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AN OVERVIEW AND BASAL GANGLIA VULNERABILITY IN KERNICTERUS: INSIGHTS INTO BILIRUBIN NEUROTOXICITY

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Kernicterus, a severe neurological condition, is a direct result of high neonatal hyperbilirubinemia. This syndrome occurs when an excessive amount of free, unconjugated bilirubin breaches the blood-brain barrier, a protective barrier that keeps potentially hazardous compounds in the blood from entering the brain. The neurological effects of kernicterus follow the geographical topography of bilirubin-induced neuronal damage, with the basal ganglia, cochlear, and oculomotor nuclei being the most impacted.

The basal ganglia, a set of brain regions involved in different functions such as motor control and learning, are particularly vulnerable to the neurotoxic effects of bilirubin. This sensitivity can result in acute bilirubin encephalopathy (ABE), a disorder marked by the sudden development of neurological symptoms caused by high levels of bilirubin in the blood. If not treated immediately and appropriately, ABE can proceed to chronic bilirubin encephalopathy (CBE) or kernicterus, causing long-term brain damage.

Bilirubin is thought to produce neurotoxicity through a variety of ways. One such mechanism is the overproduction of glutamate, a neurotransmitter important in most areas of normal brain function, including cognition, memory, and learning. Excessive glutamate release can cause neuronal damage and death, a process known as excitotoxicity.

Finally, elevated intracellular calcium levels can lead to bilirubin neurotoxicity. High calcium levels inside cells can activate a variety of enzymes that can damage cell structures, resulting in cell death. These processes are similar to those that occur following a hypoxic- ischemic insult in newborns, in which a lack of oxygen and/or blood flow to the brain causes neuronal damage.

Infants with bilirubin levels above 25 mg/dL are at a much higher risk of developing kernicterus. Levels exceeding 30 mg/dL are associated with a very significant risk of permanent harm. As a result, early detection of hyperbilirubinemia-related risk factors, prompt diagnosis, and appropriate therapy are critical in controlling newborn hyperbilirubinemia.

The standard treatment for this illness is LED phototherapy and exchange transfusion. LED phototherapy exposes the infant's skin to a specific form of light, which alters the structure of bilirubin molecules, making them simpler for the infant's liver to handle and remove. To swiftly reduce bilirubin levels, an exchange transfusion replaces the infant'sblood with donor blood.

However, new therapy options seek to reduce bilirubin generation, improve liver clearance, and/or reduce enterohepatic circulation. These innovative medicines are predicted to benefit patients with severe hyperbilirubinemia and impending bilirubin-induced neurologic dysfunction (BIND), despite standard therapy. As research continues, it is anticipated that these new medications may give more effective and safe choices for controlling this critical illness.