11.3A: Blood-Brain Barrier

Tight junctions present in the blood-brain barrier separate circulating blood from cerebrospinal fluid, regulating diffusion into the brain.

Learning Objectives

- Describe the function of the blood-brain barrier

Key Points

- The blood–brain barrier (BBB) endothelial cells restrict the passage of substances from the bloodstream to a greater extent than endothelial cells in capillaries elsewhere in the body.
- The BBB results from the selectivity of the tight junctions between endothelial cells in central nervous system (CNS) vessels that restrict the passage of solutes.
- Several areas of the human brain are not protected by the BBB, including the circumventricular organs.
- Tight junctions are composed of transmembrane proteins such as occludin and the claudins.
- The BBB effectively protects the brain from many common bacterial infections. However, since antibodies and antibiotics are too large to cross the BBB, infections of the brain that do occur are often difficult to treat.

Key Terms

- **astrocyte**: A star-shaped neuroglial cell.
- **claudins**: This family of proteins is the most important component of tight junctions, where they establish the paracellular barrier that controls the flow of molecules in the intercellular space between the cells of an epithelium.
• **blood-brain barrier**: A structure in the CNS that keeps substances found in the bloodstream out of the brain while allowing in substances essential to metabolic function such as oxygen.

• **occludin**: A protein forming the main component of the tight junctions, along with the claudin group of proteins.

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**EXAMPLES**

• An exception to the bacterial exclusion are the diseases caused by spirochetes, such as *Borrelia*, which causes Lyme disease, and *Treponema pallidum*, which causes syphilis. These harmful bacteria seem to breach the BBB by physically tunneling through the blood vessel walls.

• Modalities for drug delivery through the BBB entail its disruption by osmotic means, biochemically by the use of vasoactive substances, or by localized exposure to high-intensity focused ultrasound.

The blood-brain barrier (BBB) is a separation of circulating blood from the brain extracellular fluid in the central nervous system (CNS). Bacteriologist Paul Ehrlich observed that chemical dye injected into an animal would stain all of its organs except for the brain. In a later experiment, his student Edwin Goldmann found that when dye is directly injected into the cerebrospinal fluid (CSF) of animals’ brains, the brains were dyed while the rest of the organs were unaffected. This clearly demonstrated the existence of some sort of compartmentalization between the brain and the rest of the body. The concept of the BBB (then termed hematoencephalic barrier) was proposed by Lewandowsky in 1900. It was not until the introduction of the scanning electron microscope that the actual membrane could be observed and proven to exist.

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**Blood-Brain Barrier Structure**

**The Blood Brain Barrier at the Small Scale**: Astrocytes send projections to completely encircle capillaries. This allows tight regulation of passage of molecules into and out of the CNS.

The BBB results from the selectivity of the tight junctions between endothelial cells in CNS vessels that restrict the passage of solutes. At the interface between blood and the brain, endothelial cells are joined by these tight junctions, which are composed of smaller subunits, frequently biochemical dimers that are transmembrane proteins such as occludin, claudins, and junctional adhesion molecule. Each of these transmembrane proteins is anchored into the endothelial cells by another protein complex. This barrier also includes a thick basement membrane and astrocyte cell projections called astrocytic feet (forming the thin barrier called the glia limitans) that surround the endothelial cells of the BBB, providing biochemical support to those cells.
Function and Importance of the Blood-Brain Barrier

The BBB endothelial cells restrict the passage of substances from the bloodstream to a greater extent than endothelial cells in capillaries elsewhere in the body. The diffusion of microscopic particles (e.g., bacteria), large molecules, and hydrophilic molecules into the CSF is restricted, while the diffusion of small hydrophobic molecules (O2, CO2, hormones) is permitted. Also, BBB cells actively transport metabolic products such as glucose across the barrier.

Non-Protected Areas of the Brain

Several areas of the human brain are not protected by the BBB. These include the circumventricular organs such as the area postrema, median eminence of the hypothalamus, pineal gland, and the posterior pituitary. The posterior pituitary and pineal gland are not covered by the BBB because they secrete hormones into circulation. The median eminence is not covered by BBB because the pituitary secretions collect in this area before release into circulation. The area postrema detects noxious substances present in the blood and is therefore not covered by the BBB.

Role of Blood-Brain Barrier in Infectious Processes

The BBB effectively protects the brain from many common bacterial infections, so brain infections are very rare. However, since antibodies and antibiotics are too large to cross the BBB, brain infections that do occur are often very serious and difficult to treat. However, the BBB becomes more permeable during inflammation. This allows some antibiotics and phagocytes to move across the BBB, but also allows bacteria and virus to cross. Diseases caused by spirochetes are exceptions to this bacterial exclusion. These include Borrelia (the cause of Lyme disease), and Treponema pallidum, which causes syphilis. These harmful bacteria seem to breach the BBB by physically tunneling through the blood vessel walls. Some toxins are made up of large molecules that cannot pass through the BBB. Neurotoxins such as botulinum toxin in food might affect peripheral nerves, but the BBB can often prevent such toxins from reaching the CNS, where they could cause serious or fatal damage.