

Fig. 7.1. Schematic representation of SPE results (cellulose acetate strip and densitometer tracing). Proteins are separated during electrophoresis in an alkaline medium on cellulose acetate. Albumin migrates the farthest toward the anode, and globulin fractions separate into bands or fractions (e.g., α_1 -globulins, α_2 -globulins, β_1 -globulins, β_2 -globulins, and γ -globulins). After electrophoresis, the strip is stained with a protein stain (e.g., Ponceau S). Bands that contain the most protein stain the darkest. When scanned with a densitometer, the tracer pen draws a line that corresponds with the intensity of protein staining. The darkest band causes the highest peak on the tracing, and other peaks are relatively lower depending on the relative staining intensities of the corresponding bands. One peak may represent the staining of one protein (e.g., albumin) or may represent the sum of multiple proteins (e.g., the α_2 -globulin region contains Hpt and α_2 -macroglobulin). α_1 ACT, α_1 -antichymotrypsin; α_1 AT, α_1 -antitrypsin; α_1 LP, α_1 -lipoprotein; α_2 MG, α_2 -macroglobulin; β LP, β -lipoprotein; and PA, prealbumin.

Fig. 7.2. Schematic structure of an immunoglobulin. Immunoglobulin consists of two heavy chains of the same class (α for IgA, γ for IgG, δ for IgD, ϵ for IgE, and μ for IgM) and two light chains (either κ or λ but not both). The combination of a light chain and the slanted segment of a heavy chain is a fragment (F) that contains an antigen-binding site (ab) ($F + ab = Fab$). The tail of the Y (vertical segments of two heavy chains) is called the crystallizable (c) fragment ($F + c = Fc$).

Fig. 7.3. Illustration of fluid movements because of Starling's law in a typical capillary bed.

A. Peripheral capillary, arterial to venous blood.

- Hydraulic pressures in health
 - The plasma hydraulic pressure in the arterial side of the capillary bed is much higher than the hydraulic pressure in the interstitial fluid. The difference in the hydraulic pressure is called the hydraulic pressure gradient (Eq. 7.2). A typical hydraulic pressure gradient (ΔP) on the arterial side of the capillary is about 33 mmHg.
 - The plasma hydraulic pressure in the venous side of the capillary bed is higher than the hydraulic pressure in the interstitial fluid. A typical ΔP on the venous side of the capillary is about 13 mmHg.
 - The hydraulic pressure in the interstitial fluid is about -3 mmHg. The negative pressure is created by the actions of valves in the lymphatic vessels and pressure changes in vena cava vessels.
- Oncotic (colloidal osmotic) pressures in health.
 - The plasma oncotic pressure is greater than the interstitial oncotic pressure because the plasma [total protein] is greater than the interstitial fluid [total protein]. The [total protein] essentially does not change in the capillary beds, and thus the oncotic pressure gradient ($\Delta\pi$) remains the same from the arterial side to the venous side of the capillary bed. For most capillaries, the $\Delta\pi$ is near 20 mmHg.
 - Most of the oncotic pressure (both in plasma and in interstitial fluid) is due to albumin, but globulins do contribute. See the text for more information about plasma oncotic pressure (colloidal osmotic pressure).
- The difference between the ΔP and $\Delta\pi$ (i.e., $\Delta P - \Delta\pi$) is a major factor that determines the rate of flow of fluid out of and into capillaries. On the arterial side, the difference is about 13 mmHg, and thus fluid leaves the capillary and enters the interstitial space. On the venous side, the difference is about -7 mmHg, and thus fluid leaves the interstitial space and enters the capillary.

B. Average pressures for peripheral capillary bed.

- Even though the ΔP on the arterial side is much greater than the ΔP on the venous side, the net difference in tissues is only about 0.3 mmHg. Most fluid returns to the capillaries because of two factors: (1) there are more venous capillaries (entering venules) than arterial capillaries (leaving arterioles), and (2) the venous capillaries are more permeable than arterial capillaries.¹⁰⁵

Fig. 7.3. continued

- As long as the lymphatic system removes the interstitial fluid, a transudate does not accumulate.
- Even though the oncotic (colloidal osmotic) pressure is greater in plasma than in interstitial fluid, there is very little difference in the osmolalities of the fluids because proteins contribute very little to total osmolality, and the concentrations of major solutes (i.e., electrolytes, glucose, and urea) are nearly the same in the two fluids (see Chapter 9). The Gibbs-Donnan effect (see Fig. 7.4) creates differences in the osmolality.

Fig. 7.4. Conceptual representation of the Gibbs-Donnan equilibrium.

The protein concentration in plasma is greater than in interstitial fluid, and most plasma proteins have a negative charge (at pH 7.4). The typical capillary wall is nearly impermeable to the proteins but is permeable to Na^+ and Cl^- . Movement of cations and anions is controlled by concentration and charge gradients. At equilibrium, electroneutrality occurs on each side of the capillary wall; for example, 12 cation charges and 12 anion charges in the plasma, and 9 cation charges and 9 anion charges in interstitial fluid. Because of the negatively charged protein molecules, there are more cations and fewer diffusible anions in plasma (12 and 6, respectively) than in interstitial fluid (9 and 8, respectively). Osmolality (determined by the number of solute molecules or ions) is greater in the plasma (24 particles) than in interstitial fluid (18 particles). The COP is generated by the presence of nondiffusible proteins, which causes a greater osmolality in plasma than interstitial fluid (Gibbs-Donnan effect). The Gibbs-Donnan effect increases with the square of the protein charge. Since the average protein molecule has > 1 negative charge, the Gibbs-Donnan effect is proportionately greater at greater protein concentrations.

Fig. 7.5. Schematic representation of the principles of colloid osmometry.

- A.** Two fluids are present in an open-tube system: a solvent (such as isotonic saline) and a similar fluid that also contains large solute colloidal particles (e.g., proteins). The fluids are initially separated by a semipermeable membrane—a membrane that is permeable to the solvent and its small solute particles but not permeable to the large colloidal particles. The presence of large colloidal particles on one side results in a higher osmolality (see the Gibbs-Donnan effect in Fig. 7.4) and thus an osmotic gradient. This gradient creates osmotic pressure; thus the term *colloidal osmotic pressure*. The colloidal osmotic pressure initiates the movement of solvent towards the colloidal particles (movement from **A** to **B**).
- B.** When the system's pressures equilibrate, solvent has moved to the fluid that contained the colloidal particles. The difference in the fluid levels is primarily due to the colloidal osmotic pressure that was created by the colloidal particles. Other factors (such as bulging of the membrane in this open system and gravity) also affect the difference.
- C.** In the closed system of a colloid osmometer, the effects of membrane bulging and gravity are reduced. However, the same general principles apply and the colloidal particles attract the fluid. The colloidal osmotic pressure is measured by a pressure transducer.