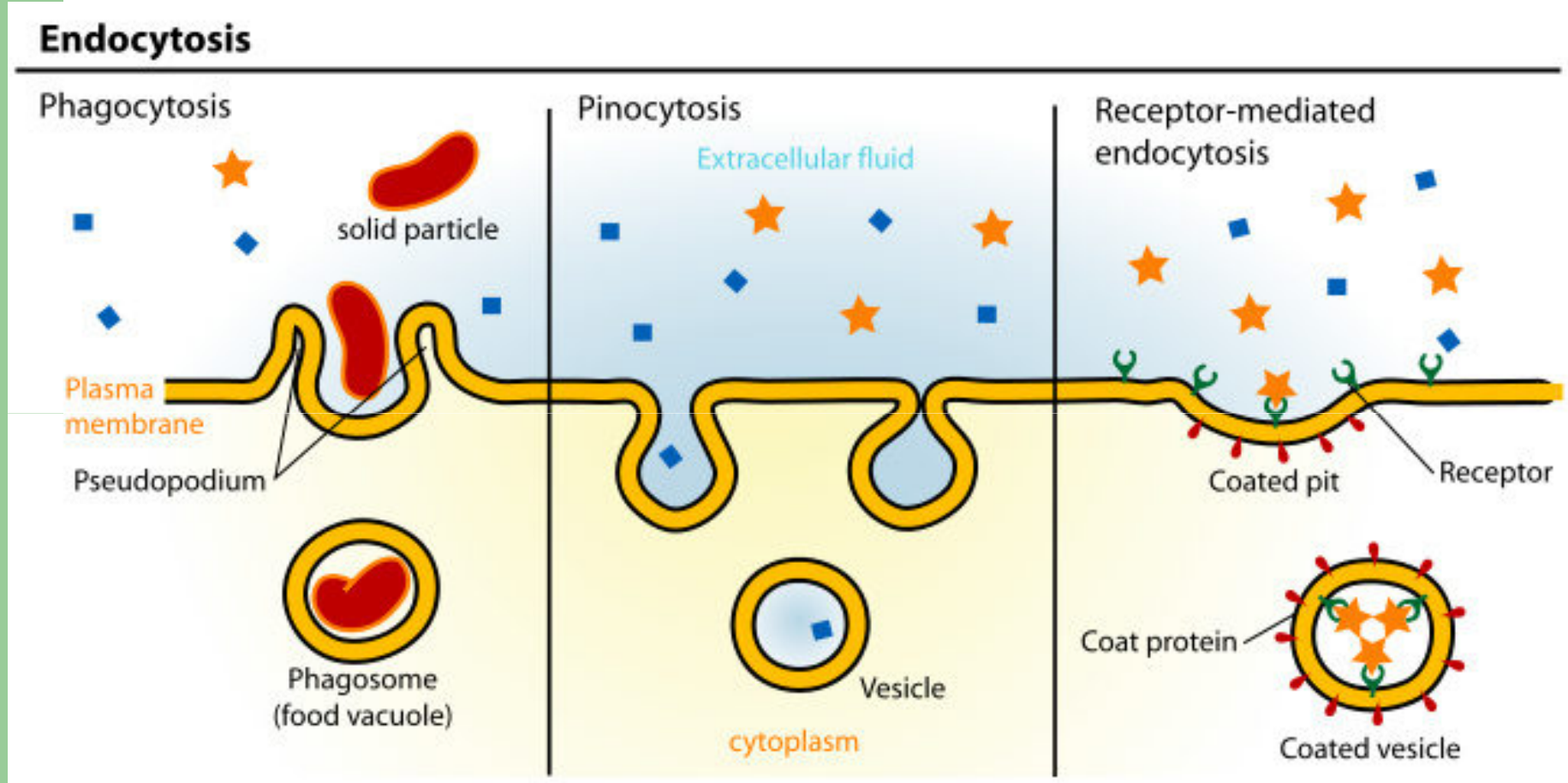
Step 5: The coated vesicle may fuse with other vesicles which are not coated.

Step 6: The clathrin coat is released and recycled back to the plasma membrane.

Step 7: An ATP-dependent proton pump acidifies the vesicle. The acidification causes the ligands and receptors to separate. Ligands are processed further for the important part (cholesterol, or iron) to be utilized by the cell. Receptors are recycled back to the plasma membrane.

Bulk Transport – *Receptor-Mediated Endocytosis:*




Endocytosis
Phagocytosis
Pinocytosis
Receptor-mediated endocytosis
Extracellular fluid
solid particle
Plasma membrane
Pseudopodium
Phagosome (food vacuole)
Vesicle
cytoplasm
Coated pit
Receptor
Coat protein
Coated vesicle