EPILEPSY

Epilepsy is defined as a brain disorder characterized by a predisposition to recurrent epileptic seizures. Epileptic seizures have been recognized for millennia. Hippocrates wrote his treatise about epilepsy "On the Sacred Disease" almost 2500 years ago. Today, epilepsy is the most common serious neurological condition affecting around 50 million people worldwide.

Seizures are the result of abnormally synchronized electrical discharges from nerve cells in the brain. The discharges interrupt normal brain function resulting in clinical manifestations that depend on the parts of the brain from which the seizure arises and to which seizure discharges spread. Seizures may temporarily lead to loss of awareness, jerking movements and abnormalities of the senses (including changes in vision, hearing and taste). Seizures can also vary in frequency, from less than one per year to several per day. Traditionally, the diagnosis of epilepsy requires the occurrence of at least 2 unprovoked seizures or one seizure in the setting of an inciting cause such as traumatic brain injury or genetic predisposition.

Seizure types and epilepsy syndromes are classified primarily upon clinical grounds, assisted by neurophysiologic, laboratory, and diagnostic imaging tests. There are two broad categories of seizures: focal (or localization-related) and generalized. Partial seizures involve only a portion of the brain, typically part of one lobe of one hemisphere. A partial seizure can evolve over seconds into a tonic-clonic convulsion, referred to as a secondarily generalized seizure. Generalized seizures are caused by electrical discharges originating from both hemispheres of the brain.

Many types of generalized epilepsy begin in childhood and adolescence and several are genetically determined. The focal epilepsies may begin at any age but are more likely to be due to a brain injury or lesion acquired during life. Unfortunately, although these causes of epilepsy have been identified, there are no treatments that are effective in preventing the development of epilepsy. The prognosis of different epilepsy syndromes is variable. Some types of childhood epilepsy will remit at puberty. In contrast some forms of focal epilepsy respond poorly or not at all to medical treatment but surgical removal of the part of the brain giving rise to seizures results in cure. The appropriate treatment is dependent on the correct diagnosis of the type of epilepsy affecting an individual. This is crucial for selecting the right antiepileptic drug (AED) to use.

In treating epilepsy, efforts are focused on two main goals: maximising seizure control while minimising or avoiding treatment side effects and maintaining or restoring quality of life. AED treatment is generally started after two or more unprovoked seizures, because the recurrence indicates a substantially increased risk for repeated seizures, well above 50 percent. Seizures can be completely controlled with AEDs in up to 70% of newly-diagnosed children and adults with epilepsy. Some people with focal epilepsy in whom seizures continue despite drug treatment benefit from surgical removal of the area in the brain responsible for the seizures. An implanted vagal nerve stimulator and dietary therapies such as the ketogenic diet are sometimes used when seizures do not respond to drug treatment and surgical treatment is not feasible.

Epilepsy causes a high burden of disease. It causes 10% of the global burden of brain and mental disorders. It affects at least 8 of every 1000 Australians with at least 10,000 new people with epilepsy in Australia per year. Two percent of Australians will have a seizure at some time in their life. It affects all age groups and is often a lifelong disorder. People with epilepsy suffer increased mortality and 35% of people with epilepsy report seizure-related injuries each year. Thirty percent of people with epilepsy will suffer an impairment of mental health such as depression. Estimated direct medical costs of epilepsy in Australia range from AUD$4,000 per person per year for those with infrequent seizures to AUD$15,000 per person per year for those with very frequent seizures. Epilepsy also has a substantial impact on caregivers and family members. It carries significant social stigma leading to social exclusion. It affects education and

employment and people with poorly controlled epilepsy are unable to drive leading to loss of autonomy and reduced employment prospects. For Indigenous Australians, seizures and epilepsy account for most neurological hospital admissions. Indigenous Australians present with more serious epilepsy and are 6 times more likely to be admitted to hospital with epilepsy than non-Indigenous Australians.

The field of epilepsy research has undergone a dramatic transformation in the past two decades due to the unravelling of the human genome and advances in scanning technologies. However, substantial gaps exist in our understanding of epilepsy, from its causes and prevention to its clinical impact and treatment. Hastening progress toward understanding the fundamental mechanisms of epilepsy at the genetic, molecular and cellular levels will speed the development of more effective therapies prevent and treat the disorder.