Neonatal encephalopathy describes a brain injury process experienced by newborn infants, with problems including reduced level of alertness, abnormal muscle tone and power, poor feeding and in severe cases impairment of breathing regulation, and seizures\(^1\). While neonatal encephalopathy may result from various causes, including intracranial bleeding, metabolic problems and infections, the most common known cause is newborn hypoxic-ischemic encephalopathy, also known as ‘HIE’. HIE is a brain injury which is presumed to result from disruption to a baby’s oxygen supply (hypoxia) or blood flow (ischemia) at or around the time of birth. This remains a serious and unfortunately relatively common condition in our community, occurring in approximately 1 in every 2000 births. It can result in death in up to 50% of affected infants, and may also lead to long term and serious disability in survivors\(^2\). This is a great tragedy for the affected babies and their families, and also contributes to the strain on our society’s disability and health care resources.

Death of important brain cells, such as neurones which generate our electrical impulses and connections, and supportive brain cells called glia, usually begins to occur immediately following injury. However, after the initial injury, a further very damaging cascade of events takes place, including tissue inflammation, swelling and loss of energy reserves in the brain tissue, which leads to a secondary wave of cell death and extends the initial brain injury\(^3\). The final brain injury consists of loss of neurones, and also loss and disruption to important brain pathways, with areas of excessive scarring. Consequences to infants to who survive this injury may include lifelong serious movement disorders, cerebral palsy, cognitive delay, hearing, vision and language impairment and ongoing seizure disorders.

The condition is diagnosed by a combination of clinical features, characteristic findings on brain MRI scan, and changes in brain electrical activity, measured on a study called an electroencephalogram. The severity of these clinical signs and investigation findings can also be used to provide information about a baby’s prognosis for survival and long-term development, to assist their family and medical staff in making decisions regarding suitable therapy. For example, involvement of multiple brain areas as seen on MRI scan, including deep structures such as the basal ganglia which are vital for control and co-ordination of movement, may be associated with a more concerning prognosis, and have a particularly strong association with poor motor outcomes, such as cerebral palsy.

Current treatment for neonatal encephalopathy includes supportive management in a neonatal intensive care unit, including support for breathing with oxygen and mechanical ventilation, treatment of low blood pressure with medications such as
adrenaline, and treatment of seizures with anti-epilepsy medications and other sedatives. When severe brain injury is identified quickly in a full term baby, attempts may also be made to reduce the temperature of the baby for the first 3 days of life, called hypothermia or cooling, as this has been shown to reduce inflammation and swelling after the initial brain injury. Even with such treatment, however, mortality remains high and new and better therapies are urgently needed.

Despite advances in obstetric care and monitoring of labour, HIE remains to some extent unpredictable and difficult to prevent. It is therefore important to develop treatments that minimise the second wave of brain injury, to improve survival and long term outcomes for affected babies. Research is continuing into new treatments that reduce the inflammatory response and brain swelling after the initial injury, and also treatments that may assist the brain in its recovery and regeneration after injury.

In the past, it was thought that brain cells once lost, were gone forever and could not regenerate. In recent years, however, it has been found that ‘neural stem cells’ which can give birth to new brain cells, remain in the mature brain in critical niche areas, and that neurones and glia continue to be created from these stem cells right through to adult life. This process of regeneration increases naturally after brain injury. Current research into new treatment for stroke includes exploring ways to maximise the regenerative behaviour of neural stem cells. The newborn brain is particularly rich in stem cells, so such therapies are likely to be even more successful in babies experiencing brain injury than in older children and adults. Moreover, the neural stem cells appear to secrete anti-inflammatory factors which further reduce the extent to the final brain injury. Research trials are proceeding to identify whether new treatments such as injection of umbilical stem cells following injury, administration of medications to enhance stem cell behaviour within their existing brain niches, or alternative neuroprotective and anti-inflammatory therapies can be added to existing management strategies to reduce brain injury and maximise repair. This ongoing research is vital, to allow us to discover the safest and most effective ways to enhance the brain’s natural protective and regenerative mechanisms, and to improve survival and long term outcomes for this serious condition.

References: