Physiology of Nerve Conduction -Miller

The neural membrane is able to maintain a voltage difference of 60 to 90 mV between its inner and outer aspects because at rest it is relatively impermeable to sodium ions but is selectively permeable to potassium ions. An active, energy-dependent mechanism, the Na+ -K+ pump, sustains the ion gradients that drive this potential difference by constant extrusion of sodium from within the cell in exchange for a net uptake of potassium, using adenosine triphosphate as an energy source. Although the membrane is relatively permeable to potassium ions, an intracellular-to-extracellular potassium ratio of 150 mmol/L to 5 mmol/L, or 30:1, is maintained because of the membrane's impermeability to other, potentially cotransported ions and the active removal of potassium.

The nerve at rest behaves largely as a potassium electrode, according to the Nernst equation:

where Em is the membrane potential; Ek is the potassium equilibrium potential; R is the gas constant; T is temperature (Kelvin); F is Faraday's constant; and [K+] is the potassium ion concentration inside (i) and outside (o) the cell. For potassium, therefore,

An opposite situation exists for Na+, which is at higher concentration outside the cell and has a Nernst potential, ENa, of about +60 mV. During an action potential, the nerve membrane transiently switches its permeability from K+ selective to Na+ selective, thus changing the membrane potential from negative to positive, and back again. **8** The progress of this potential change and the underlying events are graphed in **Figure 13-6**. They provide a basis for understanding local anesthetic conduction block.

Ion permeation through membranes occurs via special proteins called ion channels. **9** The conformation of these channels is often sensitive to the membrane potential; both Na+ and K+ channels in nerve membranes are activated to an open conformation by membrane depolarization. Sodium channels, in addition, close to an inactivated conformation following their initial activation. A small membrane depolarization, extending along an axon from a region of excited membrane for example, begins to open both Na+ and K+ channels. The Na+ channels open faster, however, and because the membrane potential is initially much further from the Nernst potential for Na+ than from that for K+, the inwardly directed Na+ current is larger (see **Fig. 13–6)**. Sodium ions thus entering the nerve depolarize it further, leading to the opening of more Na+ channels and increasing the current even further **(Fig. 13–7)**. This sequence of events continues in the *positive feedback of the depolarizing phase* until some of the Na+ channels have become inactivated and enough of the potassium channels have opened to change the balance of current, resulting in a net outward current that produces membrane repolarization (see **Fig. 13–7)**. After one action potential, the concentrations of Na+ and K+ have changed very little. The small amount of Na+ entering and K+ leaving the cell as a result of this process is restored by the Na+ -K+ pump. **10**

Depolarizations too weak to activate enough Na+ channels to produce a net inward current are below the membrane's excitability threshold. The precise value of the threshold varies among different regions of the cell and also changes with time. Directly after an impulse, when some Na+ channels are still inactivated and some K+ channels still activated, the threshold is higher than the resting value, and the membrane is refractory to stimulation. In the immediately repolarized membrane, as Na+ inactivation decays and as K+ channels return to their closed conformation, the original threshold value is progressively restored.

The impulse is a wave of depolarization that is propagated along the axon by a continuous coupling between excited and nonexcited regions of membrane. Ionic current (the action current) entering the axon in the excited, depolarized region flows down the axoplasm and exits through the surrounding membrane, thus passively depolarizing the adjacent region (see **Fig. 13–3)**. Although this *local circuit current* spreads away from the excited zone in both directions, the region behind the impulse, having just been depolarized, is absolutely refractory, and impulse propagation is thus unidirectional.

The local circuit current spreads rapidly along a length of insulated internode in a myelinated axon (see **Fig. 13–3)**, and many nodes of Ranvier in sequence are depolarized to threshold with little intervening delay. Single impulses do not jump from node to node as separate, discrete events, but instead the active

depolarization occurs simultaneously along several centimeters of the largest axons **11** (see **Fig. 13-10**). Indeed, the local circuit current is so robust that it can skip past two completely nonexcitable nodes and may successfully stimulate a third. **12** If nodal excitability is partially reduced, by inhibition of some of the Na+ channels for example, the amplitude of impulses in successive nodes falls decrementally, a process that can continue for many centimeters. **13** This situation probably occurs during certain phases of local anesthesia, as discussed later. However, when the inhibition of Na+ channels is sufficient, so that local circuit current fails to bring the adjacent resting region to threshold, then the impulse is extinguished.