

WHO-Facts Sheet

EPILEPSY

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1. EPIDEMIOLOGY, ETIOLOGY AND PROGNOSIS

What is epilepsy?

Epilepsy is a neurological disorder that affects people in every country throughout the world. Epilepsy is also one of the oldest conditions known to mankind. It is characterized by a tendency to recurrent seizures and is defined by two or more unprovoked seizures.

The widely-held belief in many countries is that a person with epilepsy is seized by a supernatural force or power. The ancient belief is reflected in the name of the disorder - the word "epilepsy" being derived from the Greek word "epilambanein" which means "to seize or attack". We now know, however, that seizures are the result of sudden, usually brief, excessive electrical discharges in a group of brain cells (neurons) and that different parts of the brain can be the site of such discharges. The clinical manifestations of seizures will, therefore, vary and depend on where in the brain the disturbance first starts and how far it spreads. Transient symptoms can occur, such as loss of awareness or consciousness and disturbances of movement, sensation (including vision, hearing and taste) mood or mental function.

Seizures

Seizures may vary from the briefest lapses of attention or muscle jerks to severe and prolonged convulsions. They may also vary in frequency, from less than one a year to several per day. Seizures are classified according to where in the brain they arise, for instance:

Partial or focal seizures

These seizures arise from an electric discharge of one or more localized areas of the brain regardless of whether the seizure is secondarily generalized. Depending on their type, they may or may not impair consciousness. Whether seizures are partial or focal, they begin in a localized area of the brain, but then may spread to the whole brain causing a generalized seizure.

Generalized seizures

The electrical discharge that leads to these seizures involves the whole brain and may cause loss of consciousness and/or muscle contractions or stiffness. They include what used to be known as *igrand mali convulsion* and also the brief *ipetit mali* absence of consciousness.

Status epilepticus

This is a state in which a person has frequent seizures without recovery of consciousness between each episode. It is a dangerous state and if not treated may lead to brain damage or death.

It is unclear why particular seizures occur at a particular age or time and not at other ages or times. Provocative factors, however, are recognized in some patients. For example, certain flashing lights (discos, television, video games etc.), over-breathing, over-hydration, loss of sleep, and/or emotional and physical stress, may stimulate seizures. Although these are not causes of epilepsy, they may influence the timing and frequency of seizures.

Different epileptic syndromes are based on the age of onset, the type of seizure, the presence or absence of detectable brain disease and genetic

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background. However, medical science is only at an early stage in understanding these different types.

Epidemiology: Prevalence, Incidence and Mortality of Epilepsy

Epilepsy knows no geographical, racial or social boundaries. It occurs in men and women and can begin at any age, but is most frequently diagnosed in infancy, childhood, adolescence and old age. Anyone can be affected by seizures. In fact, up to 5% of the world's population may have a single seizure at some time in their lives, but a diagnosis of epilepsy is reserved for those who have recurring seizures, at least two unprovoked ones.

Prevalence

The prevalence of a disorder is the proportion of a population with that disorder at a given point in time. From many studies around the world it has been estimated that the mean prevalence of active epilepsy (i.e. continuing seizures or the need for treatment) is approximately 8.2 per 1,000 of the general population. However, this may be an underestimate as some studies in developing countries (such as Colombia, Ecuador, India, Liberia, Nigeria, Panama, United Republic of Tanzania and Venezuela) suggest a prevalence of more than 10 per 1,000.

Incidence

The incidence of a disorder is the number of new cases at a given time. Studies in developed countries suggest an annual incidence of epilepsy of approximately 50 per 100,000 of the general population. However, studies in developing countries suggest that this figure is nearly double that at 100 per 100,000.

One of the main reasons for the higher incidence of epilepsy in developing countries is the higher risk of experiencing a condition which can lead to permanent brain damage. These conditions include neurocysticercosis, meningitis, malaria, pre and perinatal complications and malnutrition.

Mortality

Epilepsy is associated with an increased risk of mortality. Death may be related to:

- An underlying brain disease, such as a tumour or infection;
- Seizures in dangerous circumstances, leading to drowning, burns or head injury, for example:
- Status epilepticus
- Sudden and unexplained causes, or a possible respiratory or cardio-respiratory arrest during a seizure
- Suicide

Whilst studies on this subject are sparse, epilepsy-related deaths in young adults in the UK, for example, are 3 times higher than standard age-related mortality rates.

Etiology of Epilepsy

Epilepsy is often, but not always, the result of an underlying brain disease. Any type of brain disease can cause epilepsy, but not all people with the same brain disease will have epilepsy. In view of the fact that only a proportion of people who have a brain disease experience seizures as a symptom of that disease, it is suspected that those who do have such symptomatic seizures are more vulnerable due to biochemical/neurotransmitter reasons.

There are still many people for whom the cause of their epilepsy cannot, as yet, be identified. In such cases, the theory most commonly accepted is that this epilepsy is the result of an imbalance of certain chemicals in the brain (especially chemical messengers known as neurotransmitters) causing them to have a low convulsive threshold.

Children and adolescents are more likely to have epilepsy of unknown or genetic origin. The older the patient, the more likely it is that the cause is an underlying brain disease, such as a brain tumour or cerebrovascular disease, or is the result of head injury.

Trauma and brain infection can cause epilepsy at any age, and as mentioned previously may account for a higher incidence of epilepsy in developing countries. For example, a common cause in Latin America is neurocysticercosis cysts on the brain caused by tapeworm infection, while in Africa, malaria and meningitis are common causes, and in India neurocysticercosis and tuberculosis often lead to epilepsy.

Febrile illness of any kind can trigger seizures in young children. About 3% of children who have febrile convulsions go on to develop epilepsy in later life.

Treatment and prognosis

Recent studies in both developed and developing countries have shown that up to 70% of newly diagnosed children and adults with epilepsy can be successfully treated (i.e., their seizures can be completely controlled for several years) with anti-epileptic drugs. After 2-5 years of successful treatment, drugs can be withdrawn in about 70% of children and 60% of adults without relapses.

However, up to 30% of people may not respond to drug therapy. A factor which leads to worse prognosis is the presence of an underlying brain disease.

Partial seizures, especially if associated with a brain disease, are more difficult to control than generalized seizures.

Secondary seizures- not epilepsy- such as those related to an acute, short-lasting brain disease, may run a self-limiting course. However, a significant proportion of people will develop established epilepsy.

For economic and social reasons, 3 out of 4 people with epilepsy do not receive any treatment at all. Most of these people live in developing countries.

2. SCIENTIFIC AND MEDICAL ADVANCES

Research into epilepsy falls into two main categories: basic and clinical. However, the vast majority of the technology required to carry out this research and the benefits which accrue from the research are available in developed countries.

Basic Research

This focuses on the fundamental mechanisms which underlie the development of epilepsy, the cause of spontaneous seizures, their different manifestations, their timing and duration, and the consequences of repeated seizures on brain function. Understanding the cellular (neuronal) and brain processes responsible for individual seizure types and epileptic disorders will lead to new approaches to prevention, treatment and care. The following are key points in this research.

- Recent work has traced specific types of seizures to distinct disturbances in neuronal connections in the brain, and the chemical transmission of information between neurons.
- Neuropharmacologists have subsequently identified or designed compounds which selectively interfere with these abnormal brain functions, leading to the development of new anti-epileptic drugs which are able to treat specific types of epilepsy with less impairment of normal brain function. This is because they are less sedative and have fewer cognitive side-effects.
- In the past few years, there have also been advances in research on the genetic basis of some epileptic syndromes, mainly in childhood and adolescence, with the identification of specific chromosomal linkages which increase the probability that an epileptic disorder will appear, usually in association with other acquired or environmental factors.
- Identification of some of the genes responsible for a predisposition to epilepsy may reveal the basic neurochemical or physiological defects which need to be prevented or corrected. This, in turn, may help scientists to develop new anti-epileptic treatments.

- It is quite possible that research over the next decade on molecular genetics of human epilepsy will result in an entirely new classification of epileptic disorders and a better understanding of the fundamental causes of the many forms of epilepsy.

Clinical Research

This research is primarily concerned with the application of new diagnostic technologies and therapeutic interventions. It also includes understanding regional differences in the various types of epilepsy and their cause, studying the provision of health services for people with epilepsy and the cost-effectiveness of treatments. Further research, in the fields of psychology and sociology, and which is not detailed here, has improved to understanding of the impact of the disease on people with epilepsy and enabled the formulation of rehabilitation programs.

Diagnostic Research

It is only in the last decade that clinical neuroscientists have been able to look directly at the structure and function of the living human brain. This has been through the use of:

- Magnetic resonance imaging (MRI) has enabled the majority of structural brain abnormalities responsible for epileptic seizures to be visualized.
- Positron emission tomography (PET) and single photon emission computed tomography (SPECT) can help pinpoint an epileptic region by looking at localized dysfunction in brain blood flow, metabolism and chemical processes during and between seizures.
- Computerized electroencephalography (EEG) and magnetoencephalography (MEG) can readily locate the sites of origin of epileptic discharges.
- Magnetic resonance spectroscopy (MRS) is also being used to non-invasively identify areas of brain damage as well as disturbances in brain metabolism and neurotransmitter function.
- Although MEG and MRS remain experimental diagnostic tools, most of these techniques are being used in epilepsy centres in developed countries not only for research but also for evaluation of people who may benefit from brain surgery as treatment for intractable, drug resistant forms of the disease.

Pharmacotherapy

- It has recently been shown that early effective treatment with anti-epileptic drugs will control seizures in up to 70% of newly-diagnosed adults and children.
- Attention is now being directed at the most

appropriate choice of drug for specific epilepsy syndromes.

- The reasons why some people develop chronic drug-resistant epilepsy is also being investigated.
- For approximately two decades, no new major anti-epileptic medications were introduced. In the last few years, however, five new anti-epileptic drugs have reached the market and several more drugs are currently in the clinical testing stages. In part, this is due to pharmacological application of the better understanding of the basic mechanisms of epilepsy.

Surgical Therapy

The last 20 years, major advance has been the recognition that certain specific epileptic syndromes, which respond poorly to drug treatment, have an excellent chance of successful treatment with surgical intervention.

- Recent advances in diagnostic technology and surgical techniques have led to an increasing use of surgical treatment of epilepsy.
- Pharmacological and surgical therapies are today based on correcting or eliminating specific epileptic disturbances. This not only provides the greatest opportunity for people to be relieved of disabling seizures and the disturbing side-effects of treatment, but it also avoids the long-term psychosocial consequences of living with an uncontrolled epileptic disorder.

3. SOCIAL CONSEQUENCES AND ECONOMIC ASPECTS

Social Implications

Fear, misunderstanding and the resulting social stigma and discrimination surrounding epilepsy often force people with this disorder “into the shadows”. The social effects may vary from country to country and culture to culture, but it is clear that all over the world the social consequences of epilepsy are often more difficult to overcome than the seizures themselves.

Significant problems are often experienced by people with epilepsy in the areas of personal relationships and, sometimes, legislation. These problems may in turn undermine the treatment of epilepsy.

Treatment

Misunderstandings about epilepsy, combined with the economic and financial barriers to availability of treatment in developing countries, play an important role in preventing treatment becoming available to millions of people in

developing countries. For example, culturally informed health-seeking strategies often lead the majority of people with epilepsy in developing countries to turn to traditional healers for treatment.

Economic Aspects

- In 1990, WHO, identified that, on average, the cost of the anti-epileptic drug phenobarbitone (which alone could be used to control seizures in a substantial proportion of those with epilepsy and which is on the WHO list of essential drugs) could be as low as US\$ 5 per person per annum.
- The World Bank report “Investing in Health” (1993) states that, in 1990 epilepsy accounted for nearly 1% of the world’s disease burden. Epilepsy commonly affects young people in the most productive years of their lives, often leading to avoidable unemployment.

4. AN HISTORICAL OVERVIEW

Basic concepts surrounding epilepsy in ancient Indian medicine were refined and developed during the Vedic period of 4500-1500 BC. In the Ayurvedic literature of Charaka Samhita (which has been dated to 400 BC and is the oldest existing description of the complete Ayurvedic medical system), epilepsy is described as “*apasmara*” which means “*loss of consciousness*”. The Charaka Samhita contains abundant references to all aspects of epilepsy including symptomatology, etiology, diagnosis and treatment.

Another ancient and detailed account of epilepsy is on a Babylonian tablet in the British Museum in London. This is a chapter from a Babylonian textbook of medicine comprising 40 tablets dating as far back as 2000BC. The tablet accurately records many of the different seizure types we recognize today. In contrast to the Ayurvedic medicine of Charaka Samhita, however, it emphasizes the supernatural nature of epilepsy, with each seizure type associated with the name of a spirit or god - usually evil. Treatment was, therefore, largely a spiritual matter.

The Babylonian view was the forerunner of the Greek concept of “*the sacred disease*”, as described in the famous treatise by Hippocrates (dated to the 5th Century BC). The term “*seleniazetai*” was also often used to describe people with epilepsy because they were thought to be affected by the moon’s phases or by the moon god (Selene), and hence the notion of “*moonstruck*” or “*lunatic*” (the Latinized version) arose. Hippocrates, however, believed that epilepsy was not sacred, but a disorder of the brain. He recommended physical treatments and stated that if the disease became chronic, it was incurable.

While both Hippocrates and the Charaka Samhita provided this less spiritualized understanding, the perception that epilepsy was a brain disorder did not begin to take root until the 18th and 19th Centuries AD. The intervening 2,000 years were dominated by more supernatural views. In Europe, for example, St. Valentine has been the patron saint of people with epilepsy since medieval times. Sites where St. Valentine was thought to have lived or visited became pilgrimage destinations to get cured. These sites included Rome and Terni (where St. Valentine was Bishop) in Italy, Ruffach in France (where a hospital for epilepsy was later built), Poppel in Belgium, and Passau in Germany.

Throughout this time people with epilepsy were viewed with fear, suspicion and misunderstanding and were subjected to enormous social stigma. People with epilepsy were treated as outcasts and punished. Some, however, succeeded and became famous the world over. Among these people were Julius Caesar, Czar Peter the Great of Russia, Pope Pius IX, the writer Fedor Dostoevsky and the poet Lord Byron (for more information on famous people with epilepsy you may wish to visit the following web site: <http://www.epilepsiemuseum.de>)

In the 19th Century, as neurology emerged as a new discipline distinct from psychiatry, the concept of epilepsy as a brain disorder became more widely accepted, especially in Europe and the United States of America (USA). This helped to reduce the stigma associated with the disorder. Bromide, introduced in 1857 as the world's first effective anti-epileptic drug, became widely used in Europe and the USA during the second half of the last century.

A hospital for the "paralyzed and epileptic" was established in London in 1857. At the same time a more humanitarian approach to the social problems of epilepsy resulted in the establishment of epilepsy colonies for care and employment. Examples include Dianalund in Denmark, Chalfont in England, Bielefeld-Bethel in Germany, Heemstede in Holland, Sandviakain in Norway and the epilepsy centre in Zurich in Switzerland.

The foundation of our modern understanding of the derangement of function seen in epilepsy (pathophysiology) was also laid in the 19th Century with the work of Hughlings Jackson. In 1873, this London neurologist proposed that seizures were the result of sudden brief electrochemical discharges in the brain. He also suggested that the character of the seizures depended on the location and function of the site of the discharges. Soon afterwards the electrical excitability of the brain in animals and man was discovered by David Ferrier in London, Gustav Theodor Fritsch and Eduard Hitzig in Germany.

Working in Germany during the 1920's, Hans Berger, a psychiatrist developed the human electroencephalography (EEG "brainwaves"). Its important application from the 1930s onwards was in the field of epilepsy. The EEG revealed the presence of electrical discharges in the brain. It also showed different patterns of brainwave discharges associated with different seizure types. The EEG also helped to locate the site of seizure discharges and expanded the possibilities of neurosurgical treatments, which became much more widely available from the 1950s onwards in London, Montreal and Paris.

During the first half of this century the main drugs for treatment were phenobarbitone (first used in 1912) and phenytoin (first used in 1938). Since the 1960s, there has been an accelerating process of drug discovery, based in part on a much greater understanding of the electrochemical activities of the brain, especially the excitatory and inhibitory neurotransmitters. In developed countries in recent years, several new drugs have come into the market and seizures can not be controlled in 70% to 80% of newly diagnosed children and adults.

Another recent stimulus towards the understanding and treatment of epilepsy in the last few decades has been the development of neuroimaging equipment. Such technology has revealed many of the more subtle brain lesions responsible for epilepsy. Any type of brain lesion (for example, trauma, congenital, developmental, infection, vascular, tumour, degenerative etc.) might lead to epilepsy in some people.

During the last few decades, greater attention has been paid to quality of life, i.e., psychological and social issues, for people with epilepsy, although progress is slow and services are still poor. It is also the case that most of the advances in developed countries are of relevance but not available for the 80% of people with epilepsy who live in developing countries. Stigma is still the same in both developed and developing countries. For many of these people supernatural views, social stigma and discrimination still prevail. Even in developed countries the disorder is still shrouded in secrecy and people refer not to reveal or discuss their condition.

Of the 50 million people in the world with epilepsy, some 35 million have no access to appropriate treatment. This is either because services are non-existent or because epilepsy is not viewed as a medical problem or a treatable brain disorder.

In 1997, the International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE) joined forces with the World Health

Organization to establish the Global Campaign Against Epilepsy to address these issues. (The ILAE was founded in 1909 and is a professional organization with chapters in 60 countries. The IBE was founded in 1961 and is a lay organization with around 55 national chapters). The aim of the ILAE/IBE/WHO Global Campaign Against Epilepsy is to improve prevention, treatment, care and services for people with epilepsy. It also aims to raise public awareness about the disorder. It is hoped that the end result will be a supportive

environment in which people with epilepsy can live better.

REFERENCES

1. Neurocysticercosis occurs when humans inadvertently become the intermediate host for the pork tapeworm, *Taenia solium*. Under normal circumstances, the adult *Taenia solium* organism lives in the human intestine, and gravid proglottids and ova are passed in the stool. If human inadvertently ingest ova, larvae may encyst in the CNS, producing NCC. Epilepsy is the most common manifestation of NCC, occurring in two thirds of affected patients.