Epilepsy and seizures

As one of the oldest medical conditions known to mankind, epilepsy is a chronic neurological disorder affecting over 50 million people worldwide and disproportionately affecting developing countries. About 30% to 50% of patients with epilepsy are medically refractory, i.e. fail to achieve adequate control of their seizures despite appropriate pharmacological intervention. There is a bimodal distribution in the incidence of epilepsy with peaks in childhood and old age although it can occur at any one time. In fact, up to 10% of the world population will experience a single seizure during their lifetime but a person is formally classified as having epilepsy only when he or she has had two or more unprovoked seizures. An estimated 3% of the population will develop epilepsy by the age of 75. Epidemiological studies from different parts of the world estimate that the prevalence of active epilepsy (i.e. continuing seizures or the need for ongoing anti-epileptic drug treatment) is in the range of 4 to 10 per 1000 people in most locations, and higher in resource-poor countries due to inadequate medical treatment, poor socio-economic status and high incidence of trauma and infectious diseases affecting the brain. The burden associated with epilepsy is great, both for the individual with epilepsy and for society at large. Epilepsy can negatively impact cognitive function, is a source of social stigma and legal marginalization, causes increased mortality, economically contributes 0.5% of the global burden of disease, and is associated with an increased risk of psychiatric disorder. Since epilepsy significantly impairs the quality of life of those living with it, this therefore highlights the need for future research to improve the outcomes from anti-epileptic treatments, and find new therapies that could prevent epilepsy from developing in the first place, or that could stop or reverse the condition once it begins.

Classification of seizures

Instead of being viewed as a singular disease entity, the term epilepsy covers a heterogeneous collection of syndromes with varying aetiologies that are defined by recurrent spontaneous seizures resulting from paroxysmal and abnormal hypersynchronous discharges of neurons residing primarily in the cerebral cortex or the limbic system. The classification of seizures and epilepsy is complex, and has evolved over time. It is periodically revised by the International League Against Epilepsy (ILAE) so that the modifications can lead to an accurate diagnosis, reliable prognosis and effective treatment. According to the most recent ILAE report, seizures are classified into two major categories – focal and generalized, based on their mode of onset. Focal epileptic seizures are now viewed as originating within networks limited to one hemisphere. Generalized seizures on the other hand are viewed as originating at some point within, and rapidly engaging, bilaterally distributed networks. They can be further sub-classified by the clinical and electroencephalographic (EEG) manifestations of the seizure into: tonic-clonic (in any combination), absence (loss of consciousness), myoclonic (sudden and brief involuntary muscle contraction), clonic (repeated jerking), tonic (muscle stiffening) and atonic (loss of muscle tone or drop attacks). Most seizures, either focal or generalized, end after a few moments or a few minutes. If seizures are prolonged or occur in a series continuously, there is an increased risk of status epilepticus (SE) where the ILAE defines the term as “a seizure which shows no clinical signs of arresting after a duration encompassing the great majority of seizures of that type in most patients or recurrent seizures without resumption

of baseline central nervous system function interictally" but has not set a fixed duration criterion.

Classification of epilepsies

As with seizures, the clinical classification of the epilepsies is complex and has evolved over time. Over 50 epilepsy syndromes are described and they are divided into those due to specific 'structural/metabolic abnormalities', which may be genetic (such as tuberous sclerosis) or acquired (e.g. stroke, trauma, and infection) and those due to inherited epileptogenic cerebral dysfunction – 'genetic'. When the underlying pathological substrate has not been identified, it is referred to as 'unknown cause'.

Among the various forms of human epilepsy, temporal lobe epilepsy and the absence epilepsies represent two of the most common examples of "structural/metabolic" focal epilepsies and "genetic" generalized epilepsies respectively. The underlying neurobiologic processes by which a "normal" brain becomes epileptic after genetic and/or environmental insults (referred to as epileptogenesis) remain poorly understood.