Step by Step
TREATMENT OF EPILEPSY
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Step by Step
TREATMENT OF EPILEPSY

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This book is dedicated to my postgraduate teacher and a great Epileptologist, Dr med. Erwin Stenzel.

Former Medical Chief of Epilepsy Centre in Bethel, Bielefeld, Germany, who inspired me to specialize in the field of epileptology.
A teacher to a student:

More than the calf likes to suck cow’s milk,  
the cow likes to be suckled
Epilepsy is a common health problem affecting 0.5-1% of the general population worldwide. In a neurological practice, patients with epilepsy are encountered so often that epilepsy makes probably the second most common condition after the cerebrovascular disorders. Over the past fifty years much advancement has been made in the field of drug treatment and considerable improvement also in the neurosurgical treatment of partial epilepsies. Brain research leading to a better understanding of neurophysiological aspects of epilepsy, as well as advanced investigations for the diagnostic clarification of seizures, have contributed much for the clinical evaluation of epileptic seizures and epilepsies. Major contributions are done by the International League against Epilepsy in formulating the classifications of epileptic seizures, epilepsies and epileptic syndromes. Around fifty years ago there were two potential drugs for the treatment namely Phenobarbitone and Phenytoin, which had to be used in all forms of epilepsies. Even though both are effective anti-epileptic drugs, they have severe side-reactions particularly in higher doses. The identification of different forms of seizures under long-term monitoring with EEG and video-recording as well as brain research have contributed considerably for the development of further anti-epileptic drugs. Accordingly we have several drugs of newer generation which are indicated in specific forms of epilepsies and epileptic syndromes.

However, much remains unknown in the pathophysiology of epileptic disorders particularly in intractable epilepsies. In spite of new developments in the field of
pharmacotherapy, several aspects of drug-effects and resistance are not properly understood. This makes the situation difficult for the treatment of a patient with epilepsy particularly in the general practice. Not only the selection of a drug but also the handling of a patient on a proper dosage requiring the optimal conditions between therapy effectiveness and over dosage become difficult for a clinical judgement. The patient with new occurrence of epileptic seizures, however, goes in the first place to his family physician for evaluation of his or her embarrassing condition. Even though epilepsy needs further clarification through a neurologist for proper diagnosis and initiation of treatment, the patient generally continues to stay in the care of a family physician for further treatment.

This book on epilepsy has been particularly prepared for the use of a general practitioner as a help for diagnostic clarification and selection of proper antiepileptic drugs. However, the book is based on the International Concept of Epileptology, particularly regarding the terminology of epileptic seizures and epilepsies including childhood syndromes. Epileptology has evolved into a special discipline within the field of neurology which is not only advantages in the clinical practice but also essential for adequate management of a person with epilepsy. The international classifications of epileptic seizures and epilepsies have been simplified wherever possible, however, without going out of the recognized baseline. The drug treatment in different forms of epilepsies, epileptic syndromes but also in undetermined epilepsies have been categorized depending upon the international guidelines. Even though most of the anti-epileptic drugs have been
covered in the chapters on drug treatment, the drugs, which are widely used have been emphasized giving proper indications to the extent possible. Attempts have been made to give a broad based idea on the EEG-studies both under normal conditions but also in case of milder and severe forms of epilepsies. The enclosed small photo CD-ROM in the book contains different EEG-recordings in benign epilepsies as well as in severe forms of partial and generalized epilepsies with special reference to Lennox-Gastaut syndrome.

This book is the result of my over 35 years of clinical experience in the field of neurology particularly epileptology in two European countries namely Germany and Switzerland. I had the opportunity to be a senior resident in the largest Epilepsy Centre Bethel in Bielefeld, Germany, under the able guidance of Dr med. Erwin Stenzel. Later I moved to Switzerland, to the Swiss Epilepsy Centre in Zürich where I worked for fifteen years, finally as medical chief II and associate medical director, also as chief of a large outpatient department. Swiss Epilepsy Centre in Zürich was once rated as one of the six best epilepsy centers worldwide. Over my twenty years of hospital service in Europe, I had the opportunity to be in charge of out-patient department, acute hospital setup, neurophysiology, long-range-care and rehabilitation of patients.

I would like to thank all my colleagues who have been of assistance to me in someway or other. In particular I would like to thank Mrs Silvia Kürsteiner for writing the manuscript of this book in an extremely painstaking manner. She showed great patience in preparing the manuscript even during repeated corrections. My thanks are hereby offered
to Mrs Isabelle Kürsteiner for making all the digital photos for this book. My medical career of around forty years in Western Europe would not have been possible without the moral support of my wife Nirmala and my sons Vijay, Vinay and Anil as well as their families. I am thankful for the useful suggestions of Mrs Helga Steiner during the preparation of this book. Finally I am thankful to my thousands of patients, who have helped me in some way or other to stick on to the specialized field of epileptology for nearly four decades. Last but never the least, I offer my thanks to the publisher M/s Jaypee Brothers Medical Publishers (P) Ltd., New Delhi, for their patience in waiting for the manuscript.

June 2007

PV Rai
EEG Atlas
with short history of patients under different clinical situations

1. **Photo No. DSCN 0003.JPN**
   **Text:** Normal background alpha activity
   Adult patient with a history of occasional grand mal seizures, cryptogenic epilepsy, under medication.

2. **Photo No. DSCN 2211.JPN**
   **Text:** Alpha-theta background activity with beta waves.
   Adult patient under medication for a partial epilepsy with occasional simple partial seizures with secondary generalization.

3. **Photo No. DSCN 0016.JPN**
   **Text:** Sleep activity in an adult patient without epilepsy. K-complexes are seen.

4. **Photo No. DSCN 0013.JPG**
   **Text:** K-complex during light sleep in an adult patient without the diagnosis of epilepsy.

5. **Photo No. DSCN 0011.JPG**
   **Text:** K-complex epileptic in an adult patient with partial epilepsy (right temporal) having complex partial seizures.

6. **Photo No. DSCN 0034.JPG**
   **Text:** Normal alpha background activity in a young adult with partial epilepsy, under medication, mixed with beta-waves in the bifrontal regions.
<table>
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<td>DSCN 0035.JPG</td>
<td>Alpha activity blocked by opening of eyes in an adult patient without the diagnosis of epilepsy.</td>
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<td>DSCN 2224.JPG</td>
<td>Artefacts caused by eye movements in an adult patient.</td>
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<td>Artefacts caused by electrodes in an adult patient (right temporal).</td>
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<td>Slow background activity of theta (and delta) waves in an adult patient with epilepsy under high medication.</td>
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<td>Beginning of drowsiness in an adult patient with epilepsy.</td>
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<td>Diffuse generalized delta- and beta-activity in an adult patient with epilepsy on drug over dosage.</td>
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<td>Diffuse irregular alpha-theta background activity in an adult patient with generalized epilepsy under medication.</td>
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   **Text:** Artefacts caused by electrodes during hyperventilation in a patient without epilepsy.

17. **Photo No. DSCN 0006.JPG**  
   **Text:** Electrode artefact (mirror image) in an adult patient with drug controlled generalized epilepsy.

18. **Photo No. DSCN 0033.JPG**  
   **Text:** Bilateral synchronous and generalized spike wave complexes in an adult patient with idiopathic generalized epilepsy under hyperventilation.

19. **Photo No. DSCN 0018.JPG**  
   **Text:** Bifrontal dominant generalized spike and poly spike wave complexes in an adult patient with idiopathic generalized epilepsy also under hyperventilation.

20. **Photo No. DSCN 0017.JPG**  
   **Text:** Bundles of spike and waves in an adult patient with grand mal epilepsy (slow background activity).

21. **Photo No. DSCN 0026.JPG**  
   **Text:** Diffuse generalized sharp and slow wave complexes in a young adult with undetermined generalized epilepsy and mental retardation.

22. **Photo No. DSCN 2209.JPG**  
   **Text:** Diffuse generalized spike and slow wave complexes in a young adult with undetermined generalized epilepsy and mental retardation.

23. **Photo No. DSCN 2202.JPG**  
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40. Photo No. DSCN 2212.JPG
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41. Photo No. DSCN 2246.JPG
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   Text: Same child as in No. 41, under hyperventilation.
A Short History of Epilepsy
INTRODUCTION

Epilepsy is an ancient illness almost as old as the humanity itself. Not only human beings but also primates with a developed brain can get epileptic seizures. Already in the antic, different systems of medicine have made reference to epilepsy. Ayurveda, the ancient system of Indian medicine has made a detailed description of epileptic seizures. In Charaka Samhita (500 BC) the seizure description is comparable to major grand mal attacks, psychomotor seizures (complex partial) and absences. Ayurveda classifies seizures according to the provocation of humors namely tridoshas Vata Pita, and Kapha. The Greek physician and philosopher Hippocrates considered as the father of western medicine described epilepsy as a disease of the brain after he examined the brains of patients who suffered from epileptic seizures. However, epilepsy remained a mysterious disease for several centuries even after Hippocrates because of various superstitions. Some of the historical personalities like Alexander the Great and Julius Caesar seem to have had epilepsy.

The great warriors like Alexander and Julius Caesar would suddenly fall down in an epileptic fit, get unconscious and have convulsions, only to stand up after some time with energy and vigour. So people might have thought that these great persons were either in possession of some outside spirits or had such over abundance of energy, that they had to have such trance like phenomena, as outlet. Hence this illness was also called a holy disease, great disease and falling sickness. Over the centuries epilepsy was shrouded in mystery either as an influence of bad spirits or as a psychiatric illness. All kinds of magical treatments were recommended for the control of seizures, probably without any considerable benefits.
The terminology of epilepsy which is now being used in many languages worldwide dates back to the antic years. The term epilepsy originates from the Greek language and means “a condition of being attacked or sized”. The concept of being attacked or sized refers to some external force influencing the human organism during an epileptic seizure. This Greek notion of demons causing an epileptic seizure must have existed over the centuries, not only in the countries which came under the influence of antic Greek civilization, but also in other cultures of the world which were not exposed to the Greek way of thinking. In the Indian subcontinent, people believed on the influence of devils causing such diseases as epilepsy and schizophrenia, even though the ancient Indian medicine Ayurveda considered the illnesses clearly as psychosomatic disorder caused by the imbalance of bodily humors. The Hippocratic school considered epilepsy “a great disease” of brain, which was later translated to Latin as morbus sacer (and morbus divus), which terminology existed until recent years also in the German literature.

From the literature on medical history, it is known that ancient tribes in different parts of the world tried to cure people with epilepsy by making holes in the cranial bones probably with the idea of making outlet for evil spirits which caused epilepsy. Several ancient cultures considered epileptic seizures as being provoked through the different phases of the moon, which incidentally seems to be a belief in some cultures event at the present time. An early contribution for the diagnostic concept of epilepsy came from the writings of Hippocrates 400 BC. Written in a rather mystical language usual for the antic literature; Hippocrates...
considered the brain as the seat of epileptic phenomena. As in the case of Ayurveda, Hippocrates also considered the disturbances of humors in the brain as responsible for the occurrence of epileptic seizure.

Most of the ancient schools of medicine in the eastern and western cultures considered some kind of disturbance of bodily humors as responsible for various diseases. Similar were the views of Hippocrates, however, with a difference that he located the pathophysiology directly to the brain and not to the heart or other organs of the body. However, the concept of treatment recommended by Hippocrates was similar, to other systems of medicine namely dietetic and rigorous hygiene. Other schools of ancient medicine recommended consumption of various animal organs as well as magical methods to cure epilepsy. Around 400 years after Hippocrates the Greek physician Galen accepted the Hippocratic idea of brain as the seat of epileptic seizure, giving his own interpretation to the humoral basis of pathophysiology in the brain. He however considered that pathological influences outside the brain namely from other parts of the body may play a significant role in the occurrence of epileptic seizures. It was Galen, who gave the concept of classifying epilepsy as idiopathic meaning caused by brain humors and sympathetic as being caused by irritating factors originating from other parts of the body. Galen also differentiated genuine epileptic seizures from other types of non-epileptic phenomena. Galen prescribed several kinds of diets mostly vegetarian, drugs both of plant and animal origin as well as blood letting as treatment for epilepsy. Galen’s concept of theory and practice related to epilepsy dominated the medical profession for several centuries.
In the French literature the terminology found its way as grand mal meaning major illness. A Swiss physician Georgius Zechius referred to this disease in 16th century as elephantiasis meaning a disease which is so serious that it cannot be conquered at all. A major contribution for the scientific understanding of epilepsy came from the writings of another famous Swiss physician, Samuel André Tissot, in the 18th century. Tissot during his medical practice in Lausanne described in detail about the clinical course of epilepsy. He considered, however, mostly grand mal seizures as epilepsy and named the non-convulsive phenomena as “petit mal”, giving them lesser significance. Tissot considered epilepsy clearly as a disease of the brain and noted that several nutritional and stress factors such as strong emotions, as well as too much consumption of spices, fluids, wine, cognac and coffee may provoke seizures (Krämer and Karbowski, 1999).

The modern concept of epilepsy as a sub-speciality of neurology is mostly the result of writings of two English neurologists, William A Gowers (1845-1915) and John Hughlings Jackson (1835-1911), who made scientific evaluation of epilepsy as a distinct functional disease of the brain. Jackson devoted practically the greatest part of his professional career for the evaluation of epilepsy. He showed the correlations between the excessive discharges of neuronal cells in one hemisphere of the brain leading to contralateral epileptic seizures in the bodily extremities in a definite pattern of “march of spasm”, which are historically termed as Jackson seizures. Beginning with Jackson’s contribution, epilepsy developed as a further speciality in neurology into epileptology. Jackson during
his professional career of over 40 years mostly at the national hospital for the cure of epileptics in Queens Square London made over 300 publications about epilepsy and founded with other neurologists 1879 the Journal of neurology “Brain”. Further contributions for the scientific development of epilepsy as a specific disorder of brain function came from different parts of Europe already in the 19th century. The introduction of Bromide 1857 as a medication for epileptic seizures dominated the therapeutic scene for the next half a century. From the organizational point of view, epileptology started gaining ground around the first part of the 20th century. 1909 an organization called International League against Epilepsy was founded in Budapest, which is even today an active organization worldwide for the promotion of medical and social aspects. A major milestone in the diagnoses was established by the invention of electroencephalography by Hans Berger 1929 in Jena, Germany. This biomedical instrument in a much improved form is even at present an important method for diagnoses and differentiation of epileptic seizures.

During the earlier periods when epilepsy was not clearly established as a brain disorder, it was often associated with psychiatric conditions partly because of psychomotor symptoms associated with certain forms of epilepsy and partly because of the mental deficits seen in patients with chronic epilepsies with accompanying brain damage. Right from the beginning two kinds of people with entirely different grades of intellectual functions were connected with this disorder, namely on the one hand great personalities in whom the disease was considered a holy sickness and those at the other end of the scale who were suffering from moderate to sever degrees of mental retardation.
Actually there is hardly any other condition of neurological disorder where the contrast of intellectual state in patients is as variable as in the case of epilepsy. On the one side genius personalities such as Vincent von Gogh and Fyodor Dostoyevsky are known to have had epilepsy, but on the other side about 20% of the people with chronic epilepsies have this illness because of their congenital or acquired brain damage. It is this group of patients with chronic epilepsies and mental deficits who attracted the attention of European missionaries in the second part of 19th and first part of 20th centuries who then founded in different European countries colonies for the long-term treatment and care of these patients. Such centres were founded in Germany, Switzerland, England, Netherlands and Scandinavia. These centres have developed over the past 150 years into modern comprehensive medical centers for the diagnoses, treatment and rehabilitation of epilepsy patients. However such centres can today take care of only a minority of the people having epilepsy (Rai 1990). The majority of people are being treated worldwide under the care of practising physicians, children specialists and neurologists, as well as at the outpatient departments of neurological and pediatric hospitals. As in the case of many other acute or chronic diseases the diagnosis and treatment of epilepsy has made enormous advances in the 20th century.
Brain Function Related to Epilepsy
INTRODUCTION

Before the nature of epilepsy is described, a clear difference must be made between an epileptic seizure and epilepsy. An epileptic seizure is a symptom of the brain which can occur because of various provocations to the brain. Any person can get an epileptic seizure at any time of life if the brain is provoked to the maximum extent. Such isolated seizures are cerebral symptoms, which need not necessarily lead to a condition of “illness epilepsy”. However, if such epileptic seizures repeatedly occur in an individual with or without provocations, such a condition will be diagnosed as epilepsy. A common example for an isolated epileptic seizure is the febrile convulsion which children can get under high fever mostly in the age group of one to five years. If such febrile convulsions repeat several times in a child, then there is already a risk of getting epilepsy in later life. It is therefore necessary to diagnose every epileptic seizure at any age of life to evaluate the cause of the seizure including the provocations and the risk of further seizures.

Various irregularities in adult life can be a provocation to the brain in respect of epileptic seizures. The common ones are irregular sleep habits with long-term reduction of sleep, irregular and over consumption of alcohol, different kinds of drug abuses, extreme physical and mental stress, infections which have a direct affect on the brain and several other factors which will be discussed later in this book. Even though much brain research has been done over the last six to seven decades; still many things are yet not known about the mechanism of an epileptic seizure.

The anatomy and physiology of the brain will be presented here in short and only in relevance to epilepsy.
The brain is a part of the nervous system which consists of a central nervous system meaning the brain and the spinal cord, a peripheral nervous system involving nerves of the brain and spinal cord as also an autonomic nervous system controlling the involuntary functions of different bodily organs. The brain consists of cerebrum, cerebellum and the brainstem (Fig. 2.1). In the central nervous system the two kinds of cell formations are grey matter and white matter differentiated according to the color. The grey matter in the brain is the seat of nerve cells or neurons which are responsible for major coordination. The white matter consists mostly of cables which are responsible for the connections of nearly 20 billion nerve cells with even higher number of connecting cell groups.
Different groups of nerve cells in the brain have specialized functions. For example, there are specialized groups of nerve cells for vision, speech, feeling of pain, etc. Within the brain there is an intense coordination between the cerebrum, cerebellum and brainstem including stem ganglions. The brainstem is responsible for the basic functioning of breathing and circulation that means for the basic biological functions as this also is the case in animals. The cerebrum is divided into two mirror-image like halves, the hemispheres. It is further divided into frontal, temporal, parietal and occipital lobes. Among other functions the frontal lobe is also responsible for the bodily movements. Behind the frontal lobe is the parietal lobe which is also responsible for the feeling of warm and cold. The occipital lobe is mostly responsible for vision. The lateral temporal lobes are responsible for such functions as memory, concentration, hearing, tasting and smelling. The temporal lobes are very sensitive in regard to epileptic seizures (Figs 2.2 and 2.3).
The upper motor neurons initiate movements in opposite side of the body. These parts are represented in the brain in a particular order from below upwards as follows: tongue, face, hand, forearm, arm, trunk, thigh, leg, foot and peripheral areas. These fibres of the upper motor neurons continue downwards through the cerebral areas leading to the brainstem and medulla oblangata. In this area they form a pyramid and then most of the fibres cross to the opposite side of the body through the spinal cord. Depending on their pathophysiology certain neurological diseases involving muscle weakness and paralysis are termed as motor neuron diseases and the others extra pyramidal diseases.

Even though the entire function of the brain is a highly coordinated mechanism, the two hemispheres have some special functions. In about 95% of all people the left brain hemisphere is responsible for speech and most of them are...
correspondingly right handed persons. In about 1-2% of the people the speech center is located in the right hemisphere. In about 2-3% of the people the speech center is located in both hemisphere. If in the right handed people the speech center is located in the left hemisphere then it is the dominant hemisphere. In the case of left handed people roughly 50% have their speech center also in the left hemisphere the remaining in the right hemisphere. This estimation is important in dealing with focal epileptic seizures but also in the event of any brain surgery, where the speech center must be determined in order to prevent neurological deficits after the operation. Depending upon this anatomical-physiological correlate generally one hemisphere of the brain is responsible for the movements and functioning of the contralateral side of the body. The actual reason for such a functioning is not clearly known, one thinks that it is an evolutionary process. In the event of an epileptic seizure of the right side of the body and extremity, generally the epileptic activity in the left hemisphere is responsible, which because of being the speech center may also lead to speech disturbances during and after an epileptic attack. However, this happens in case of people who are right handed. The opposite is the case in the event of an epileptic seizure occurring over the left side of the body, in which case the patient will probably not have speech disturbances if he or she is at the same time also a right handed person.

The peripheral nervous system comprises of 12 pairs of cranial nerves and 31 pairs of spinal nerves. The autonomic nervous system consists of sympathetic and parasympathetic subdivisions. Functionally all the different...
parts of the nervous system are extremely interrelated to one another. Each system is made of millions of neurons and neuroglial cells, both of which are present in the brain and the spinal cord. The neurons are the basic units of the nervous system; the neuroglial cells support the neurons. The neurons have specific functions and properties of excitation and inhibition, as well as electrical and chemical conductivity involving their inner and outer surface. This impulse is dependent upon a high concentration of sodium ($\text{Na}^+$) outside the cell and a high concentration of potassium ($\text{K}^+$) in the cell which results in an unequal electrical charge across the cell membrane. In the resting state there is a negative charge of 70 mV inside the cell membrane in relation to the outside surface. This difference is the result of cell’s relative impermeability to sodium and the sodium-potassium pump mechanism, whereby sodium is pumped continuously out of the cell and potassium is pumped into the cell. With an adequate stimulus the permeability of the cell membrane changes with increase of sodium and decrease of potassium which results in the cell activity namely depolarization and conduction. After depolarization the ionic flow gets reversed leading to repolarization whereby the cell membrane is again returned to its resting potential. During depolarization and part of the repolarization process the neurons cannot be restimulated with another action potential so that a repeated excitation of the neuron is prevented.

Even though there are billions of neurons in the human brain, they are arranged in a chainlike pathway so that impulses must travel from one cell to another through functional junctions the synapses. The synaptic
transmission is a chemical process that occurs because of the release of different neurotransmitters. In addition the synapses are polarized so that the impulses flow in one direction only for example from the axon of one neuron to the axon or dendrite or cell body of another neuron. The micro anatomic structures of the synapses consist of presynaptic terminal, synaptic cleft and postsynaptic membranes. The presynaptic terminals contain hundreds of very small vesicles that store excitatory or inhibitory neurotransmitters. This micro world of chemical and electrical activities, when disturbed, plays a major role in the production of epileptic seizures.

About 40% of the structures of the brain and the spinal cord are made up of neuroglial cells, which protect, support and nourish the cell bodies and processes of the neurons (Fig. 2.4). There are 4 distinguished types of neuroglial cells namely astroglia (astrocyte), ependyma, microglia and oligodendroglia. Where as neurons cannot divide, neuroglial cells can divide and multiply by mitoses which in a pathological process may lead to brain tumors. As already mentioned the millions of neurons are not directly connected to one another but through the synapses and chemical channels the neurotransmitters. This way every neuron has interconnection with hundreds and thousands of other neurons for exchanging information through electrical and chemical pathways of neurotransmitters. If a cell becomes overactive it sends electrical impulses through the synapses so that chemical neurotransmitters are liberated, which can then excite the neighboring cells. In this process there are neurotransmitters which can excite the activity of further cells or inhibit their activity depending
on the chemical structure of the neurotransmitters. An example for an excitatory neurotransmitter is glutamate and an inhibitory neurotransmitter is gamma-aminobutyric acid (GABA).

Fig. 2.4: Neuron with axons and dendrites
In this fascinating microworld of neurons, neuronal synapses and neurotransmitters there is a constant bioelectrical and chemical activity in the form of excitation and inhibition, which under physiological conditions remains fairly stable (Fig. 2.5). An acute or chronic abnormality of this cellular stability relating to excitation and inhibition can be the main reason for the production of an epileptic activity in brain consequently leading to an epileptic seizure. Even though much information has been accumulated through animal experiments, the exact nature of the beginning of an epileptic activity in brain is not yet fully understood. A disturbance in the bioelectrical activity of a few neurons is not sufficient to produce an epileptic activity and seizure. When we mean an epileptic activity it has to be understood as a disturbance of the bioelectrical
activity of a large number of neurons within the brain, which may temporarily remain constricted to the neuronal activity only. On the other hand when thousands of neuronal cells are disturbed in their physiological activity of excitation and inhibition leading to an excessive discharge of neurons, they may lead to an epileptic seizure with corresponding consequences in the neuromuscular activity and at the level of consciousness. This abnormal neuronal activity can be recorded in electroencephalogram (EEG) which in the absence of an epileptic seizure is termed interictal activity. If a patient is examined in EEG during a seizure this disturbed activity may show another pattern depending on the type of the seizure which is then called ictal activity. Both these phenomena are important in the diagnosis of epilepsy which will be discussed later.

An over excitation of the neuronal activity is represented in EEG in the form of a spike; the inhibitory activity represents a wave. When we imagine the number of nearly 20 billion nerve cells in the brain which are continuously in connection with one another and are constantly exchanging a bioelectrical and chemical activity in the form of excitation and inhibition through the neurotransmitters, an excessive discharge of thousands of cells may lead to a real firework within the brain.

Already in the year 1870 Hughlings Jackson described an epileptic seizure as “a symptom of an occasional burst of excessive neuronal discharge”. This definition holds good, even today in spite of the enormous advances made in the field of neurophysiology for the past 60 - 70 years. An epileptic seizure is the result of an abnormal excitation of neurons either in a particular area of the brain or as a result.
of the trigger mechanism from the deeper structures which lead to similar abnormal over activity in the cerebral cortex either in one hemisphere or in both hemispheres. Depending upon the intensity of this abnormal excitation and localization in the brain, an epileptic seizure may be characterized as a focal, partial or generalized seizure. The different forms of epileptic seizures have various grades of intensity, beginning with mild muscle twitching without any loss of consciousness up to the most serious form of generalized tonic clonic seizures with complete loss of consciousness which is the grand mal. The spread of neuronal activity may show the following pattern:

- Abnormal activity of trigger neurons
- Associated activity of neighboring neurons
- Involvement of a high level of excitation leading to the breakdown of inhibition
- Involvement of otherwise normal neurons leading to epileptic seizure.

The above pattern shows the process of an epileptic seizure beginning as an abnormal neuronal activity in the brain which then activates the healthy neurons in the neighborhood leading to an excessive discharge of a large number of neurons and resulting in an epileptic seizure. In the absence of this complete process there may be a trigger activity in a smaller number of neurons in the brain more or less continuously but without resulting in the further process leading to a seizure. For example if there is a concussion to the brain after an accident resulting in a bleeding or injury to brain tissue, this concussion may irritate local neurons leading to excitation but without necessarily resulting in a epileptic seizure. If there is a further provocation to this
concussion through other internal or external factors such as an infection in the brain or excessive alcohol or sleep deprivation, the irritant cells may cause further excitation which can then result in an epileptic seizure. Similar situation is possible in the event of a brain tumor, which in the early stages may cause only irritation but during its further progression may lead to excitatory mechanism mentioned above resulting in an epileptic seizure.
INTRODUCTION

Epilepsy is a common neurological disorder, probably the second common illness after neurovascular disorders. Epilepsy is characterized by recurrent epileptic seizures, which because of the chronicity is a treatable condition. The symptom of epilepsy is a cerebral seizure which can occur on a variety of conditions and at different age groups. It is a paroxysmal disorder occurring in intervals with or without provoking factors. An isolated epileptic seizure is a symptom, which may or may not be associated with brain pathology. Recurrent seizures, however, may lead to a condition of illness with various medical and psychosocial consequences. Any disease of shorter or longer duration can be a burden to the patient, but some diseases may have various degree of repercussions on the familial, professional and social surroundings of the patient. Some common diseases in the population such as cardiovascular disorders, metabolic disorders and diseases of the skeletal system which generally start in the middle age may have serious consequences for the patients with reduction of quality of life directly or indirectly. These conditions can be, however, evaluated better on the basis of population oriented epidemiological studies.

Epidemiology in the field of epilepsy is rather a later development. However, over the last forty to fifty years several epidemiological studies on epilepsy have been published from different parts of the world, from the western and eastern hemispheres. Because of these studies there is not only increased information regarding the incidence and prevalence of epilepsy but additional knowledge is available
in regard to clinical course as also morbidity and mortality. However, there is not sufficient standardization regarding the evaluation of epilepsy as a chronic disorder. The reasons could be that epilepsy may be a single diagnosis in many otherwise intellectually and socially integrated people, whereas the diagnosis of epilepsy in case of mentally retarded people or such other patients with additional syndromes may be of secondary importance. The parameters of epidemiological assessment may be rather difficult because of these heterogeneous factors in the population studies.

**Terminological Differences**

There is an international classification of epileptic seizures and epilepsies for the last forty years which is accepted as diagnostic criteria by the neurologists. People with epilepsy are, however, not always treated by neurologists but more so by general practitioners, pediatric and psychiatric specialists. These specialized disciplines in medicine may not always use the accepted terminology of international classification. The epidemiologists have to depend on medical practitioners of different disciplines for the evaluation of their studies. The criteria for epilepsy definition are generally based on the occurrence of two or more clear unprovoked cerebral seizures. A further problem lies in the assessment of patients with active epilepsy and such others who are free of seizures under medication. Population studies should ideally include not only the diagnosis of epilepsy but several individual factors namely family, profession, psychosocial and even geographical factors including cultural, rural and urban settings. The infor-
Information for the epidemiological studies is mostly obtained from the following sources:

- General practitioners, family physicians
- Neurologists, pediatricians, psychiatrists
- Neurological departments
- Pediatric departments
- Psychiatric hospitals
- Special epilepsy centers
- Protected homes for the mentally retarded and disabled.

Unlike other common diseases in the general population, epilepsy carries still some social prejudice and as such a clear epidemiological estimation may not be readily available. Further there may be considerable lapse of time between the occurrence of first seizure and the actual clinical diagnosis, as many patients may not report to a physician until the seizures recur. It is generally known in the neurological practice that the first epileptic seizure reported by patients to the general physician, is not always considered as epileptic. This is particularly the case in case of intellectually normal adults who are otherwise healthy and socially well integrated. The occurrence of second and further seizures are generally taken seriously for further diagnosis and treatment. The phenomenology of seizures plays also an important role in the early or the late diagnosis of epilepsy. A grand mal seizure occurring during day may be reported early to the physician, whereas a grand mal seizure in sleep may go unnoticed for quite some time. It is generally the partner of the patient who notices a grand mal seizure at night, and sends the patient for clinical examination. In case of an epilepsy beginning with simple partial or complex partial seizures, there may be even longer lapse of time before the patient goes to a physician for the
diagnosis of his seizure-like condition. On the other hand several non-epileptic seizures such as syncoes, cerebrovascular and cardiovascular problems may be wrongly diagnosed as epilepsy and even treated with antiepileptic drugs (Rai et al 1988). Probably these factors are responsible for the disparity in the statistical analysis of incidence and prevalence presented in many important epidemiological studies from different parts of the world.

**INCIDENCE OF EPILEPSY**

Epidemiological studies are involved in the assessment of the morbidity of a disease in relation to the frequency of occurrence in a specified population and with relation to a particular place and a period of time. Incidence is the assessment of the rate at which new cases of a disease occur. Prevalence is the assessment of all existing cases of a particular disease in the population at a defined time. In case of epilepsy the incidence is usually estimated on the basis of new cases within one year for a population of 100,000. The prevalence on the other hand is the evaluation of the total number of people with epilepsy for a population of 1,000 at a given period of time. The difficulties in assessing the incidence because of diagnostic problems have already been mentioned. In all chronic cases such as epilepsy the prevalence becomes high because of the multiplication of people living with epilepsy, even though the rate of incidence may be rather low. The population at risk for epilepsy must be therefore indirectly estimated depending upon the statistics of incidence and prevalence. Authors on larger epidemiological studies on epilepsy have taken different standards for the measurement of estimation of epilepsy risk for general population.
Considering the studies of various authors the annual incidence rate for epilepsy vary from 17 per 100,000 to as high as 70 per 100,000 (Zielinsky, 1988). Considering the 16 studies referred by Zielinsky, 1988, the average rate of incidence for epilepsy is 36 per 100,000. On the whole the statistics available regarding the incidence of epilepsy from different studies vary from 20 to 50 per 100,000 of the population. The rate of incidence varies depending upon the nature and method of studies carried out. The authors who have made assessments from the reports of medical practitioners have showed higher rates of incidence than those who have conducted their studies directly under the general population. The studies show also different figures depending upon the criteria of diagnosis for epilepsies.

The rates of incidence are higher when isolated epileptic seizures such as febrile convulsions are considered in the epilepsy diagnosis. There are other problems in the assessment of statistics as well. Patients who after the withdrawal of medication get free of seizures may not come for medical consultations. This problem occurs both in the assessment of incidence and prevalence, where it becomes uncertain whether a patient who has remained free of seizures for a particular period of time without medication should be included in the study or not. For the estimation of incidence it is, however, important to assess even those patients who are cured of epilepsy after some years of drug treatment with consequent withdrawal of drugs. Most of the epidemiological studies are retrospective studies based on the estimation of patient case histories from general practitioners, specialized clinics and hospitals. Mani, 1987, conducted direct population based studies in a remote South
Indian village for the assessment of incidence and prevalence based on a defined population in a particular period of time. This study was specific for a developing country like India which however showed similar figures of incidence and prevalence comparable to the studies in socially and industrially developed Western countries. The studies conducted by Mani in 1987, refers to the underdeveloped rural areas in India. Considering the less developed socioeconomic structure in these areas, one would expect higher figures of incidence for epilepsy, which, however, was not the case. One of the explanations could be the higher rate of child mortality in these socio-economically poorer areas.

Age factor plays an important role in the incidence of epilepsy. From the various studies available it is clear, that the rate of incidence is highest among children particularly in the first decade of life. The incidence gets lower in the adult life with a later increase of incidence in the older age after 60 years. The higher incidence in the first decade is understandable from the possibilities of various prenatal, postnatal and childhood diseases and injuries to the brain which are important etiological factors in the occurrence of epileptic seizures. The higher incidence in later part of life is probably due to the presence of diseases which begin after midlife particularly the cerebrovascular disorders. In respect of predominance of sex related to incidence, there is however less clarity. Some studies show higher incidence in males and the others again higher rates in females. It is however known that certain kinds of epilepsies can be slightly higher in women such as the juvenile myoclonic epilepsy and childhood absence epilepsy. The epilepsies
which begin in early childhood or later in life, particularly of the symptomatic forms seem to make no difference in the matter of males and females.

PREVALENCE OF EPILEPSY

Various epidemiological studies have been conducted worldwide to estimate the prevalence of epilepsy. The overall prevalence rates per 1,000 of the general population vary from 1.5 to as high as 19.5 depending upon the various studies (Zielinsky, 1988). For the determination of prevalence of epilepsy in the general population we have to consider again different diagnostic aspects related to epilepsy. Because of these problems, the epidemiological studies here are much more complex than for example in other diseases such as multiple sclerosis, cerebral tumors, diabetes or coronary heart disease. In these diseases a diagnosis can be estimated because of the clinical condition correlating with the more or less standard laboratory findings. In diseases of the central nervous system such as multiple sclerosis or tumors of the brain and spinal cord, even though a clinical diagnosis cannot always be quickly estimated, the MRI can give definite findings to confirm the diagnosis. So also is the case in common diseases such as diabetes or arthritis of the joints where milder or sever symptoms are associated with definite organic or laboratory findings. Epilepsy even though mainly a symptomatic disorder, can cause some problems in the estimation of nosological diagnosis.

The present tendency of accepting two unprovoked epileptic seizures as a criterion for the diagnosis is a rather simplified procedure. There are for example patients who get isolated seizures during puberty and adolescence with
or without traceable provocations and remain seizure free sometimes for a decade or longer. Only the second or the third seizure may bring these patients to a medical examination when epilepsy can be diagnosed after EEG findings or clearer clinical verification. The first seizures in this case would not contribute for the diagnosis of epilepsy whereas only the seizure after a decade may lead to the diagnosis. Similar is the case in regard to febrile convulsions, where only a certain number of children get epilepsy later in life. There are other problems of epidemiological survey. If a study is done directly under the general population with a questionnaire for example “have you ever suffered from an epileptic seizure?”, “did you ever have an attack with the loss of consciousness?” may be answered in different ways. People without clear orientation of epilepsy may find it difficult to give a proper answer for the first question and in the case of second question all kinds of answers are possible which may be suggestive of vago-vasal synapses, complicated migraine, narcolepsy, cerebro vascular disorders. If the studies are carried out from the patient files of general practitioners there may sometimes be an over diagnosis of epilepsy because of the above mentioned factors mentioned by patients. In other cases, real cases of epilepsy may also be overlooked.

The situation may be different if the case files of pediatricians, neurologists or special departments for neurology, pediatric and seizure clinics are studied. These specialists are oriented with the diagnostic criterion of epilepsy as a nosological condition and as such the number of recorded cases about epilepsy may be comparatively low. Any epidemiological study on epilepsy may encounter such
difficulties for proper assessment of the condition as epilepsy. It is actually an unsettled problem because of the terminological difficulties of calling a seizure “epileptic” and a disease “epilepsy” which is often confusing. These terminological problems are not specific in the field of epilepsy as even an coronary attack may be called as a part of a coronary disease, the difference being however that there is another terminology for a pain syndrome namely angina pectoris. All epidemiological studies therefore give a description of the criterions for their analysis and assessment.

Even if the diagnosis of epilepsy is properly estimated based on the nosological assessment of seizure, etiology, EEG finding, there may be some further difficulties related to an “active epilepsy” and such epilepsies which are compensated for a long time with antiepileptic drugs eventually with withdrawal of drugs. One encounters in the clinical practice that patients who come in adult life for conditions such as migraine, TIA, sometimes mention that they had as children epilepsy which without medication was completely healed. Such cases are possible under childhood absences of the idiopathic primary generalized epilepsy or there could have been a wrong diagnosis of epilepsy related to febrile convulsions or other conditions which were of non-cerebral nature. Depending upon these various factors the following points regarding the diagnosis must be considered for the evaluation of an epidemiological study.

- Febrile convulsions
- Isolated seizures, provoked
- Isolated seizures, unprovoked
• Seizures after head injuries
• Seizures due to brain tumors
• Reflex seizures
• Epileptogenic activity in EEG without seizures
• Photosensitive reaction without seizures
• Non-epileptic seizures.

The vast difference in the statistical analysis related to the prevalence of epilepsy presented in various studies may be associated with the above mentioned factors. If we stick on to the concept of defining epilepsy as a nosological entity, based on the occurrence of two unprovoked seizures irrespective of the duration between the seizures, then these aspects must be emphasized in the questionnaire on epilepsy epidemiology namely whether the patient had at least two epileptic seizures in his or her life time. Even in such a case error is possible because it may be difficult to ascertain whether the two epileptic seizures were both provoked or partly unprovoked. However, such a compromise is necessary for estimation of a global epidemiological study. Epidemiological studies on epilepsy carried out some twenty to thirty years ago might have shown other figures regarding prevalence than the studies of present day. This may be due to the factor that for the last twenty years there are many more potential antiepileptic drugs than in the earlier days. Accordingly nearly seventy to eighty percent of the patients with epilepsy are today free of seizures under the new line antiepileptic drugs.

Depending on the etiology and prognosis of epilepsy, a withdrawal of antiepileptic medication is possible after remission of seizures for a period of around five years. Even though there is no clear understanding regarding the
duration of time after seizure freedom, there are neurologists who withdraw drugs after already two years of seizure freedom the others more careful one’s wait for a duration of five years of seizure freedom before they begin to withdraw the drugs. The criteria for withdrawal of medication after seizures freedom are not clear, as the total neurophysiologic mechanism of seizure freedom under medication or after drug withdrawal, is not properly understood. Patients who respond well to a monotherapy with freedom of seizures within weeks or month after introduction of an antiepileptic drug are proper candidates for earlier withdrawal of the medication, even though there are individual variations. Generally adults getting epileptic seizures under cryptogenic epilepsies without proper pathological clinical or EEG findings seem to respond well to a properly selected monotherapy. The withdrawal of a medication is not only based on purely clinical or electroencephalographical findings but also considering the psychosocial situation of the patient. These aspects of active epilepsies where patients are under medication and such others who are considered “cured” without medication must also be considered for epidemiological studies.

**Long Time Prevalence**

Epilepsy can be considered as a “chronic disease” only because of the recurring paroxysmal seizures and the necessity of the patients to take long range medication. In several other chronic diseases such as arthritis and other painful conditions patients take medication on a long range basis mostly to relieve pain and other symptoms associated with such conditions. The situation however is different in
Epilepsy. The long range medication is necessary mostly as a prophylactic measure to prevent the occurrence of further epileptic seizures. In the previous years when much less was known about the mechanism of different kinds of epilepsies, the disorder was considered a lifelong disease and as an incurable condition. As such the concept of epidemiological evaluation was also somewhat different, in that once a patient had epilepsy she or he would be considered as epileptic for whole life. Such a notion is present sometimes even today in respect of issuing driving licences for heavier categories such as buses, lorries, trains and for aeroplanes. The issue of a flight licence is for example not possible in Switzerland once a patient had even one epileptic seizure or some similar clinical phenomena with epileptogenic finding in EEG. The reasons are that the risk of further seizures in such a person is too high to take over the responsibility of a pilot in a civil or military aircraft. In considering such a decision, it does not make much difference whether the seizure was a provoked or an unprovoked one. It is generally believed the risk involved for these persons to get further seizures is higher than the risk for the general population even though this aspect has not been properly studied. The global prevalence of epilepsy has been generally agreed to be 0.5 - 1% of the general population. The figures for people who may have an isolated epileptic seizure sometimes or other in their lifetime are considerably higher with 5% for the population.

We do not yet have proper epidemiological statistics about the people who are considered “cured” after the withdrawal of long range medication. It is generally known that nearly 70-80% of the patients with epilepsies remain
seizure-free under medication but it is not clear as to what percentage of people continue to remain seizure-free without medication for longer years. Different pattern of evaluation may be necessary to estimate such a group of people in the long time epidemiological studies. This would then make difference in considering epilepsy not necessarily as a chronic recurring disorder but also as a curable condition. In the clinical practice it is known that people who suffer from severe attacks of migraine for a definite period of time, may completely remain free of further migraine attacks with or without medication. A similar situation is possible in certain cases of milder epilepsies.

The problem arises because of the risk of loosing consciousness in the event of an epileptic seizure, which is generally not the case in migraine. The clinical studies have shown that a person having more than two unprovoked or sometimes even provoked seizures runs the risk of having further seizures and as such must be treated with anti-epileptic drugs to prevent further seizures. The neurologists are influenced by the historical concept of Gower’s theory that every epileptic seizure could be the reason for further seizures. Such a concept is also supported by the experimental phenomena of Kindling. Accordingly it would be difficult if not impossible, to deny treatment for a person who had more than two epileptic seizures. This is particularly because of the professional and social circumstances common in the urban areas where driving licence becomes a necessity and the risk of accidents during professional activity is considerably raised because of seizures. It may however be useful to include these aspects in the future epidemiological studies, which might
eventually change the clinical picture of epilepsy to a certain extent. The epidemiological study of a condition like epilepsy can not be carried out on parameters which are suitable for such common diseases involving skeletal, metabolic and cardiovascular systems. These chronic diseases have a different morbidity compared to paroxysmal and partly non age dependent condition epilepsy.

**Factors Related to Age and Sex**

From the different epidemiological studies available it becomes clear that the maximum incidence of epilepsy is in the first decade of life particularly in the first one to two years. The incidence rate decreases in the second decade and later become considerably lower, with another peak after sixty years. Several authors have found higher incidence rates in males, the others found again the higher incidence in females so that a conformity is not possible. Similar figures are available also in regard to prevalence of epilepsy related to male and female population. Some authors mention about the higher rate of prevalence among female patients having “inactive” epilepsy compared to male patients. The figures for patients with active epilepsy seem to be however same for both sexes. In other studies again a higher rate of prevalence for male population is suspected because of the probability of more frequent head injuries. The prevalence rates for post-traumatic epilepsy were estimated at 1-1.5/1000 (Zielinsky 1988).

Prevalence based on age specific factors has been studied by many authors. Higher prevalence rates have been registered in different studies among children in the age group of 2-15 years, which show figures of 2-7% prevalence
according to various studies. There were however different criteria for the assessment of prevalence in various studies. Some authors made a survey of younger children from the birth records of different regions, whereas the other authors studied children having epilepsy as well as mental and neurological disorders. On the whole, it seems certain that the incidence and prevalence of epilepsy in the first decade of life show higher figures compared to the second and succeeding decades. Regarding the type of seizures occurring in the early years of life, there are conflicting figures. This is probably due to the fact that there are many childhood syndrome which begin in the first decade of life with variety of seizures such as complex partial, primary generalized, secondary generalized and other kinds of seizures. Epidemiological figures related to the incidence and prevalence of epilepsy in the urban and rural areas are also variable. Some studies show higher figures for the urban areas, the others again for rural areas. Somewhat clearer is the picture related to socioeconomic conditions where higher rates of epilepsy related to incidence and prevalence are recorded in the population belonging to low socio-economic structures.

**Epilepsy and Mortality**

The estimation of mortality associated with epilepsy is based on the death certificate available from medical institutions. There is however some difficulty in the assessment of the actual cause of death in a person with epilepsy. The certificate may mention the immediate cause of death as an epileptic seizure which is however rare, when a person dies during an epileptic seizure as in the case of status
epilepticus, aspiration or severe head injuries associated with an epileptic attack. If the cause of death is not clear, the certificate may mention only about “the death of a person with epilepsy” in which case the assessment of mortality remains unclear. In the European studies available the mortality because of epilepsy was considered 1.1 and 2/100,000 (Goldberg and Kurland, 1962). The studies from industrially less developed countries show slightly higher figures of mortality for epilepsy patients. The cause of death in epilepsy patients may be due to the following factors:

- Status epilepticus
- Death during a single seizure
- Fatal accidents due to seizure.

The indirect causes of death in a epilepsy patient may be due to other factors such as:

- Accidents not clearly estimated
- Suicide
- Unclear death in a person with epilepsy.

From the studies available so far it can be found that the rates of mortality for people with epilepsy are higher than for the general population. However with the improvement in the antiepileptic medication and public education, the situation must have improved during the last few decades. Further studies are necessary considering the newer trends in the diagnosis and treatment of epilepsy, which could give information about the various epidemiological aspects; perhaps with certain changes in the statistical figures.
CHAPTER 4

Epileptic Seizures
As mentioned in the earlier pages, an epileptic seizure is a symptom of the brain irrespective of etiology. In the earlier days an epileptic seizure was classified mostly as grand mal meaning in French “major illness” or Petit mal meaning “minor illness”. A grand mal is characterized by generalized tonic clonic seizures with the loss of consciousness, whereas a petit mal was the expression of minor convulsive or non-convulsive symptoms with or without the loss of consciousness. Over the past 50 years the analysis of epileptic seizures improved considerably because of the development in neurophysiology particularly the long-term monitoring in electroencephalography. As a result there is an elaborate and rather complicated classification of epileptic seizures formulated by the International league against epilepsy, which gets recorrected from time to time according to the further development in the field of neurophysiology. Consequently the terminology of grand mal can generally hold good even today for the description of a generalized tonic clonic seizure (GTCS), whereas the terminology of petit mal is no longer valid because of further differentiated information made available through EEG studies with video recordings.

However there is some basic concept for describing an epileptic seizure namely as generalized seizure or focal seizure. When we talk of a generalized seizure it means that the epileptic activity begins somewhere in the deeper structures in the brain and spreads very fast in both cerebral hemispheres which follows clinically a seizure involving both sides of the body (Fig. 4.1). This may refer to convulsive seizures such as grand mal where the convulsions are seen
more or less symmetrical in both sides of the body. On the other hand non-convulsive seizures such as absences should also be considered as generalized seizures because there are no local or one-sided symptoms in the body. In the event of absences, the patients show almost symmetrical blinking of eyelids or myoclonical jerks in both sides of the body which may or may not be accompanied by disturbed consciousness. In both these cases of convulsive and non-convulsive generalized seizures, the electroencephalography shows during the seizure a symmetrical generalized epileptic activity without predominance of one brain hemisphere.

**Fig. 4.1:** Concept of brain with generalized seizures

On the other hand there are focal epileptic seizures or partial epileptic seizures with or without loss of consciousness. Actually there is no clear terminological difference between focal and partial seizures. When we mean a focal
seizure we are referring to such clinical phenomena which are seen mostly in one part of the body, which may then remain localized to this part or spread further even to the extent of becoming a secondary generalized tonic clonic seizure (grand mal). When we talk of a partial seizure more parts of the body are involved, sometimes with different psychosomatic epileptic phenomena mostly with disturbed consciousness. These seizures also may lead to secondary generalized seizures. Actually any seizure focal, partial, convulsive or non-convulsive may end up in a major convulsive generalized tonic clonic seizure. In the event of focal-partial seizures there is mostly localized neuronal disturbance in the brain in one hemisphere or in the limbic system. The EEG shows during such a seizure at the beginning a focal activity which triggers off in one particular area in the brain, which may then spread to further brain areas (Fig. 4.2). The modern classification of epileptic seizures is the result of the improved clinical observation through video monitoring of an epileptic phenomenon, with simultaneous recording of EEG during a seizure. Consequently it should be clear that the diagnosis of an epileptic seizure even though a clinical matter, can be clarified only through EEG examinations particularly ictal EEG recordings. We have at present an International classification of epileptic seizures as a result of the studies done over the past 50 years worldwide and there is a classification of epilepsy as a disease including different forms of epileptic syndromes both in case of children and adults. These classifications improve the possibility of specialized treatment of different kinds of epilepsies with modern drugs, sometimes also through brain surgery.
In the analysis of epileptic seizures much progress has been made compared to the earlier periods when seizures were described as grand mal or petit mal. At present several forms of epileptic seizures have been identified through long-term EEG monitoring. When we mean an epileptic seizure, there is a particular clinical phenomena experienced by the patient or seen by the environment which must have a corresponding correlation to the epileptic activity in brain which can be recorded in an EEG. For example there are several epileptic like clinical phenomena which do not have a correlation with brain activity, which must then be classified as non-epileptic seizures. An epileptic seizure however simple or complicated must always have a correlation to a generalized paroxysmal or focal epileptic activity in the brain (Fig. 4.3). Before the actual classification
of the epileptic seizure formulated by the International
league against epilepsy is presented, attempts will be made
here to describe the seizures as far as possible also in a
simplified terminology.

Fig. 4.3: Concept of brain with secondary
generalization of seizures

EPILEPTIC SEIZURES (CRITERIA FOR DEFINITION)

- Clinical seizure type
- Electroencephalographic seizure type
- Electroencephalographic interictal expression
- Anatomical substrate
- Etiology
- Age.
General Concept of Seizure Classification

- Focal/partial seizures with or without impairment of consciousness.
- Generalized seizures, convulsive and non-convulsive forms.

Focal/Partial Seizures

Under this group of focal/partial seizures we have to make further two broader classifications.
- Simple focal/partial seizures without loss of consciousness.
- Complex partial seizures with impaired consciousness.

The classification of focal/partial seizures is based on the neurophysiological concept that these seizures are relatively localized in particular areas of the cerebral cortex or the grey matter. Usually these seizures particularly simple partial seizures are localized in one hemisphere of the brain. However, in the case of complex partial seizures the localization may be in one temporal lobe, in the limbic system or in the fronto-basal structures. Simple partial seizures without loss of consciousness are further divided into motor, sensory and autonomic forms. The classification of complex partial seizures is more complicated as the structures involved in the brain can produce complex symptoms which cannot be correlated to only one particular area of the brain. Consequently these seizures are also called psychomotor seizures involving different psychic and motor phenomena with impaired consciousness. The following are rather simplified presentations of simple partial and complex partial seizures.
Classification of simple partial seizures (without loss of consciousness):

- With focal motor signs, such as muscle jerks with or without march of spasms
- With adversary movement of head and/or body
- With postural component, change of body posture
- With sensory or somatosensory symptoms such as disturbed experience of sensory organs
- With autonomic symptoms like change of body feeling, sweating, epigastric sensation
- With psychic symptoms like illusions, delusions, déjà vu, anxiety.

Classification of complex partial seizures (with impairment of consciousness):

- Begin with simple partial seizure developing into a complex symptomatic with impairment of consciousness
- From the beginning with impairment of consciousness followed by different kinds of automatism like chewing, walking, automatic movements
- Beginning with epigastric feeling going into states of disturbed thinking for example “dreamy state”, illusions, hallucinations.

Generalised Seizure

As in the case of partial seizures the classification of generalized seizures is based on the clinical and electro-encephalological aspects. A generalized seizure whether convulsive or non-convulsive is a symmetrical phenomena clinically and associated with a bilateral synchronous and generalized spike wave correlation in EEG. Broadly the generalized seizures can be divided into various types of
absences and lesser varieties of convulsive seizures. Absences are further divided into simple and complex forms in accordance with such phenomena like myoclonus, differences in muscle tone, autonomic and automatic symptoms. The convulsive seizures consist of myoclonic, tonic clonic and atonic clinical phenomena. In addition there are less specified seizures such as infantile spasms and akinetic phenomena. There have been debates about the inclusion of some seizure forms such as infantile spasms and akinetic seizures, under the generalized forms. These seizures are generally the symptoms of epileptic syndromes and as such can not be classified as partial seizures, and accordingly the phenomenology of these seizures belongs to generalized forms. The following simplified presentation shows generalized seizures with non-convulsive and convulsive forms (Table 4.1).

Table 4.1: Classification of generalised seizures

<table>
<thead>
<tr>
<th>Clinical seizure type</th>
<th>EEG expression</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Absence seizures:</td>
<td></td>
</tr>
<tr>
<td>1. Absences (typical):</td>
<td></td>
</tr>
<tr>
<td>- With impairment of</td>
<td>Usually bilateral, regular, symmetrical 3-4 Hz spike and wave complexes with multiple spike and wave discharge</td>
</tr>
<tr>
<td>consciousness only,</td>
<td>- Usually normal background activity</td>
</tr>
<tr>
<td>onset and cessation</td>
<td>- Usually irregular, asymmetrical, paroxysmal discharge of fast activity and spike and slow wave complexes</td>
</tr>
<tr>
<td>abrupt</td>
<td>- Background activity usually abnormal</td>
</tr>
<tr>
<td>- With other components</td>
<td></td>
</tr>
<tr>
<td>(e.g. clonic, tonic,</td>
<td></td>
</tr>
<tr>
<td>atonic automatisms)</td>
<td></td>
</tr>
<tr>
<td>2. Absences (atypical):</td>
<td></td>
</tr>
<tr>
<td>- With pronounced changes in tone</td>
<td></td>
</tr>
<tr>
<td>- With onset and cessation not abrupt</td>
<td></td>
</tr>
<tr>
<td>B. Myoclonic seizures:</td>
<td></td>
</tr>
<tr>
<td>- Single or multiple myoclonic jerks</td>
<td>Polyspike and wave, spike and wave complexes</td>
</tr>
</tbody>
</table>

Contd...
Clinical seizure type | EEG expression
--- | ---
C. Clonic seizures:
  - Predominantly clonic components | Fast activity (about 10 c/sec) and slow waves
D. Tonic seizures:
  - Predominantly tonic components | Low voltage fast activity with increasing amplitude (about 10 c/sec)
E. Tonic-clonic seizures:
  - Major generalised seizures without focal onset | Rhythmic about 10 c/sec decreasing in frequencies and increasing in amplitude, interrupted by slow waves
F. Atonic seizures:
  - Astatic, drop seizures | Fast activity, low voltage or polyspike and waves
G. Infantile spasms:
  - BNS seizures | Discontinuous, asynchronous short paroxysms of spikes, alternating with flattening activity (hypsarrhythmia)

Description of Seizures

Partial Seizures

The description of partial seizures is based on the general concept of the focal onset in cerebral grey matter. This concept holds good mostly for simple partial seizures and to a lesser extent for complex partial seizures. The definition of a partial seizure must be on the basis of a clinical diagnosis which however must confirm the neurophysiological correlation in the grey matter. The classification is rather easy in the event of simple partial seizures without impairment of consciousness, where as in the case of complex partial seizures with impairment of consciousness the situation is rather complicated. Neurophysiologically
the complex partial seizures involve neuronal structures which are of greater complexity and have more organized functions than the primary motor and sensory areas. Accordingly several forms of complex partial seizures can not be simply standardized with one or other form of clinical pattern. Even though many complex partial seizures may show psychomotor symptoms, some seizures may be bland like absences. This differentiation is however important in view of the diagnosis and treatment.

*Simple partial seizures:* Simple partial seizures are characterized mainly by such clinical phenomena of localized symptoms without impairment of consciousness. The subdivision of simple partial seizures as experienced by the patient can be as follows.

The patient experiences generally a motor phenomenon such as clonic jerking of extremity or a part of the extremity such as a thumb or a tow or a sensory phenomenon with change of smell or taste. If such a sensory phenomenon is experienced just before the change of consciousness it is called an aura, which actually is the earliest part of an epileptic seizure. During the history taking and clinical examination every attempt must be made to differentiate a simple partial seizure from a simple absence as this differentiation has an enormous significance in the treatment of these seizures. The simple partial seizures involving motor symptoms do not generally make much difficulty in the differentiation, whereas the simple partial seizures with autonomic symptoms or somatosensory symptoms are somewhat difficult to differentiate from complex partial seizures. Such is the case also in regard to simple partial seizures with psychic symptoms such as illusions or
delusions. However the occurrence of psychic symptoms as an entire manifestation of a simple partial seizure is rather uncommon and may be already the beginning of a complex partial seizure.

Complex partial seizures: As mentioned above a complex partial seizure may begin with a simple partial seizure and develop into a complex phenomenon in the symptomatic and as well as in the EEG pattern. In this case the beginning is a simple partial seizure without impairment of consciousness, which consequently goes into a complex symptomatic resulting in impaired consciousness. The patient will be able to mention some phenomena such as the aura and will be completely helpless in describing further details of the seizure experienced by him. In other cases which are considerably common, the patient experiences an epigastric phenomenon like nausea when he is still without impairment of consciousness. But this feeling of nausea extends upwards very fast up to the region of neck when the patient goes into a state of impairment of consciousness. Usually the patient can not describe further experiences. As such by history taking it is important to ask the dependents or accompanying persons regarding further details of seizure phenomena.

There are other kinds of complex partial seizures in which the patients are with impairment of consciousness right from the beginning and cannot describe anything regarding the seizure. Often however the environment notices different kinds of automatic psychomotor phenomena such as chewing, walking like a robot, starring with a rather fearful look and so on. There are various phenomena involved in complex partial seizures which have to be estimated during
history taking. Some patients experience déjà-vu, which means getting an experience of having seen things before and déjà-vac, getting a feeling of having not seen the things before at all. There are others who experience a trance like phenomena “dreamy state” and some experience sexual fantasies leading into an orgasm.

Complex partial seizures are the most common seizures in adult life, which are also generally therapy-refractory. Many of these patients are of normal intelligent and experience an active professional and social life. The complex partial seizures are mostly the result of an early childhood brain damage resulting in temporomesial sclerosis. The damage can be so minimal that cognitive disturbances are not always noticed during early childhood and school age. In others a “minimal brain dysfunction” is diagnosed during school age but without epilepsy.

**Generalized Seizures**

When we call a clinical phenomenon as a seizure, it is generally understood that this symptom is of a convulsive nature. This is not always the case in respect of generalized seizures as these seizures are both, convulsive and non-convulsive. There is no better terminology for describing an epileptic phenomenon adequately than as a seizure. In non-medical language, an epileptic seizure can be called a fit, which is much more vague than a seizure. Accordingly we have to stick on to the concept of a seizure however calling it as convulsive or non-convulsive in the generalized form. The earlier description as grand mal and petit mal as already mentioned is totally inadequate at the present stage of development in the clinical neurology and neurophysiology.
Absence seizures (non-convulsive): An absence means a brief period of unresponsiveness to the environment because of an impairment of consciousness. The absences begin mostly in childhood or in early adolescence and are characterized by different kinds of clinical phenomena. Automatic behavior may be present both in absences and complex partial seizures, which however must be clinically and electroencephalographically differentiated. The absence is of short duration usually 10-20 seconds and rarely longer than 40 seconds. The onset of absences is sudden and without warning, the cessation is likewise abrupt. Certain automatisms such as blinking of eyelids or myoclonias may be present. In the case of typical absences there is only impairment of consciousness because of which the children may lose contact with the surrounding for a few seconds, may make mistakes in writing, may forget what they have read, but continue their activity immediately after. One observes in such children after an absence a mild embarrassment with a smile before they continue their activity further. These absences are called typical absences as they are devoid of other symptoms.

In this group of typical absences are also included such absences with mild tonic, clonic and atonic phenomena. The myoclonias on the other hand are very heterogeneous which may be present in atypical absence also. The myoclonic jerking is not always an epileptic phenomenon and as such must be distinguished from other kinds of pseudo-seizures.

Other kinds of absences are called atypical absences. These absences are characterized by such associated phenomena as increase of muscle tone and somewhat
different clinical pictures with onset and cessation not being so abrupt, as in the case of typical absences. A diagnosis of these atypical absences can be evaluated through ictal EEG recordings in which, not regular bilateral synchronies spike and wave discharges are registered but somewhat irregular and asymmetrical paroxysmal activity of spike and slow waves complexes are seen.

The clonic seizures are characterized by predominantly clonic components during an absence whereas tonic seizures show an increased muscle tone. In the case of clonic seizures an ictal correlation of fast activity of spikes and slow waves are seen and in tonic seizures low voltage fast activity with increasing amplitude is generally registered in EEG.

Generalised tonic clonic seizures (convulsive): The tonic clonic generalized seizures (GTCS) are the classical form of epileptic seizure which can also be termed grand mal seizure. Clinically it is a dramatic phenomenon where the patient suddenly falls down in a tonic contraction and goes on into a convulsive phase of clonic jerks during which he may bite the tongue, pass urine and stool involuntarily with total loss of consciousness. Postictal, the patient may go into a sleepy condition or sometimes even to a state of agitation. The generalized tonic clonic seizures are a very heterogeneous group. Whether seizures in this group occur simultaneously in both hemispheres or whether they are triggered off from the deeper structures in one or the other hemisphere remains still a debated subject. However in the event of a primary generalised tonic clonic seizure the ictal activity in EEG is from the beginning without a focal dominance. In other cases a tonic clonic seizure may generalized with focal onset because of a focal or partial
seizure with the beginning in one hemisphere only. However in cases of a secondary generalization the ictal activity in EEG should be able to give some information about the beginning of the seizure as of focal onset. Attempts should be made to determine the exact nature of a tonic clonic generalized seizure as primary or secondary generalized for the purpose of better drug treatment.

In addition to grand mal, there are unclassified epileptic seizures which cannot be classified under the above mentioned criteria of clinical judgement or EEG findings. Example for such seizures are neonatal seizures, erratic seizures in infancy and seizures occurring suddenly because of some intoxication.

Repeated Seizures

Under the title repeated epileptic seizures we understand a phenomena of status epilepticus which can be a partial status epilepticus such as with Jackson seizures or psychomotor seizures and a serious form of generalized status epilepticus in the way of repeated tonic clonic seizures which is a life-threatening condition. There can also be epileptic status consisting of absences where a clinical diagnosis from a status of partial seizures is rather difficult. A rare condition is epilepsia partialis continua (after Kozhevnikov) which represents a continuous localized/partial motor status. Other than these there are rarely some other kinds of cluster seizures as those which occur during menstruation and the others which are the result of so-called reflex provocation through television, computer, etc.
Status epilepticus:
- Generalized status epilepticus (tonic clonic, absence status)
- Partial status epilepticus (Jacksonism, psychomotor)
- Localized motor status (epilepsia partialis continua).

Cluster seizures:
- For example menstrual cycle, some reflex seizures.

Generalized status epilepticus with convulsive seizures: A status epilepticus is characterized by a condition of repeated epileptic seizures for a period of 5 to 30 minutes or longer without a clear cessation of seizures. In this condition either the seizures repeat one after another as in the case of generalised tonic clonic seizures where a very brief cessation may be noticed. In other cases the patient may be in a state of unconsciousness when the generalized seizures occur in cluster for a period of 30 minutes or much longer. This is a very serious condition and must be treated as an emergency with parenteral antiepileptic drugs, which will be discussed in the chapters under “Treatment of Epileptic Seizures”.

Absence status epilepticus without convulsive seizures: In the case of absence status the clinical diagnosis is rather difficult. The patients will not have convulsions but may be in a state of reduced consciousness or disorientation without losing control of their motoric functions. The absence status are common among children in school age who have generalized epilepsies, however adults with primary generalized epilepsies may also get status epilepticus with absences. The diagnosis can be confirmed if the patients are examined under an EEG which will show the typical generalized spike and wave discharge. Even though the
clinical condition is not so dangerous like the status of generalized tonic clonic seizures (grand mal status), there is a risk of these patients going over into generalized tonic chronic seizures if untreated. In case of adults the diagnosis of an absence status is even more difficult without an EEG examination as the condition may be confused for psychiatric disorders.

Partial status epilepticus with focal/partial seizures: Similar is the situation concerning a status of complex partial seizures where the patients may be in a condition of reduced consciousness but without being totally unconscious. However in the case of a status of complex partial seizures the patients may show by reduced consciousness several psychomotor automatisms such as chewing, lip smacking, playing with the cloth or moving around without a proper direction or motivation. Even in this case of complex partial seizures a diagnosis can be confirmed only through an ictal EEG recording which might show a continuous activity of uni-temporal, bi-temporal or diffuse frontal-temporal sharp waves. A status of focal motor seizures such as Jacksonian seizures is easier to diagnose clinically as there are continuous muscle jerkings of a particular extremity or a part of the body leading sometimes to a march of spasms as described by Hughlings Jackson about 150 years ago.

There are other forms of rare seizures involved in a status epilepticus such as a localized motor status epilepsy partialis continua (Kozhevnikov) in which case one part of the body may be continuously affected by epileptic seizures over hours and even days which is a very difficult condition to treat. Parenteral anticonvulsive drugs and even an anesthesia is necessary to control the seizures. Every kind
of status epilepticus described above such as absences, Jacksonian seizures and complex partial seizures may all sometimes lead to a status of generalised tonic clonic seizure which then becomes a real medical emergency.

Unclassified seizures: The phenomenology of certain cluster seizures which occur during the menstrual cycle is somewhat unclear. These seizures are classified under catamenial epilepsy and are triggered through hormonal factors mainly an imbalance between estrogen and progesterone. It is considered that estrogen lowers the threshold and progesterone raises the threshold for seizures. The nature of seizures can be variable but they are mostly partial or generalized seizures probably in form of secondary generalized seizures. Similar is the case in respect of reflex seizures which are triggered through the influence of, for example television, computer and other kinds of video provocation. It is not uncommon that people particularly in adolescence get their first seizure by video games, in discotheque or by switching on a television. There are several kinds of reflex phenomena which may trigger off to epileptic seizures. One of the types described by Mani 1987 is called “hot water epilepsy”. It is a heterogeneous group of reflex epilepsy with different phenomenology of seizures.

Epileptic Seizures in Childhood

Some of the epileptic seizures in childhood are age dependent which means they are the expressions of a brain at the early developmental stages. Some seizures are restricted only to a definite period in the brain development, as in the case of BNS seizures which start in the first year of a child’s life. The pattern of these seizures may change as
the child grows, into other kinds of seizures such as tonic, atonic or myoclonic seizures. Most of these seizures are classified under childhood epileptic syndromes and occur as the result of early childhood brain damage mostly prenatal or postnatal.

**BNS seizures (epileptic spasms):** BNS seizure is the short form for Blitz-Nick-Salaam seizure which refers to the phenomenology of epileptic spasms in early childhood. These seizures occur in children mostly because of severe brain damage and the seizures are classified under West syndrome. The characteristics of these seizures are a sudden blitz like forward bending of head and trunk with the arms folded like the oriental form of greeting – Salaam. These seizures occur in clusters with the duration of seconds and can repeat in children up to 100 times a day. During and after these seizures the children mostly cry. Because of this repeated crying of children sometimes the parents and even the doctors mistake the seizures for some kind of abdominal colic. These seizures are also called infantile spasms. The infantile spasms have the phenomenology of myoclonic and tonic components, however in a rapid sequence.

**Tonic seizures:** Tonic seizures are characterized by sudden increase of muscle tone of an extremity or even of the entire body. During the tonic seizures there may be a brief loss of consciousness and the patients may suddenly fall down in a drop attack. Even these seizures are common in children however not in the infantile age but some what later in childhood. The seizures are generally the expression of a serious childhood epileptic syndrome Lennox-Gastaut syndrome. Some other epilepsies in childhood may also show this kind of tonic seizures. The duration of tonic
EPILEPTIC SEIZURES

Seizures can be about 10 seconds or occasionally even 1 minute. The seizures may be accompanied by certain neurovegetative disturbances including flow of saliva.

**Atonic seizures:** Atonic seizures are due to a loss of muscle tone which may also lead to a sudden fall resulting in head injuries for the patient. These seizures were also termed as akinetic and astatic seizures, which terminology has not been used much at present. The difference between tonic seizures and atonic seizures is the pattern regarding the muscle tone, the actual differentiation can be made with the help of polygraphic EEG recording and simultaneous video registering of seizures.

**Clonic seizures:** Clonic seizures are convulsive phenomena of a generalized seizure where in, the tonic phase is lacking. It should be considered as a reduced form of a generalized seizure without the tonic component, in other words an incomplete generalized (GTCS) seizure. The patients generally do not fall down and do not also completely lose consciousness but may have generalized clonic jerks which may then under circumstances proceed to a generalized tonic clonic seizure.

**Description of a Generalized Tonic Clonic Seizure (Grand Mal)**

**Tonic phase**

- Loss of consciousness preceded sometimes by aura
- Sudden dropping to the ground with a noise (if the patient is standing)
- Increase of muscle tone in the whole body
- Dilated pupils without reaction to light
- Brief stoppage of breathing.
**CLONIC PHASE**

- Generalized convulsions in the regions of face and extremities including trunk
- There may be biting of tongue, loss of urine, stool and cyanosis.

**POSTICTAL PHASE**

- Beginning of normal breathing
- Recovery of consciousness
- Postictal sleep or irritability, maybe also headache or clouded state.

**AURA**

A short mention has to be made to an epileptic phenomena, which is popularly known as aura. Several patients mention about a diffuse experience before an epileptic seizure. This is mostly a sensory phenomena experienced by the patient in the form of a simple partial seizure without impairment of consciousness. In other cases it could be the beginning of a complex partial seizure as it is often experienced by patients in the way of an epigastric sensation. In every case either it is a short simple focal seizure or the first part of a complex partial seizure and not an independent phenomena. It can be registered as the beginning of a seizure when the patients are recorded under long-term monitoring with EEG and video. Several epilepsy patients with complex partial seizures are made aware of the oncoming of an epileptic attack through this kind of an aura, so that they may try to suppress this sensation through their own strategy. In some cases of simple partial or complex partial seizures partly controlled through antiepileptic medication, the patients may be able to suppress the aura and prevent
an epileptic attack. But in majority of cases patients report of having had an aura like experience and then there is an impairment of consciousness during the further occurrence of the seizure. There can be different kinds of aura corresponding to sensory experiences such as vision, hearing and taste. Other patients can experience different neurovegetative phenomena or disturbances of memory with such illusions as déjà-vue and déjà-vac.

In case of simple partial seizure of the Jacksonian type the patients are without impairment of consciousness. One can see that the patients are in a position to suppress their motoric jerks by pressing their hand or leg tightly with the other hand or both hands, as the case may be. In other kinds of simple partial seizures without impairment of consciousness the patient may feel the experience of loss of one limb depending upon the localization of ictal activity in cerebrum. This is a very fearful experience for the patients particularly if they are engaged in motoric activities such as walking, operating a machine or driving a vehicle.

**NON-EPILEPTIC SEIZURES**

An epileptic seizure is the symptom of a cerebral dysfunction leading to an excessive neuronal discharge and is not the result of other kinds of psychosomatic phenomena. However there are different kinds of seizure like phenomena which can be confused with an epileptic seizure. As epileptic seizure is a frequent condition occurring in about 5% of the population sometimes in their lifetime, there is a risk of other seizures being wrongly diagnosed as epileptic (Rai et al 1988).
The most frequent wrong diagnosis of seizure-phenomena involves syncope particularly when associated with convulsive symptoms. The other wrong diagnosis are related to different kinds of psychogenic seizures both in adults as well as in children. Such seizures are common among people with conversion hysterical symptoms and must be clearly differentiated from epileptic seizures as otherwise there is a risk of such patients being treated with antiepileptic drugs. In the diagnosis of such seizures a negative interictal EEG is not contributory, but much more help can be got through an exhaustive history taking. A short mention of the common non epileptic seizures will be made here.

**SYNCOPE**

A simple fainting due to a transient drop in blood pressure accompanied by slowing of pulse, pallor and sweating occurs mostly while standing. Loss of consciousness is gradual with a feeling of dizziness and the falling is less abrupt, is usually not associated with injuries. Tongue biting does not occur, incontinence is very rare. The patients when they lie down on ground with brief unconsciousness mostly do not have convulsions. However in some cases of so called convulsive syncopes which are comparatively rare, there may be a few tremor like convulsions of the arms, which may last only seconds. Generalized tonic clonic convulsions as in the case of grand mal seizure are never observed in the case of syncopes. Recovery with nausea and sweating is usually rapid once the patient comes to a horizontal position. These syncopal episodes are sometimes called vaso vagal attacks and may be frequent in adolescence and young
adults of both sex, sometimes under such circumstances as suddenly rising from a chair or being exposed for a while in very closed surroundings such as in a church, temple or supermarket with stuffy conditions. Similar synapses may occur also among sensitive people during such situations as experiencing pain during an injection or seeing blood or getting a shocking news, etc. Such synapses are the result of a failure of certain reflexes to adjust heart rate and vascular resistance to abrupt changes in posture. Syncope can also result from situations like intensive coughing, during micturition of men in standing position particularly in elderly men.

**TRANSIENT ISCHEMIC ATTACKS**

Epileptic seizures may be confused with episodes of transient cerebral ischemia which is a fairly common complaint among elderly people having long-term hypertension and cerebrovascular disturbances. The patients may suddenly lose orientation, may partly continue their activities, however with amnesia for the work done before. This is generally due to a transient circulatory disturbance in the vertebral basilar artery.

**CARDIAC DYSRHYTHMIAS**

In elderly people with vascular disease there may be sometime abrupt cessation of heart beat or rapid change in rhythm which may provoke a drop attack with short unconsciousness. These are called Stokes-Adams attacks and should be diagnosed with careful history taking. Sometimes such Stokes-Adams attacks may lead on to partial complex seizure because of a cerebral ischemia (Marsden and Reynolds 1988).
NARCOLEPSY

Narcolepsy is characterized by frequent daytimes sleep attacks leading to collapse and hypnagogic hallucinations. With a good history taking narcolepsy is easy to diagnose and cannot be confused with epileptic seizures. Difficulty may arise in case of a patient having a car accident because of such sleep attacks. In these cases however consciousness is rarely impaired and the attacks are mostly due to sleeping episodes.

PSYCHOGENIC SEIZURES

Psychological problems particularly in young adults and children may lead to seizure like phenomena which should be differentiated from epileptic seizures. Such behavior is the expression of neurotic hysterical character disturbance particularly when such people are exposed to a stressful situation. These seizures can show dramatic clinical phenomena like a grand mal epileptic seizure however without real loss of consciousness. The patients may fall down, make a loud noise, show excessive jerkings of all the extremities sometimes with a bow like bending of their body and the attack may proceed for 5 minutes or longer. There may be salivation, biting of cheek rarely even slight passing of urine. Some of these seizures are very difficult to differentiate from the real epileptic seizures and require long-term EEG monitoring with video. If the seizures are examined properly there are some significant differences to the phenomenology of a grand mal attack. The drop is not sudden, the convulsions are extremely dramatic and last longer, the consciousness is not lost (however difficult to be estimated during an attack), the pupils are not dilated and
the postictal recovery is not typical as for a grand mal. The patients may however hyperventilate during the attack and may be exhausted. The differentiation from an epileptic seizure is in some cases difficult even for experienced neurologists.

**Panic Attacks**

Panic attacks may be often confused to complex partial seizures beginning in a similar kind of aura with abdominal discomfort, nausea, a feeling of choking sensation and anxiety leading to neurovegetative symptoms. The consciousness is however not impaired and the patients may be able to explain their experiences fairly fully. During history taking the personality of the patient must be considered in detail to explore the situation concerning phobic anxiety and the circumstances which lead to the provocation of seizure like phenomena. A differential diagnosis can sometimes be made only through the help of ictal recording with an EEG.

**Complicated Migraine Attacks**

Certain complicated forms of migraine particularly basilaris migraine may be confused for epileptic seizures. This happens mostly among young women who might get during a migraine attack accompanying symptoms such as diplopia, disartrhria, ataxia, paraesthesia and even drop with a reduced consciousness. These patients may show in an interictal EEG certain focal findings. A complete history taking is necessary to differentiate the migraine attacks from epileptic seizures. However a combination of migraine and certain kinds of partial epilepsies is possible and requires
then further diagnosis also in view of the need for a drug treatment.

**TRANSIENT GLOBAL AMNESIA**

Transient global amnesia is a condition where the patients have amnestic episodes of shorter or longer duration. They are generally patients of middle age or older who develop an amnesia and loose memory for situations they experienced during the hours or days or even months before. Due to this amnesia they lose orientation for the immediate situation and may act wrongly but without making serious mistakes. There are instances where taxi drivers have taken their passengers in a wrong direction but without making traffic mistakes. Asked about the situation for wrong handling they were very embarrassed but could not explain the reason. There are others who drive in wrong directions and reach a place which they did not intend to. These disturbances are most probably the results of a transient functional disturbance in the region of hippocampus, thalamus or singulum of fronto-orbital cortex. A differential diagnosis regarding epileptic seizures is generally not very difficult if a proper history taking is done. However repeated episodes of transient global amnesia may increase the risk for these patients to get partial epilepsy later in life.

**TWILIGHT OR FUGUE STATES**

There are case descriptions where people have been noticed as having lost memory for long periods in which, they have carried coordinated acts with complete amnesia. Such cases have been often described in the novels and press. A clear diagnosis of such fugue states is generally difficult. Cases
EPILEPTIC SEIZURES

are recorded in which the patients were missing for one or more days, they have travelled by train or bus and were found in different destinations with total amnesia for that period. Under this condition of fugue there are several clinical possibilities including twilight states after a major grand mal seizure, a cluster of complex partial seizures or an absence status. However in most cases it is a psychiatric condition where the patient may be in a state of delusion, hallucination and/or amnesia. A diagnosis of epilepsy should be avoided until it is clearly proved through clinical and electroencephalographical studies.

SEIZURE LIKE CONDITIONS IN CHILDHOOD

Some seizures like phenomena in childhood may be confused with epileptic seizures. They are muscle jerks of several kinds, without loss of consciousness which may be present even in the first year of life. The difference being that this kind of myoclonias happen during a clear consciousness of the child. There are other conditions in which children show a tonic contraction of the arms for example during abdominal colics which may be mistaken for epileptic symptoms. They do not lose consciousness and they are mostly children of normal milestones. Other children have sleep disturbances where they may wake up from sleep and have jerk like phenomena in a state of half sleep but without clear symptoms of epileptic seizure (Pavor nocturnes). Children in later years may have behavioral problems, as a result of which there may be episodes of hyperventilation leading to temporary disturbance of consciousness and even drop attacks. Hyperventilation may be the result of anxiety in children and young adults, which
however may further aggravate anxiety resulting in neurological symptoms such as giddiness, visual disturbance, headache, muscle jerks and even loss of consciousness. The symptoms must be clearly explored to differentiate them from epileptic seizures. Sometimes a long-term-monitoring with EEG and video is necessary to make a proper diagnosis.
CHAPTER 5

Epilepsy as an Illness, Etiology
INTRODUCTION

The classification of an epileptic seizure depending upon clinical phenomenology and the cerebral correlation in EEG has been possible to a considerable extent because of the growth of knowledge in clinical neurology and neurophysiology. The classification of epilepsy as a nosological entity based on etiology, seizure pattern, age dependence and prognosis is much more challenging. The task of defining epilepsy as a disease or illness is more than an academic matter, must be considered not only from the clinical and pharmacological aspects but also from psychosocial standpoint. Epilepsy is characterized by occurrence of occasional or frequent epileptic seizures with or without provocations to the brain. There maybe a definite brain pathology associated with the epileptic seizures or the etiology may be totally unknown. Even though an epileptic seizure is a symptom of the brain, the whole personality of the patient is involved during a seizure particularly in serious form of seizures. The social impact of a seizure on the surroundings is considerable, particularly in the case of generalized tonic clonic and complex partial seizures. In the interval between the seizures the patient can be completely a normal person and may be fully integrated in the professional and family surroundings.

Such is the case in around 75% of patients with epilepsy, who do not have serious brain pathology. The situation is different in case of around 25% of children and adults who have severe brain damage or disease which is the cause for their epileptic seizures. Accordingly the classification of epilepsy must be considered from the aspects of etiology and brain pathology. On the one hand there are fairly
uncomplicated cases of partial or generalized epilepsies. A
differentiation has to be made however considering the
etiology of epilepsy as idiopathic and symptomatic forms.
The idiopathic generalized epilepsies may show a genetic
predisposition but this is not always the case. In the case of
a genetic predisposition depending upon the EEG findings
we may classify the epilepsy as primary generalized or
simply as idiopathic generalized epilepsy. On the other
hand there are idiopathic forms also in the partial epilepsies
where the diagnosis of a seizure as partial is possible
clinically and electroencephalographically, however
without knowing the etiology. Such is the case in children
where certain benign childhood epilepsies are present. A
classification of the epilepsy only as idiopathic or
symptomatic is not sufficient for defining different age
related epilepsies which must be then classified as
syndromes.

The classification of epileptic seizures and epilepsies
was originally formulated by Henry Gastaut 1969 and
adopted by the International League against Epilepsy,
which then reclassified the terminology in the later years.
The rational of classification is the result of the growth of
knowledge over the last 50 years in the field of epileptology.
Even today there is no general consensus regarding the
complicated terminology involved in the classification of
seizures and epilepsies, as a particular model or pattern
cannot hold good for longer duration because of newer
developments. However a classification, whatever
terminological differences it may possess, is necessary for
better understanding and communication within the
medical profession. The classification of an epilepsy as
illness must help us to give some information about the etiology, which in turn would help us to consider such epilepsy as a benign or serious form from the point of view of prognosis. The earlier concept of defining epilepsy only as idiopathic (etiology not known) as opposed to symptomatic where a clear cerebral pathology is recognized, has changed over the years leading to further differentiated definitions. The childhood epilepsies are mostly age-related syndromes associated with or without brain pathology and developmental age of the child. The serious forms of these epilepsies are the manifestations of a complexity of neurological disorders, wherein only the epileptic seizures can be treated to a certain extent. The psychosomatic retardation of the child remains to a large extent uncontrollable. Table 5.1 shows a simplified classification of epilepsies and epileptic syndromes.

A reference must be made to the concept of classification regarding idiopathic and symptomatic form. The classification of epilepsy as a nosological entity is based mostly on the evaluation of etiological factors. When no etiology is found, sometimes the epilepsy is called genuine, which is generally a mistake. The developments in neurophysiology over the years have contributed considerably for the exploration of etiology. However in several cases in spite of our available technological methods the etiology remains undetected. Accordingly the terminology of idiopathic epilepsy has to be maintained for better understanding of the differences. In reality however epilepsy seems to be mostly a symptomatic disorder associated with organic or functional disturbance in the brain. In the event of siblings for example, it is possible that
One person gets the primary generalized epilepsy with typical bilateral synchronous generalized spike wave distribution in EEG clinically associated with absences and grand mal seizures. The other sibling may show a similar EEG pattern if examined but without having clinical epilepsy. This shows that the sibling who has epilepsy could have eventually a minimal brain dysfunction causing the clinical condition. In the matter of clinical diagnosis however we must consider only such factors which are:

<table>
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<tr>
<th>Table 5.1: Classification of epilepsies</th>
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<td>1. Partial (focal) epilepsies:</td>
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<tr>
<td>• Idiopathic age-related form, e.g. benign childhood epilepsy with centrottemporal spikes</td>
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<tr>
<td>• Symptomatic form which is not age related, e.g. many varieties of partial epilepsies having different clinical patterns and etiological factors</td>
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<tr>
<td>2. Generalized epilepsies:</td>
</tr>
<tr>
<td>A. Generalized idiopathic epilepsies:</td>
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<tr>
<td>• Benign neonatal epilepsies</td>
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<td>• Childhood absence epilepsy</td>
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<td>• Juvenile absence epilepsy</td>
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<tr>
<td>• Juvenile myoclonic epilepsy</td>
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<tr>
<td>• Idiopathic generalized epilepsy with tonic clonic seizures</td>
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<tr>
<td>B. Generalized symptomatic epilepsies:</td>
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<tr>
<td>• Age Related generalized symptomatic epilepsies (e.g. West syndrome, Lennox-Gastaut syndrome)</td>
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<tr>
<td>• Other forms of generalized epilepsies with accompanying brain damage and/or encephalopathy</td>
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<td>3. Undetermined epilepsies or epileptic syndromes:</td>
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<tr>
<td>For example febrile convulsions, neonatal seizures, progressive epilepsies</td>
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(Simplified from the International Classification of 1970 and 1985)
relevant as symptoms. In the genetics involving epilepsy it is known that epilepsy is not inherited as such, but only the neurophysiological pattern which leads to epilepsy. Probably some other unknown factors are necessary for getting a clinical epilepsy.

**TERMINOLOGICAL DIFFERENCES**

Regarding the definition between epileptic seizures and epilepsies, one does not make much difference in a general medical practice or even in a neurological practice. However this differentiation is necessary not only from the academical point of view but also in view of proper diagnosis and treatment. A single epileptic seizure, even a grand mal seizure does not make the diagnosis of epilepsy, as this is only an isolated cerebral symptom. An investigation may be necessary to find out the cause for the seizure, but in the absence of brain pathology and if there is no risk of further seizures, then a medical treatment is not indicated. When do we make a clear difference between isolated epileptic seizures and epilepsy? There are no hard and fast rules. The criteria is the risk of chronification of epileptic seizures. Febrile convulsions for example in a child to the extent of two or three seizures during high fever over a period of one or two years can not be considered as epilepsy unless the EEG shows a pathological finding or there is some evidence of brain pathology. If the febrile convulsions however continue repeatedly several times in a child under low fever or without fever, then the diagnosis has to be revised and the necessity of treatment should be reconsidered. Such is the case in other isolated seizures provoked by severe consumption of alcohol or drugs. Even in this case we cannot
define the seizure as a diagnostic entity for epilepsy but should be considered as isolated seizure until the cause is determined. Accordingly if the seizures continue even without consumption of alcohol or drug then the diagnosis has to be reconsidered also in view of the necessity of treatment.

The epilepsies in childhood are generally different from the epilepsies in adult life, even though the seizures may be similar. Certain seizures of childhood may not occur in adult life. However the seizures started in childhood such as myoclonic, atonic seizures may continue to adult life. The epilepsies in children whether benign or severe forms, show some definite patterns which are generally age dependent as already mentioned earlier. Descriptions of the syndromes are mentioned in the coming chapters.

Epilepsy can start in children at very early age, among adults mostly at the age of adolescence and somewhat in later years. There is another peak age which is generally in very elderly people. Symptomatic epilepsy for example as a result of brain damage due to accidents, diseases, tumor can begin in any time of life. The most common epilepsy in adult age is the partial epilepsy or the symptomatic type of epilepsy. The partial epilepsies are characterized by focal or partial seizures of the simple or complex partial forms and such epilepsies which lead to secondary generalization leading to grand mal. Partial epilepsy should be diagnosed on the basis of clinically occurring partial seizures, associated with focal EEG findings during interictal or ictal recordings. In some cases these patients with partial epilepsies may have neurological deficits; in others the neurological status could be completely normal. Most of the
patients with partial epilepsies in adult life are intellectually intact people pursuing normal professional and family activities. Table 5.2 shows a further classification of the epilepsy as a disease entity with epileptic syndromes particularly of childhood based on the International Classification of Epilepsy.

### Table 5.2: Classification of epilepsies and syndromes

<table>
<thead>
<tr>
<th>1. Partial epilepsies and epilepsy syndromes, idiopathic and symptomatic forms:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Idiopathic age related forms:</td>
</tr>
<tr>
<td>- Benign epilepsy of childhood with centro temporal spikes (Rolando Epilepsy)</td>
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<tr>
<td>- Benign epilepsy of childhood with occipital spikes</td>
</tr>
<tr>
<td>- Primary reading epilepsy</td>
</tr>
<tr>
<td>• Symptomatic forms (not always age related):</td>
</tr>
<tr>
<td>- Chronic progrediant epilepsy partialis continua in childhood (Kozhevnikov epilepsy)</td>
</tr>
<tr>
<td>- Epileptic syndrome with special provocations (reflex epilepsy)</td>
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<tr>
<td>- Temporal lobe epilepsy</td>
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<tr>
<td>- Frontal lobe epilepsy</td>
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<tr>
<td>- Parietal lobe epilepsy</td>
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<tr>
<td>- Occipital lobe epilepsy</td>
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<tr>
<td>• Undetermined forms of partial epilepsy</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2. Generalized epilepsies and epilepsy syndromes:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Idiopathic age related begin of epilepsies:</td>
</tr>
<tr>
<td>- Benign familial neonatal seizures</td>
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<tr>
<td>- Benign neonatal spasms</td>
</tr>
<tr>
<td>- Benign early myoclonic epilepsy</td>
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<tr>
<td>- Absence epilepsy of childhood</td>
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<tr>
<td>- Juvenile absence epilepsy</td>
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<tr>
<td>- Juvenile myoclonic epilepsy</td>
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<tr>
<td>- Other idiopathic generalized forms of epilepsy</td>
</tr>
<tr>
<td>- Reflex epilepsies</td>
</tr>
<tr>
<td>• Undetermined epilepsies or epileptic syndromes</td>
</tr>
<tr>
<td>- West syndrome (infantile spasms)</td>
</tr>
</tbody>
</table>

Contd...
- Lennox-Gastaut syndrome
- Epilepsy with myoclonic astatic seizures
- Epilepsy with myoclonic absence

• Epilepsy with undetermined etiology:
  - Childhood myoclonic encephalopathy
  - Childhood epileptic encephalopathy with Burst suppression in EEG
  - Other undetermined symptomatic and generalized epilepsies

• With specific syndromes:
  - Epilepsy due to brain deformity (phakomatose, Aicardi’s syndrome)
  - Congenital metabolic disorders including Pyridoxine or Vitamin B6 dependent disturbances, which may lead to progrediant myoclonus epilepsy

• With focal and generalized seizures:
  - Neonatal seizures
  - Severe childhood myoclonic epilepsy
  - Epilepsy with continuous spike wave pattern in sleep (ESES)
  - Aphasia epileptic syndrome (Landau-Kleffner syndrome)
  - Other undetermined epilepsies
  - With several generalized tonic clonic seizures in sleep (sleep grand mal epilepsy)

3. Special epilepsy forms and syndromes:
• Occasional seizures
  - Febrile convulsions
  - Isolated seizures or isolated status epilepticus
  - Seizures in context of acute metabolic disorders or toxicity (alcohol, drugs, eclampsia, hypo- or hyperglycemia)

• Isolated unprovoked seizures
• Reflex epilepsy
• Chronic progrediant epilepsy partialis continua of childhood

From the above rather complicated classification of epilepsies and epileptic syndromes, it should be clear that...
many forms of epilepsies are still poorly understood particularly from the point of view of etiology. Under the above mentioned classification we have also such epilepsies and epileptic syndromes where people may get only a few epileptic seizures in their whole life, the mechanism of which cannot be properly understood. Not only the brain pathology remains unclear but also the situation concerning a clinical judgement in view of initiating a medication. On the other hand there are childhood syndromes, where a child (because of a severe brain damage or an encephalopathy) may have up to hundred seizures per day or more. In the case of such severe encephalopathic syndromes the focus of attention is centred on epileptic seizures, because of the necessity of treating the seizures. The seizures however are difficult to treat and remain mostly therapy-resistant, but without treatment the condition may lead to a status epilepticus with fatal consequences. Although epilepsy is known since centuries as clinical phenomena with cerebral seizures, the concept of classifying the seizures and the epilepsies began only after developments in the neurophysiology particularly after the practice of EEG studies with video monitoring. The classification by Gastaut 1969 was modified over the years through the International League against Epilepsy which makes revisions from time to time depending upon the availability of new scientific information. Even though epilepsy is primarily a clinical diagnosis based on the occurrence of seizures, the general physicians and neurologists rarely get an opportunity to witness a seizure particularly in the case of occasional seizures. A clinical diagnosis of epilepsy is however generally possible through correct history taking from the
patients and the dependants; a classification of the epilepsy is not possible without further diagnostic procedures involving EEG and sometimes neuroradiological methods.

It is necessary to mention here that epilepsy cannot always be considered as a chronic illness, as there are different conditions where epileptic seizure is only a temporary symptom which may or may not need a long-term treatment. As such one must be careful in labelling a patient as an “epileptic”, because of a large variability in the prognosis with or without treatment. Further, epilepsy as a diagnosis cannot be justified unless there are clinical symptoms of clear epileptic seizures. Rarely there are individuals who have in EEG epileptic changes without clinical seizures, in which cases the diagnosis of epilepsy is not correct. The idea of labeling a patient as having “a bioelectric epilepsy” should be considered as a non-diagnosis. However in such individuals careful history taking is necessary sometimes under longer observation to rule out the possibilities of mild clinical epileptic phenomena.

EPILEPSIES IN CHILDHOOD

The childhood epilepsies are in several ways different than the epilepsies which occur in adult life. The clinical symptoms, etiology and prognosis of childhood epilepsies are related to cerebral maturation and in this way very much age dependent. Different kinds of injuries to the developing brain may cause epilepsies involving various clinical course and prognosis. The damage can occur already during the pregnancy of the mother, as well as during child birth and in the following early periods of childhood. The earliest events in the embryology of nervous system can occur
around the 6th week of gestation in the way of dorsal and ventral induction of the neural plate followed by further proliferation, migration and organization of neuronal structures, followed by myelinations. Some of the disorders of neuronal proliferation leading to abnormal neuronal migration may be associated with epilepsies of early childhood. The organization of the nervous system occurs from six month of gestation to the postnatal age of several years when dendritic and axonal ramifications occur, and the synaptic contacts are established (Volpe 1981). Since birth occurs during the period of maximal organization it may be possible that perinatal insults might also lead to disorders in neuronal organization. If the childhood epilepsies are the results of disorders of neuronal proliferation, migration and organization, such epilepsies may lead to intractable conditions with severe prognosis.

Several kinds of trauma to the brain are possible already during the stages of gestation. The common ones are the abnormalities in the embryonic development, infections of the mother during pregnancy, intoxications during pregnancy such as through alcohol, tobacco, drugs or other toxic expositions. Further damage to the infant brain is possible during difficult birth through mechanical damage or lack of oxygen. The newborn child may be exposed to additional risk of brain damage through infection and trauma. The manifestation of epilepsy may be dependent in proportion to the intensity of brain damage. Some of the severe epileptic syndromes of childhood are etiologically the results of such brain damage which may lead to an epileptic syndrome including permanent intellectual retardation.
Genetics and Epilepsy

From the scientific literature available there is convincing evidence that genetic factors play a certain role in the development of epilepsies including EEG patterns. However no single genetic factor has been found responsible for causing epilepsy. Around 140 Mendalian traits in the humans carry an increased risk for seizures (Anderson et al, 1986). Obviously there is a genetic heterogeneity with different genetic pathways which may lead to the condition of epilepsy. These conditions can be affected by genetic variation, with the result that some individuals may have a reduced ability to handle the effect of environmental insults such as infections or trauma (Anderson and Hauser, 1985). However it is known that only very small proportion of patients with epilepsy may have a chromosomal abnormality, which has to be estimated through genetic studies. In the clinical practice, cases of primary generalized epilepsies are seen often with a positive family history of epilepsy in the case of close relatives such as parents and siblings. Even in the case of certain partial epilepsies in adolescence or early adult life, the possibility of genetic predisposition must be considered through careful history taking. The genetic factor has to be considered also during the classification of an epilepsy or epilepsy syndrome particularly in childhood. However at the present stage of development, the importance of genetic factor should not be overemphasized. The evaluation of genetic risks should be done in close collaboration between neurologists and specialists in the field of human genetics.
Epileptic Syndromes in Early Childhood

An epileptic syndrome is characterized by some common feature such as the type of epileptic seizures, age of onset, clinical course leading to benign or severe conditions including the prognosis. Only a few epileptic syndromes of early childhood have been identified as of a benign nature, most of the others being of severe forms. To the benign forms belong such conditions as benign idiopathic neonatal convulsions, the so called 5th day fits of infants with a good prognosis. The seizures occur mostly during 3rd or 7th day of infant’s life, predominantly among male infants. Similar is the condition in case of infants with benign familial neonatal convulsions which also occur during the early days of life with a positive family history. The inheritance is considered here to be due to autosomal dominant transmission. In both these cases of neonatal convulsions the children have mostly normal birth without any noticeable abnormalities.

As a marker for benign or severe epileptic syndromes of childhood the following clinical criteria are useful.

Benign Childhood Epileptic Syndromes

- Practically normal development of pregnancy and child birth
- Normal development of the child until the occurrence of seizures
- No neurological deficits noticeable in the child
- Clinical and EEG pattern indicate of an idiopathic benign form of epilepsy
- Fast response to medication with seizure freedom.
Severe Forms of Childhood Epileptic Syndromes

Most of the childhood epilepsies which begin in the form of syndromes are of serious nature considering the prognosis in respect of seizures, psychomotor development and the response to antiepileptic medication. Even though a clear etiology can not always be estimated, these children with severe epileptic syndrome show considerable degree of brain pathology due to prenatal or postnatal brain damages. The common intrapartum causes can be listed as follows:

- Intracranial hemorrhage
- Infection during pregnancy
- High toxic ischemic encephalopathy
- Cerebral malformations
- Maternal abuses such as drugs, alcohol, tobacco
- Inborn errors of metabolism.

The severe prenatal damages to the brain, on the one hand lead to developmental disorders in the child but on the other to an epileptic condition mostly in the form of an encephalopathy. Both of these conditions cannot be remedied, the only possibility being to control epileptic seizures to the extent possible through different antiepileptic drugs. Two of the major severe epileptic syndromes of childhood are described as below.

**WEST SYNDROME**

West syndrome is a severe form of early childhood encephalopathy with epileptic seizures in the form of infantile spasms. The syndrome is the outcome of observations of WJ West in his own child in 1841, the findings were then published in Lancet as a peculiar form of infantile convulsions. The diagnostic criteria for West
syndrome have been formulated by Jeavons 1985 which include infantile spasms in the form of Blitz-Nick-Salaam seizures, brain pathology leading to mental deterioration and typical EEG changes in the pattern of hypsarrhythmia. A similar syndrome with early childhood myoclonic encephalopathy is described by Aicardi in 1980. In the case of West syndrome the clinical symptoms begin already in the first year of child's life, mostly between 3rd and 12th month. Rarely it can start already in the first or second month or later than one year. The predominant clinical features are the occurrence of very frequent infantile spasms in the form of BNS-seizures and associated neurological deficits particularly mental retardation. In the meantime there are also discussions of subdividing the syndrome into idiopathic and symptomatic forms depending upon clinical and EEG studies. The fact remains however that this is a therapy refractory epileptic encephalopathy with a very poor prognosis.

The seizures in the form of infantile spasms can occur several times a day and may last each time only for seconds. The child may cry during the seizures which may be sometimes mistaken for non-epileptic phenomena. Other than the seizures there are abnormalities in the development of the child which is an important clinical feature of the syndrome. The diagnosis can be ascertained through the EEG findings which show a typical picture of disorganized paroxysmal rhythms in the form of hypsarrhythmia. The etiology is mostly congenital in the form of different brain disorders such as tuberous sclerosis, other kinds of brain lesions or a condition of severe brain damage during birth. It is necessary to make detailed EEG monitoring and
neuroradiological examinations such as MRI to estimate the drug treatment and all round prognosis of the syndrome. For several decades ACTH-infusions are used in the treatment; in addition cortisone injections are given during the acute stages. The antiepileptic drugs used are clonazepam, vigabatrin, valproate, vitamin B₆. In this severe form of disorder the clinical course and prognosis is very variable. About one fifth of the children die before reaching the 5th year of life, from the remaining children some get slightly better and the others go on to the other kind of epileptic syndrome called Lennox-Gastaut syndrome.

**Summary of a West syndrome**
- A rare syndrome consisting of about 3% of all childhood epilepsies which makes about 1 in 5,000 births
- Begins generally in the age group of 3 to 12 month of a childs life
- Boys are generally more affected than girls
- Predominantly infantile spasms (BNS seizure), additionally other seizures are possible
- Neurological deficits and mental retardation
- Typical EEG findings in the form of hypsarrhythmia.

**LENNOX-GASTAUT SYNDROME**

Lennox-Gastaut syndrome is also a severe childhood epileptic encephalopathy which begins generally a little later, around the age group of 3 to 5 years. In some cases it may start somewhat earlier, in others in the so called late form of Lennox-Gastaut syndrome it may begin as late as 10th year of life. This syndrome was first described by William Lennox (Lennox and Davis 1950) as a clinical entity with EEG correlation. Later it found a detailed description...
in the book by Lennox “Epilepsy and related disorders”. William Lennox devoted practically all of his professional life for the study and management of epilepsy. He described the syndrome with three characteristic clinical features which he called “a nick, a jerk and a drop”. The syndrome was later elaborately described by Gastaut in 1966 and in the succeeding years. The characteristic features of the syndrome are children with epileptic encephalopathy who have neurological deficits, mental retardation and therapy refractory epilepsy with several seizures per day. Predominantly three kinds of epileptic seizures are clinically found, which are atypical absences, axial spasms in the form of tonic seizures and drop seizures with atonic or myoclonic components. The tonic seizures in the form of axial spasms are a necessary component of Lennox-Gastaut syndrome, which may occur during day and night. Most children also have atypical absences which do not begin so abruptly as in the case of typical absences. During these absences the consciousness may be impaired; there may be loss of muscle tone, associated with myoclonic twitching of the eyelids, however generally without noticeable myoclonic jerks. The axial spasms show during polygraphic EEG recordings an increased muscle tone in the form of tonic components, whereas a drop seizure may be characterized also by atonic components with a lack of muscle tone. In addition the children may have during the course of the illness other seizures such as complex partial seizures and generalized tonic clonic seizures and even status epilepticus. The diagnostic criteria as formulated by Beaumanoir, 1985, are summarized as below:
• Childhood encephalopathy with epileptic seizures as dominant forms of the syndrome
• Mainly axial tonic seizures, atonic or myoclonic seizures as sudden falls, atypical absences (and tonic clonic seizures)
• Massive diffuse and generalized slow spike and waves in interval EEG, bursts of fast rhythms around 10/sec in sleep
• Retarded mental development associated with psychological disorders.

The children may get 50 to 100 seizures of various kinds per day and may get injuries on forehead and face because of frequent falls. There may be episodes of clouded states due to cluster of absences, and repeated axial spasms followed by tonic or atonic seizures. This condition may last for days, weeks or even months, which may be very difficult for drug treatment. In almost 90% of children there are axial spasms and tonic seizures particularly in sleep. In the etiological exploration there is mostly a definite brain pathology involved in the form of prenatal or perinatal brain damage. There may be even metabolic disorders but in some cases the etiology remains undetected. In other cases the Lennox-Gastaut syndrome is a continuation of the early childhood encephalopathy of West syndrome. In most of the cases the peak age of onset is between 3 and 5 years wherein, the children had more or less normal mile stones until the syndrome is clinically manifest. However they deteriorate in their psychomotor development very fast during the course of the active epileptic encephalopathy. The diagnosis is made clinically through clear observations of the seizures followed by intensive EEG monitoring with
video recordings. Etiologically the patients may have in addition to pregnancy and birth disorders some degree of family history as shown by Rai et al, 1988. The prognosis of Lennox-Gastaut syndrome both in respect of seizure control and as well as general psychomotor development is poor. According to the previous literature available about 5% of children with LGS die within 10 years, but later studies from Stenzel and Panteli, 1981 and Rai et al, 1988, showed that patients who are institutionalized live well up to the adult age. According to these studies there seem to be a remission of certain kinds of seizures particularly grand mal in adult life which may be due to the continuous long-term treatment with antiepileptic drugs. Even though the prognosis of epilepsy is poor, the mental retardation seems to come to a kind of stand still at certain age of life after considerable damage has already been done (Rai et al 1988).

Investigations must be carried out not only through intensive EEG monitoring but also thorough neuroradiology and sometimes (if necessary) also through genetic evaluation. The treatment of the condition is unsatisfactory, as a complete freedom of seizures is not achieved. A polytherapy of antiepileptic medication is almost always necessary which includes such drugs as valproate, lamotrigine, benzodiazepine particularly clonazepam and the newer drugs such as oxcarbazepine and topiramat. The Lennox-Gastaut syndrome (LGS) is summarized as below.

- About 3% of all the childhood epilepsies
- Onset between the ages of 3 to 5 years, sometimes earlier and rarely around the age of 10 years
- Boys slightly more affected than girls
- Seizures characterized by atypical absences, axial tonic spasms and drop seizures with atonic and tonic
EPILEPSY AS AN ILLNESS, ETIOLOGY

components as well as other kinds of seizures including grand mal
• The syndrome is almost always associated with mental retardation
• EEG shows massive diffuse and generalized slow spike and waves in interval, bursts of fast rhythms around 10/sec. in sleep (Fig. 5.1).

Myoclonic-astatic Epilepsy
This is a severe form of childhood epilepsy characterized by myoclonic and astatic seizures which can begin in children in the age group of 1 to 6 years, maximum up to 9 years. This form of epilepsy represents 1 to 2% of all epilepsies in children, the boys being more affected than
girls. The clinical course can be confused with Lennox-Gastaut syndrome because of frequent myoclonic, astatic and also generalized tonic clonic seizures. This syndrome was described in detail by Doose, (1985), who also identified the epilepsy as idiopathic and generalized form, often associated with genetic predisposition. The clinical characteristic features are the frequent occurrence of myoclonic and astatic seizures associated with atypical absences and absence status. Without proper treatment the children can also have status of generalized tonic clonic seizures. Before the epilepsy begins the children may have a normal childhood development who then suddenly develop mixed seizures. There may be history of complicated febrile convulsions. The children show myoclonic jerks around mouth, eyelids and may have drop attacks due to atonic seizures. In sleep these children may also have tonic seizures however considerably less than in the case of Lennox-Gastaut syndrome.

The EEG shows in interval a slow background activity with the occurrence of frequent and short bursts of spike wave complexes. Often the children show photosensitivity during the EEG examinations. The treatment of seizures is difficult even in the case of myoclonic astatic epilepsy, the drugs commonly being used are valproate, lamotrigine and recently also topiramate. The prognosis is on the whole unsatisfactory, however better than in the case of Lennox-Gastaut syndrome. A poor prognosis of myoclonic astatic epilepsy is possible under following conditions as stated by Doose (1985):

- Occurrence of frequent tonic clonic seizures or status epilepticus
Onset of the syndrome with tonic clonic seizures before the age of 2 years
Continued slow background activity of theta rhythm even in school age (under therapy)
Continuation of paroxysmal activity and spike waves under therapy
Failure of development of a stable parieto-occipital alpha background activity.

Progressive Myoclonic Epilepsy
Progressive myoclonic epilepsy as the name suggests is a severe form of epilepsy which is however comparatively rare. The epilepsy begins mostly in childhood with different forms of generalized seizures characterized mostly by myoclonic components. The clinical course is characterized by the presence of following seizure types accompanied by several degenerative conditions.
- Generalized asymmetrical myoclonias
- Multiple epileptic seizures including generalized tonic clonic, myoclonic and tonic seizures
- Progressive mental deterioration leading to irreversible dementia
- The occurrence of several neurological disturbances including cerebellar, pyramidal and extrapyramidal.

The progressive myoclonic epilepsy is a serious condition which may be etiologically associated with the following diseases:
- Non-ketotic hyperglycinemia
- Early infantile ceroid lipofuscinosis
- Tay Sachs and Sandhoff disease
- Phenylketonuria variant
• Late infantile and juvenile ceroid lipofuscinosis
• Sialidoses
• Juvenile Gaucher’s disease
• Myoclonus epilepsy with ragged red fibers
• Sub-acute sclerosing panencephalitis (Aicardi, 1985).

The above mentioned epileptic syndromes associated with epilepsy are difficult for drug treatment and general medical management excepting in the case of myoclonic atonic epilepsy. The prognosis is difficult because of underlying brain pathology, other neurological disorders or multiple etiologies. The disease conditions are generally not remediable, but the epileptic seizures must be treated for preventing status epilepticus which may otherwise lead to fatal consequences. The assessment of the possibility of treatment and prognosis of the disease must be carefully done in order to avoid preventable errors from the point of view of medical, medicolegal and ethical aspects. Even though the severe syndromes have something common in most of the patients, leading to poor prognosis; there are however individual variations, which must always be taken into account. Even in cases of West syndrome and Lennox-Gastaut syndrome, there are children who show a comparatively better response to treatment with a relatively better prognosis. In dealing with the parents of these children we have to take into account the severe mental agonies they undergo in managing the consequences of a family misfortune. Even though it is not correct to give false hopes, the treating physicians should however encourage the parents to undertake all that is medically and morally possible to help the affected children.
Baltic Myoclonus Epilepsy

Baltic myoclonus epilepsy is a rare degenerative epilepsy in which seizures begin around the age of ten years. The seizures may get worse if phenytoin is given in the treatment. The disease may show the presence of “Lafora bodies” or other pathological conditions.

Benign Syndromes

In the proceeding chapters certain other epileptic conditions and syndromes will be presented which have in general a much better prognosis than the one’s already mentioned.

Benign Early Myoclonic Epilepsy in Infants

In this kind of epilepsy which has been described by Dravet (1985) only one type of seizure occurs in infants, which is characterized by brief generalized myoclonics. The myoclonics involve the axis of the body and the limbs. Later when the children are able to walk there may be dropping of head on to the trunk during a seizure. The attacks usually last only a few seconds, the child is neurologically normal. There may sometimes be repeated seizures, however the consciousness is rarely impaired. The seizures respond well to treatment, the interictal EEG does not show paroxysmal changes. The children become later free of seizures under treatment particularly with a medication of sodium valproate. If untreated however they may develop generalized tonic clonic seizures which may replace the myoclonics. The prognosis is on the whole good in comparison to other severe forms of myoclonic epilepsies of childhood.
Absence Epilepsy of Childhood

Childhood absence epilepsy is a fairly common condition of idiopathic generalized epilepsy which begins in the age group of 5-10 years. The children get typical absences particularly in the early morning hours or during tiredness which can repeat up to two hundred times per day. The symptoms are characterized by bland absences, which can occur in clusters so that the children stop their activity for a few moments only to continue it later. The begin of the absences and the end is fairly abrupt. In other cases the children may have complex absences with blinking of eyelids or rolling of eyelids slightly upwards. There is generally no loss of postural control. The absence epilepsy of childhood makes almost 10% of all epilepsies and the girls are more effected than boys. There is generally a family predisposition to epilepsy. During the absences the children have typical 3/sec. symmetrical generalized spike wave complexes which may last few seconds or longer. The spike wave complexes may be generally provoked through hyperventilation during EEG recordings. The response to drug treatment is generally good, the children may however get also generalized tonic clonic seizures. On the whole the children do not have neurological or psychological deficits, there may be complete remission of seizures after adolescence.

Table 5.3 shows a summary of the age related childhood absence epilepsy which was formerly called petit mal.
Table 5.3: Childhood absence epilepsy

- Begin in the school age, mostly in the age group of 6–7 years with a variation up to 12th year
- Girls more often affected than boys
- Seizures mostly in the form of simple and complex absences, sometimes also with automatisms
- Generally no neurological and psychological abnormalities
- EEG shows typical 3/sec generalized symmetrical spike wave activity provoked by hyperventilation
- Generally good prognosis with treatment of sodium valproate, however without proper treatment later generalized tonic clonic seizures are possible.

Juvenile Absence Epilepsy

Juvenile absence epilepsy is a similar syndrome like the childhood absence epilepsy with the difference that the seizures begin mostly around puberty at the age group of around 15 years. The absences which begin at this age are generally not so frequent as the childhood absences, however they are often associated by generalized tonic clonic seizures. Sometimes the epilepsy can begin with a major generalized seizure which may be followed by occurrence of absences. There may be other symptoms such as myoclonics. Both boys and girls are equally affected in this form of epilepsy. The juvenile absence epilepsy shows considerably more generalized tonic clonic seizures than the childhood absence epilepsy. However the other findings are similar in respect of normal neurological and psychological findings and the EEG shows a similar pattern with 3/sec symmetrical generalized spike waves which are also provoked by hyperventilation (Figs 5.2 and 5.3). The drug treatment is generally successful, mostly with sodium
valproate and lamotrigine and the prognosis is on the whole good. As in the case of childhood absences also in juvenile absences there is a family predisposition.

**Juvenile Myoclonic Epilepsy (JME)**

Juvenile myoclonic epilepsy is characterized by myoclonic seizures which begin mostly in the age group of 15 to 20 years. Even this is a fairly common syndrome among young people with a family history of epilepsy. The myoclonic jerks occur frequently early morning after waking up in the region of arms and shoulders. During breakfast the young patients may have difficulty in holding a coffee cup because of the cluster of myoclonic jerks. Due to this phenomena the syndrome is also called impulsive petit mal described by
German neurologist Dieter Janz. The patients may have in addition to myoclonic jerks absences and generalized tonic clonic seizures, which may often occur also in the early morning hours. Sometimes the myoclonic jerks, absences and generalized tonic clonic seizures may occur also during late afternoons. The neurological findings as well as intellectual status in most of the patients having juvenile myoclonic epilepsy are normal. The EEG shows somewhat irregular poly spike wave complexes which can occur in bundles. There is often a tendency to photosensitivity which can be recorded during EEG examinations. The response to drug treatment is generally good, however there may be remission of seizures in case of withdrawal of drugs even after years of seizure freedom. Because of this, in spite of
good control of epileptic seizures some patients may have to take drugs very long or even for life time. The drugs of choice are sodium valproate, lamotrigine and sometimes primidone. Table 5.4 shows juvenile myoclonic epilepsy.

Table 5.4: Juvenile myoclonic epilepsy (JME)

- An idiopathic generalized epilepsy with family predisposition
- Begin of the epileptic seizures between 15 to 20 years, sometimes also later
- Men and women are equally affected
- Mostly myoclonic seizures associated by generalized tonic clonic seizures, rarely also absences
- Neurological and psychological findings are generally normal
- EEG shows in interval irregular poly spike wave complexes, sometimes in bundles with photosensitivity
- Drugs of choice sodium valproate, lamotrigine and sometimes primidone.

EPILEPSIES IN ADULTS

The epilepsies which occur in adult life are not age related syndromes, may however show some common characteristics in respect of the phenomenology of seizures, their occurrence in daily life, as also in respect of the etiologies. When we speak of epilepsies in adult life we mean epileptic seizures which begin after adolescence with or without provocations, which then lead on to a condition of chronification of seizures. We have to consider here that certain kinds of epilepsies which begin in late childhood or adolescence may continue into adult life. The benign childhood absence epilepsy which can be accompanied by generalized tonic clonic seizures may recede during late puberty even without medication. However in some cases
this epilepsy may be reactivated in adult life in the form of
generalized tonic clonic seizures, as well as with absences.
In other cases which are more common, the juvenile
myoclonic epilepsy may continue into adult life or could
remain active even much later requiring drug treatment
throughout.

In many other conditions the epilepsy may get clinically
manifest with the occurrence of partial or generalized
seizures after the age of 20 years. If patients get generalized
tonic clonic seizures abruptly and without an aura, the
epilepsy may belong to the group of idiopathic or primary
generalized form. In some patients the generalized tonic
clonic seizures may be associated with typical or atypical
absences. The situation is rather different in the case of
partial epilepsies which begin in adult life, somewhat
around the age of 20 years or later. The clinical picture here
is very much variable in respect of the seizures and the
etiologies. There may be patients who begin with simple
partial seizures or complex partial seizures with or without
secondary generalization. Most of the partial epilepsies are
of a symptomatic nature in respect of clinical phenomena,
which has then to be evaluated through EEG and
neuroradiological findings. In several cases however the
etiology can not be estimated, even though from the point of
view of seizure symptomatology the epilepsy remains a
partial form.

Most of these partial epilepsies in adult life are the
temporal lobe epilepsies, which are also the most therapy-
refractory forms. Almost 2/3 of the epilepsies in adult life
are of a symptomatic nature, clinically associated with
different forms of partial seizures mostly complex partial
ones. A differentiation of the epilepsies as generalized or partial must be done carefully depending upon exhaustive history taking related to the seizures, assisted with EEG and radiological findings. Some of the benign epilepsies in adult life with mostly generalized tonic clonic seizures may also have a focal origin, which however cannot be easily detected. Such patients who get rare generalized tonic clonic seizures only during sleep, may not be able to report the occurrence of an aura. The interval EEG in such cases may not show focal or paroxysmal findings.

This differentiation of the epilepsies into generalized or partial forms is necessary also in view of a drug treatment. An idiopathic epilepsy of the generalized form may need a drug such as sodium valproate, whereas a symptomatic epilepsy even with the generalized tonic clonic seizures may respond better to a drug like carbamazepine. In the event of an epilepsy which begins in adult life, sometimes more than one neuroradiological examination with MRI should be done to rule out the possibility of a slow developing brain tumor. Broadly the epilepsies in adult life may be classified as generalized and partial forms which however must be further differentiated into idiopathic, symptomatic or cryptogenic forms. Complex partial seizures can for example have their origin in the temporal lobe or in the fronto basal structures, which may then show different response to drug treatment. If there is resistance to drug treatment, then we have to search further into the etiological factors also in respect of a possible surgical treatment of the epileptic seizures.
Grand Mal Epilepsy

Under the title grand mal epilepsy, we have to understand a clinical condition which is characterized by the occurrence of mostly generalized tonic clonic seizures (GTCS) with or without focal onset. Some patients in adult life who start with grand mal seizures, may have only this kind of seizures in intervals of long periods, sometimes even once a year. There are patients who get a grand mal seizures only in sleep with or without provocations, others may get such seizures mostly on awakening in the early mornings. In other cases the grand mal seizures may occur irrespective of day and night rhythm. On careful observation one could notice that the people who get grand mal seizures at night generally have the seizures with a focal beginning which however can not be reported by them. Sometimes they awaken just before the seizure as in a dream but go over to a generalized tonic clonic attack which may be noticed by the partner. The interval EEG in such patients does not generally show a focal epileptogenic activity. This kind of epilepsy must then be considered as a cryptogenic grand mal epilepsy, where a symptomatic origin is suspected but can not be determined. In the case of patients who get a grand mal seizures on awakening, the EEG may show under hyperventilation a generalized spike wave activity, which is then indicative of an idiopathic or a primary generalized form. The differentiation is important from the point of view of drug treatment.

The definition of epilepsy as a nosological entity depends mainly on three factors, namely the clinical phenomena, or the seizure, the anatomical substrate in the brain and the EEG correlation under ictal and interictal
examinations. The patients who have a focal origin of a grand mal epilepsy may experience an aura. In the case of an idiopathic grand mal epilepsy, the patients may not feel an aura but suddenly drop down to the ground with unconsciousness and have generalized tonic clonic seizures. In such patients, the ictal EEG might show at the beginning of the seizure a fast activity of generalized spikes followed by spike and waves.

To summarize, a grand mal epilepsy which begins in adult life is characterized generally by the occurrence of only generalized tonic clonic seizures which however may be of the partial, cryptogenic or idiopathic form. The prognosis of such epilepsies, if not associated with definite brain pathology, is generally good with proper response to drug treatment. If a grand mal epilepsy in adult life is however the continuation of a generalized epilepsy which had started in childhood or adolescence, the phenomenology may include along with grand mal, also absences. Provocation factors such as sleep deprivation, alcohol misuse and stress play a considerable role in respect of occurrence of seizures. Along with drug treatment, the patients must learn to change their lifestyle for a better control of seizures. Withdrawal of drugs even after five years of seizure freedom is in some cases difficult. The decision of initiating a treatment after the occurrence of one or more grand mal seizures in adult life, the continuation and withdrawal after seizure freedom must always be considered according to individual variations depending upon clinical, electroencephalographical, neuroradiological and social situations. It is important to know that even though a single grand mal seizures in adult life does not make the diagnosis
of epilepsy, there is a risk of 60-70% that such patients go on to a chronicification of the condition with the recurrence of further seizures.

**Partial Epilepsies**

Partial epilepsy is a much more heterogenic condition involving variety of seizures and etiologies. Even though most of the partial epilepsies are of symptomatic nature, there may be occasions where some of these conditions are cryptogenic, that means the symptomatic nature cannot be completely assessed or even idiopathic with family disposition. The difference in contrast to generalized epilepsies is that the partial epilepsies are characterized by the occurrence of simple partial, complex partial or secondary generalized grand mal seizures. Statistically partial epilepsies are the most common epilepsies in adult life and are also difficult for seizure control with drug treatment. A partial epilepsy beginning in adult life however simple it may look like, needs a thorough investigation through most of the available methods of diagnosis, particularly neuroradiology. The epilepsy can begin in early adult life after the age of around 20 years with the occurrence of simple partial seizures in the form of motoric or sensoric phenomena. Some of the partial epilepsies may begin with a grand mal seizure however of a focal onset which should be estimated through history taking and with the help of EEG. Some of the seizure such as Jacksonian types may give us hints to the location in the cerebral cortex, the others are somewhat difficult to be located because of the complexity of the symptomatology. There may be a combination of different kinds of seizures associated in a partial epilepsy.
Accordingly a subclassification of the partial epilepsies depending upon the anatomical substrate in the brain as well as clinical and EEG findings has to be done.

Temporal Lobe Epilepsy

Temporal lobe epilepsy is one of the most common kinds of epilepsies in adult life, which (as the name suggests) has its origin in the temporal lobes. The epilepsy is characterized by the occurrence of complex partial seizures which may have their origin in one or both of the temporal lobes or in the deeper structures of the limbic system. The occurrence of complex partial seizures only, can not justify the diagnosis of a temporal lobe epilepsy as these seizures can also have their origin in the frontal, parietal or even occipital lobes and in the basal structures. However the majority of the complex partial seizures have their origin in the temporal lobes. Temporal lobe epilepsies are also difficult for treatment. Within the temporal lobes the seizures may have their origin in the mesial regions particularly in hippocampus and amygdala. The possible etiological factors are different kinds of mostly benign brain tumors, cerebral ischermias, cerebrovascular malformations, accidents causing cerebral concussions, etc. If no cerebral pathology is found a cryptogenic form must be suspected in which cases the patients as children could have suffered febrile convulsions.

The complex partial seizures from temporal lobe epilepsy generally begin slowly and end also gradually. The seizures may begin in the form of an aura as simple partial seizure mostly in the epigastric region and go on into an impairment of consciousness. Sometimes there may
be secondary generalization of the complex partial seizure into a grand mal. The occurrences of such seizures could be in longer intervals, may be also in clusters. Complex partial seizures are socially very disabling phenomena as the patients may have under impairment of consciousness different kinds of automatisms such as staring, smacking of lips, moving like a robot. In Interval the patients may not show abnormal neurological findings but these are not always ruled out. The EEG may show interictal sharp wave in the temporal regions of the left or right hemisphere sometimes in both hemispheres but this is not obligatory. Ictally the EEG shows a focal finding in the temporal or temporobasal structures. The treatment with antiepileptic drugs is difficult, often different combinations are necessary. In therapy refractory conditions epilepsy surgery must be considered, which will be discussed under the chapters on treatment.

**Frontal Lobe Epilepsy**

The frontal lobe occupies a very large portion of the cerebrum, the seizures originating in frontal lobe show even more complexity of symptoms than the seizures of temporal lobe. It is often difficult to differentiate the seizures of frontal lobe because of the possibility of varieties of seizures occurring at the same time. Even the classification of seizures as generalized or partial with convulsive or non-convulsive symptomatic becomes difficult in case of frontal lobe seizures. Some seizures which occur in sleep have to be differentiated from non-epileptic phenomena because of the bizarre symptomatic. For example simple partial seizures, complex partial seizures, even absences and
generalized tonic clonic seizures may all have their origin in the frontal lobe. The differentiation becomes difficult as the focal seizures may change their phenomena due to very fast generalization. The frontal lobe seizures are generally therapy refractory for the usual drug treatment and even the possibility of surgical treatment in case of frontal lobe seizures is limited. Even though most of the seizures are of symptomatic nature, sometime the etiology may remain undetected leading to the proposition of cryptogenic or even idiopathic types of epilepsy. The general characteristics of a frontal lobe epilepsy are the following:

- Frequent occurrence of seizure, sometimes also in longer intervals and in clusters
- Intractable seizures with wild motoric phenomena at night such as sudden getting up from sleep, shouting and even falling down from bed
- Tendency to secondary generalization of focal seizures leading even to status epilepticus.

The diagnosis of a frontal lobe epilepsy and differentiating it from a temporal lobe epilepsy is clinically difficult and must be estimated through repeated EEG recording and long-term monitoring with video also during sleep.

**Parietal Lobe Epilepsy**

Parietal lobe epilepsy is a rather rare phenomena occurring mostly as a secondary to such processes as brain tumor, cerebrovascular abnormality or other brain lesions. The epilepsy is characterized by the occurrence of simple partial seizures sometimes associated with complex partial and generalized tonic clonic seizures. The clinical phenomena include sensory and autonomic symptoms and may be
associated with other neurovegetative phenomena as well. Compared to temporal lobes and frontal lobes the parietal lobes are generally less sensitive in respect of producing epileptic seizures. However when the parietal lobe epilepsy is suspected, thorough neuroradiological investigations must be carried out to explore the brain pathology.

**Occipital Lobe Epilepsy**

Even the occipital lobe epilepsy is a comparatively rare condition and if present is mostly of a symptomatic form. The seizures are of the nature of simple partial seizures with elementary symptoms associated with visual hallucinations. The patients may report experiencing sensation of light, optical hallucinations with or without color. Complex partial seizures with secondary generalization are sometimes possible also in case of occipital epilepsy. The diagnosis must include the exploration of brain pathology.

**Reflex Epilepsies**

Under reflex epilepsy we mean such conditions where the epileptic seizures are provoked through definite sensory stimulus. One of the most common kinds of a reflex epilepsy is the occurrence of epileptic seizures because of flickering lights of television, in a disco or from such situations as during a fast driving on roads lined with trees which may filter the sunlight leading to a flickering sensation. In some adolescents and young adults the first seizure can occur during switching on a television or on exposition to a flickering light in a disco. The severe effect seems to be associated with switching on or switching off such lights.
These people show during EEG examinations mostly a positive reaction to photo stimulation.

Other kinds of reflex epilepsies have been reported under such conditions as exposures to certain noise or music, reading a text, pouring hot water on head or even the act of chewing during eating. These epilepsies are accordingly named as television epilepsy, music epilepsy, reading epilepsy, hot water epilepsy and eating epilepsy. The seizures provoked during such reflex phenomena are generally complex partial or generalized tonic clonic seizures. There may be positive findings in the EEG either in the form of focal discharges or generalized spike wave activity. The treatment consists of avoiding such stimuli to the extent possible.

OTHER KINDS OF EPILEPSIES

Kozhevnikov Syndrome

The Kozhevnikov syndrome is a chronic and severe form of epilepsy characterized by continuous frequent myoclonic jerks which are generally confined to a small group of muscles. Two types of the syndrome have been recognized namely type I in children associated with progressive neurological and neuropsychological deterioration and type II identified by Bancaud (1985), which can occur at any age because of a neurological dysfunction. Both forms are called epilepsy partialis continua and are fairly difficult to treat. The type I which can start in very early age, even in the first year of life in children, is a progressive disorder leading to a complex symptomatology of continuous seizures, mental deterioration as in cases of an encephalopathy, which remains resistant to conservative
drug treatment. In type II there may be different kinds of brain pathology, however with slightly better prognosis in respect of epileptic seizures and neurological deterioration. The syndrome is characterized by myoclonic jerks and unilateral seizures which occur daily even many times a day. The drug treatment is similar as in the case of status epilepticus which however is generally not successful. In case of identified brain lesions surgical treatment is indicated, in some cases with partial or even total hemispherectomy.

**Benign Partial Epilepsy with Centrotemporal Spikes**

This is an age related epilepsy occurring in children and adolescents, in the age group of 3-13 years with a peak age of 9 years. The boys are more affected than girls. In most of the cases there is a history of febrile convulsion. The children are generally normal in respect of neurological and psychological functions. There is a familial disposition to epilepsy in about 40% of the children. The seizures are generally not frequent but may occur in clusters particularly in the beginning of the epilepsy. In certain children the seizures occur mostly in sleep. There may be focal seizures followed by tonic clonic phenomena, however without loss of consciousness. The seizure phenomena may be observed in face, lips, tongue, pharynx and larynx leading to speech arrest. The EEG shows in the interval centro temporal spikes which may occur in short intervals followed by slow waves. The localisation is mostly in the central and mid-temporal areas sometimes accompanied by generalized spikes and waves. The seizures may recede even without drug treatment but if they continue to persist drugs like carbamazepine or
lamotrigine may be given. The prognosis of the epilepsy is good with seizure freedom before the age of 20 years.

**Benign Epilepsy with Occipital Paroxysms**

This benign childhood epileptic syndrome was described by Gastaut (1985). The age of onset is between 7 and 17 years, boys and girls are equally affected. More than half of the patients have a family history of epilepsy and the occurrence of febrile convulsions during early childhood. The seizures are characterized by occipital lobe symptoms with amourosis sometimes associated by hemianopsia, elementary and complex visual illusions and hallucinations, which may occur also in combination. There may be complex partial seizures with tendency to secondary generalization. The diagnosis is based on the EEG findings also in interval which show characteristic spike waves and sharp waves of high amplitude which are recorded over the occipital and posterior temporal regions unilaterally or bilaterally. The paroxysms can occur in bursts, at 1 - 3 /sec in irregular intervals. The drug treatment consists of carbamazepine, lamotrigine and sodium valproate. The prognosis is generally good as the seizures disappear mostly before the age of 20 years.

**SUMMARY**

A diagnosis of the childhood epilepsies particularly of the benign forms is clinically not always possible. The criteria for diagnosis as benign are normal neurological and psychological findings in children particularly in the school age, followed by seizure forms which respond well to drug treatment or show a reducing tendency even without
treatment as well as fairly typical interictal EEG findings. In contrast the severe forms of the childhood epilepsies such as West syndrome, Lennox-Gastaut syndrome and Myoclonic Astatic epilepsy begin in early childhood and show a progressive condition in respect of seizures, neurological deficits and mental deterioration. The EEG shows severe paroxysmal changes, characteristic of the syndromes.

In case of adults the clinical picture is much more heterogenic particularly in respect of partial epilepsies and must be individually estimated regarding drug treatment and prognosis. In case of generalized epilepsies in adult life or cryptogenic epilepsies associated with grand mal seizures the clinical picture may suggest more of a homogenous form. The majority of the grand mal epilepsies whether idiopathic forms showing generalized tonic clonic seizures, or the cryptogenic forms with generalized tonic clonic seizures, which begin in adult life have generally a good prognosis when they are not associated with definite brain pathology. The EEG findings in the interval and interictal EEG are helpful for the decision of a proper drug treatment and for estimating the prognosis. Accordingly before a drug treatment is initiated, there must be clarity regarding the phenomenology of an epileptic seizure making it quite sure that it is a cerebral seizure and not any other kind of seizure phenomena. Further there must be a clear assessment weather the epileptic seizure leads to a chronic condition of epilepsy as a nosological entity. This can be assessed generally through (interictal and) ictal EEG findings followed by neuroradiological examinations. Particularly in adult life the provocation factors which are
responsible for the occurrence of an epileptic seizure must be estimated to rule out the possibility of isolated seizures, which need not necessarily lead to a chronic condition of epilepsy. Without these considerations much harm can be done to a patient if he gets an antiepileptic drug, without proper diagnosis.
INTRODUCTION

In dealing with the diagnosis of epilepsy we have to consider the pathophysiology of brain responsible for epileptic seizures and for chronification of this condition. During the past 50 to 60 years of brain research, considerable information is available regarding brain lesions which are responsible for epileptogenesis in humans, even though several mechanisms are still unknown. Certain areas in the brain have a reduced threshold to epileptic seizures as shown in the previous chapter regarding the frontal and temporal lobe epilepsies in comparison to the other lobes namely parietal and occipital and certain deeper structures which are also less vulnerable. Brain lesions have to be considered as severe risk factors for the occurrence of an epileptic disorder, the location of the lesion playing thereby a definite role. Accordingly we have to distinguish following criteria as responsible for epileptogenesis in humans:

- Lesions which directly or indirectly cause epileptic neuronal discharges
- Lesions which occur as a result of repeated seizures leading to ictal brain damage in the form of secondary lesions
- Systemic factors which may influence the occurrence of epileptic seizures (Mathieson 1988).

To determine the etiological factors we have to make an exhaustive history-taking to ascertain the possibility of an epileptogenic lesion starting from the pregnancy of the mother until the first occurrence of an epileptic seizure. The history taking should include information regarding the possibility of brain involvement in the following situations of life:
• Intrauterine development
• Complications during birth
• Febrile convulsions in early childhood
• Infections and inflammations in early childhood
• Head injuries in childhood or adult life
• Acquired vascular lesions or neoplasms
• Brain related metabolic encephalopathy
• Metabolic encephalopathies of other origin
• Familial disposition to epilepsy
• Congenital or chromosomal abnormalities.

As epilepsy is a fairly common neurological condition, the patients may go for treatment to general physicians, neurologists, child specialists and psychiatrists. In case of childhood epilepsies, sufficient information is generally available from the parents particularly the mother. In case of adults the history-taking is more difficult as an occasional epileptic seizure experienced by the patient is generally not observed by another person. The patient by himself is not able to report much about the seizure. Hence, it is not uncommon that many adults do not go to the doctor after a first epileptic seizure, unless the seizure has caused some injuries or embarrassment in the way of incontinence of urine or stool. A detailed history-taking for the diagnosis of an epileptic seizure is time consuming and has to be carried out in more than one session. The history taking should follow a general medical and complete neurological examination preferably through a neurologist. It is also necessary to make an EEG examination even though almost 50% of the EEG’s in interval may not show an epileptogenic finding, sometimes even after repeated seizures. Depending on the suspected etiology, a neuroradiological examination
in the form of magnetoresonance imaging of the brain (MRI) is necessary particularly in adults but also in children with complicated forms of epilepsies.

In the diagnosis of an epilepsy, it is of utmost importance to make sure that the seizure is a cerebral phenomena showing definite clinical characteristics of the various epileptic components described in the previous chapters. Mistakes can be done when the seizure is diagnosed too fast as epileptic as shown by the studies of Rai at al, 1988. Even among the cases referred for a specialized epilepsy center almost 50% of the patients with suspected epileptic seizures had no epilepsy but other seizure-like phenomena. Some of these symptoms involving syncopes, cerebrovascular conditions and psychological episodes are difficult to differentiate from epileptic seizures, unless thorough clinical and EEG examinations are done.

**HISTORY-TAKING**

An epileptic seizure is a clinical phenomena which can be fairly well correlated to cerebral pathophysiology. As already mentioned earlier, a seizure is not generally seen by physicians, the patient himself cannot describe his experience properly, except in the case of focal motor seizures without impairment of consciousness. As such every attempt should be made to assess the clear phenomenology of a seizure with the help of third persons and the patient. Once the nature of a seizure is estimated as epileptic, further attempts should be made to find out the provocation factors, possible etiological factors and the risk of further seizures for the evaluation of a nosological diagnosis. Along with
the clinical assessment, examination should be carried out through electroencephalogram and neuroradiological methods as required to confirm diagnosis and to estimate prognosis. In spite of all the technological advances made available today, a good part of the epilepsy diagnosis is done through proper history-taking and clinical neurological examinations. History-taking should be exhaustive and as precise as possible. The physician must learn the art of history-taking so that maximum information can be gathered for the diagnosis. The patient and the dependants may put emphasis on certain details and ignore other matters which may however be very important for the clinician. A proper history-taking must include following details beginning with family history, personal history and psychosocial situation, wherein the main emphasis is however given to history particularly in respect of seizures.

**FAMILY HISTORY**

- Occurrence of seizures in parents, their siblings or siblings of the patient
- Occurrence of any other paroxysmal disorders, particularly neurological
- Whether the parents are related to each other before marriage

**PATIENT HISTORY**

- Complications during the pregnancy of mother involving infections, trauma, drug intake, intake of tobacco and alcohol
- Details regarding birth, premature, delayed or normal delivery
STEP BY STEP TREATMENT OF EPILEPSY

- Complications during birth, such as delayed birth, forceps or vacuum extraction, cesarean section
- Estimation of APGAR if available
- Early infantile development
- Early childhood milestones involving walking, speaking and further psychomotor development
- Infections or trauma during childhood
- Febrile convulsions in childhood
- Milestones also in comparison to siblings
- Infection or head injury in adult life
- History of any other accident or intoxications in adult life
- History of other illness, medication

HISTORY OF SEIZURES

- Occurrence of first seizure with date and time
- First seizure during day or night
- Seizures occurring during infection or independent of it
- Description of seizures
- Subjective experience of seizure
- Which parts of the body were involved
- Phenomenology of seizure concerning jerks, tonic or clonic symptoms
- Change of consciousness during seizure
- Duration of seizure
- Postictal condition, confusion, sleep
- Facial expression particularly expression of eyes during the seizures
- Presence or absence of automatic phenomena
- Further details concerning tongue bite, incontinence of urine or stool
• If there were further seizures: the duration between the first and the succeeding seizures
• Medical examinations and treatment if any.

PSYCHOSOCIAL HISTORY
• Details regarding schooling, further education, profession, driving
• Family situation of the patient, problems if any
• Consumption of tobacco, alcohol, drugs, if any
• Psychological structure of the patient.

CLINICAL EXAMINATION
After the history-taking, the patient should undergo a thorough medical examination with major emphasis on the neurological status. However, it is obligatory to examine the patient also from the point of view of general medicine involving: pulse, blood pressure, condition of heart, lungs and abdomen. The neurological examination must be complete and should include following aspects:
• Consciousness
• Orientation
• Memory and concentration
• Emotional condition
• Behavior pattern
• Neuropsychological aspects
• Reading and writing
• Intellectual status
• Right or left handedness of the patient.

The examination of head should include:
• Morphological examination
• Reaction to pressure
• Movement of head
• Meningismus
• Carotid examination

**CRANIAL NERVES**

<table>
<thead>
<tr>
<th>CN I (olfactory)</th>
<th>- testing the ability to smell familiar aromatic odours</th>
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<tr>
<td>CN II (optic)</td>
<td>- testing vision with vision chart</td>
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<td></td>
<td>- ophthalmoscopic examination of fundus</td>
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<td></td>
<td>- testing visual fields by confrontation and extinction of vision</td>
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<tr>
<td>CN III, IV and VI (oculomotor, trochlear and abducens)</td>
<td>- inspecting eyelids for drooping</td>
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<td></td>
<td>- inspecting pupils’ regarding size, equality and response to light and accommodation</td>
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<td></td>
<td>- assessment of cardinal fields of gaze</td>
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<tr>
<td>CN V (trigeminal)</td>
<td>- inspecting face for muscle atrophy and tremors</td>
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<tr>
<td></td>
<td>- palpation of jaw muscles for tone and strength</td>
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<td></td>
<td>- testing superficial pain and touch</td>
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<tr>
<td>CN VII (facial)</td>
<td>- inspecting symmetry of facial features with various expressions</td>
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<tr>
<td>CN VIII (acoustic)</td>
<td>- testing sense of hearing with whisper screening test</td>
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<tr>
<td></td>
<td>- comparing bone and air conduction of sound</td>
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<tr>
<td></td>
<td>- testing for lateralization of sound</td>
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DIAGNOSTIC PROCEDURES

CN IX (glossopharyngeal) - testing gag reflex and ability to swallow

CN X (vagus) - inspecting palate and uvula for symmetry
- inspecting any swallowing difficulty
- inspecting quality of glottural speech sounds

CN XI (spinal accessory) - testing trapezes muscle strength
- testing sternocleidomastoid muscle strength

CN XII (hypoglossal) - inspecting tongue in mouth and while protruded
- inspecting tongue movement toward nose and chin
- inspecting tongue strength with index finger
- evaluation of the quality of lingual speech sounds

REFLEXES

An examination of the superficial and deep tendon reflexes must be carried out which involves the following:
- Superficial abdominal reflex
- Biceps reflex
- Brachioradial reflex
- Triceps reflex
- Patellar reflex
- Achilles reflex
- Plantar reflex
- Clonus
The further neurological examinations should be done in the following order:

- Examination of the motoric function
- Examination of coordination
- Examination of sensory function
- Examination of vertebral colon

**Motoric**
- Muscle tone and strength
- Fine motoric of fingers and toes
- Evaluation of gait
- Evaluation of gait with heel-tow walking

**Coordination**
- Finger – nose test
- Romberg test for equilibrium
- Co-ordination with rapid alternating movement
- Examination of fine motor functions
- Test for tremor of hands and feet

**Sensory Function**
- Superficial touch on hands and legs
- Superficial pain on hands and legs
- Temperature and deep pressure
- Vibration tests on hands and feet

**Cortical Sensory Function**
- Stereognosis
- Two point discrimination
- Graphastasia
• Extinction phenomena
• Point location

**Spinal Cord**
• Movement
• Configuration
• Reaction to touch and pain

The further examination of the spinal cord should be performed according to necessity, which should include different spinal nerves.

The first clinical examination of a patient, be a child or an adult, should always include an exhaustive history-taking and a complete neurological examination. For an experienced neurologist this examination can be completed within one hour, for such physicians who are not experienced in neurology, probably one hour is not sufficient for history-taking and neurological examination. In such cases the preliminary examination should be divided into two sittings. One must however take into account that patients and the dependents are very anxious to know the diagnosis. In certain cases a probable or even a definite diagnosis of the seizure as epileptic or non-epileptic can be assessed only after history-taking and clinical examination. In other cases however further examinations such as electroencephalogram or computer tomogram of the brain are necessary to make a clearer diagnosis of the seizure and the etiology. Considering the psychological implications, it is useful to give some hints to the diagnosis after history-taking and clinical examination, leaving room for a definite judgement only after the further instrumental examinations are done. Such a procedure is more useful to win the
compliance of the patient than to keep her/him waiting until all the examinations are completed. Epilepsy has some social stigma and is generally considered as a long lasting chronic disease and hence nobody is happy to hear this diagnosis. When the diagnosis is announced to the patient partly or fully, care must be taken to describe the condition in a way which is tolerable for the patient and the dependents.

**STRATEGIES FOR DIAGNOSIS**

**Children**

Epilepsy as a recurring condition of cerebral seizures has a heterogenic etiology. Several factors may be responsible in the pathophysiology of epilepsy as a benign condition, or as a syndrome with progressive clinical course. It is therefore necessary to consider the essential factors which may contribute for the classification of seizure, and for the diagnosis and prognosis of epilepsy. Physicians must consider the psychological problems of the parents for example in case of their child having an epilepsy. A familial disposition for example, may cause embarrassment and certain amount of guilty consciousness for the parents. However, this information is important for the diagnosis and prognosis in most of the childhood epilepsies and epileptic syndromes. Primary generalized epilepsies which begin in school age with absences may have a good prognosis leading to remission of seizures with or without medication, whereas epilepsies beginning in earlier childhood such as West syndrome or Lennox Gastaut-syndrome have a very poor prognosis. In both cases a genetic predisposition to epilepsy is possible. In case of benign
epilepsy the children show no signs of brain damage whereas in other serious forms of epilepsy syndromes there may be additional brain damage of different grades or other metabolic disorders. For example, children with antenatal or perinatal brain damage may have an increased tendency to epilepsy but this is not obligatory. On the other hand a child showing an idiopathic primary generalized epilepsy without noticeable signs of brain damage may have siblings who have no epilepsy. In this case it is useful to ascertain whether the child with epilepsy has in addition to genetic predisposition some minimal brain dysfunctions which might have contributed for a clinical epilepsy. Generally the siblings of a child with idiopathic generalized epilepsy may have similar EEG findings as the patient, however, without clinical epilepsy. Children with cerebral paresis may have increased risks for epilepsy but it is also not always obligatory and must be differentiated carefully. Similarly some children with Down syndrome may develop an epilepsy, the others may remain without an epilepsy throughout their lives.

**Adolescents and Adults**

In case of adolescence an epilepsy may start with myoclonic jerks, absences and generalized tonic clonic seizures which may be strongly suggestive of juvenile myoclonic epilepsy. However, the patients ignore mentioning the myoclonic jerks or absences and may emphasize the occurrence of a grand mal seizure only. Other cases of generalized epilepsies which start with grand mal seizures may be a carry over of a benign absence epilepsy of childhood which was probably not diagnosed at all. In both mentioned cases namely JME
and grand mal epilepsy the diagnosis can be confirmed even with interval EEG. The partial epilepsies begin generally in later adolescence, around the age of twenty years. The patients might have had practically normal psychosomatic and intellectual developments until the beginning of epilepsy. Some of these patients in spite of all the normal findings could have had a minimal brain damage of antenatal or perinatal origin. The epilepsy can be clinically manifest in young adult age probably because of the various provocations to the brain such as sleep deprivation, alcohol and stress in this age group. The prognosis of such epilepsies is difficult to judge in the beginning. It must be emphasized here that in all cases of adult epilepsies particularly of the partial form, a neuroradiological examination to rule out neoplasm is obligatory. This must be done in case of generalized epilepsies with spike and waves in EEG also as it is not usual even for such epilepsies to begin without brain pathology after the age of around twenty years. Another peak of adult epilepsies is after the age of sixty years which may be caused by cerebrovascular factors. Even in these cases the etiology can never be taken for granted and needs further clarification through all possible diagnostic methods available today.

From the point of view of epileptology, a detailed neurological examination is necessary because of following reasons. Many healthy individuals may have mild neurological deficits which do not lead to an epilepsy. When epilepsy is present, one must try to make sure whether a particular neurological finding has clinical correlation to the seizures or not. Even though many neurological disorders with cerebral involvement may lead to epilepsy,
it is not always the case. Many patients with multiple sclerosis may not have epilepsy, but some may develop later in life. Similar is the case with patients of Alzheimer disease who rarely get epilepsy. Many people with cortical damage due to various reasons may get isolated epileptic seizures without the condition becoming chronic. It is therefore necessary during the clinical examination to make sure as far as possible whether the existing cerebral disease is responsible for an epileptic seizure or whether new factors in the cerebral pathology are playing a role. With the present development in medical technology, in all cases of uncertainty a magnetic resonance imaging (MRI) of the brain should be performed.

Similar is the case in people with intellectual retardation. If a person with intellectual retardation gets epilepsy in adult life, one must always think of an additional etiological factor. There are people with dysmorphic syndrome and intellectual retardation who might have epilepsies since childhood but seizures controlled under medication. Any exacerbation of seizures at a certain age without noticeable provocation should suggest the risk of an additional brain pathology, for example, in the form of tumors. It is important to note that an isolated epileptic seizure is possible in any human being at any phase of life. But a chronification of the epileptic seizures cannot happen without some kind of brain pathology and must be evaluated accordingly. As mentioned before the strategy of diagnosis in epilepsy is a deep analysis of the patient’s history followed by a neurological examination. The instrumental examinations are necessary to ascertain or rule out the doubts involved during this procedure. However, EEG is the primary instrumental
diagnosis useful to differentiate the epileptic seizures from the non-epileptic and for the confirmation of a classification. An epilepsy diagnosis at the present day is incomplete if it is not evaluated through electroencephalography.

**ELECTROENCEPHALOGRAPHY**

Electroencephalography is the method of recording and interpreting cerebral electrical activity on a electroencephalogram (EEG). Even though the electroencephalogram was invented by Berger as early as 1929, the instrument got refined for better recording around twenty to thirty years later. Since then EEG is the most important method of instrumental diagnosis in epilepsy, which as already mentioned should follow the procedure after history-taking and clinical examination. The EEG records the electrical activity of neurons over the scalp. This is the conservative method of examining through electroencephalogram. The examination is made typically with about twenty electrodes of roughly 1 cm² surface area over the scalp. A depth recording or stereo-electroencephalogram (SEEG) is the method of examining the neuronal activity through thinner electrodes inserted directly into the brain. This is a neurosurgical method and is done only on special indications when a patient is considered a suitable candidate for epilepsy surgery. The electrical activity of neurons involves two types of electrical changes namely slow postsynaptic potentials on a timescale of 5-50 ms and briefer action potentials lasting only about 1 ms, which hardly contribute for an EEG. Therefore, only postsynaptic potentials can be recorded through an EEG. The electrical activity of neurons depends upon a tiny change within the
cell membrane which can be described as follows: There is an increased negativity inside the cell with inhibitory potentials and decreased negativity with excitatory postsynaptic endings. This activity is in the range of 60 – 100 uV, which is measured in EEG. During the spread of this electrical impulse from one cell to another a polarity opposite to that inside the cell body will be recorded in the surface EEG. Because of the distance from the cerebral cortex to the scalp, the scalp electrodes can pick up generally the summated activity of the underlining structures. Accordingly the fast negative spikes in EEG represent cellular excitation and depolarization, whereas slow waves occur during hyperpolarization and represent inhibition. Generally there is a certain equilibrium or steadiness between the excitatory and inhibitory mechanisms during the cellular activity. This steadiness of activity is generally symmetrical and constitutes the background activity in EEG. This is classified into four frequency bands namely:

- Alpha activity or the normal background activity which is in the range of 8-13/sec.
- Beta activity which is above 13/sec.
- Theta activity which is in the range of 4-7/sec.
- Delta activity which is up to 4/sec waves.

In most of the people during a waking stage, there is a alpha background activity ranging between 8-13/sec., which is pronounced particularly in the posterior region of the brain (Fig. 6.1). The beta activity above 13 / sec. represents mostly the intake of medication, sometime it could be of other origin such as constitutional. The slower activity namely theta and delta occur generally during drowsiness or in sleep. However, there may be a constitutional difference
in certain people which show a fast theta activity around 7/sec as background activity. A much slower activity particularly in the range of delta represents either stages of sleep or other abnormal conditions with impairment of consciousness. All these bands of waves which remain symmetrical and continuous must be interpreted as belonging to a background activity.

Other than this background activity we have to deal with various kinds of asymmetrical or symmetrical focal or generalized paroxysmal activity ranging from spikes, sharp waves, spike and waves and sharp and slow waves. A clear paroxysmal activity whether focal, diffusely present or generalized, always represents a pathological activity which is important in the diagnosis of epileptogenesis.

An EEG machine must have a minimum of eight channels, however, there are EEGs now which have up to 32 channels. For depth recording of EEG there may be even

Fig. 6.1: EEG: Normal background activity in adults
more channels. Each channel of a scalp EEG writes on a paper graph a continuous tracing of the potential difference between two points. There are basically two ways of recording the EEG, namely on a common reference electrode which records on each channel the potential difference between one electrode on the scalp and the common reference electrode. This method is called monopolar recording and will produce waves on the paper which are highest on the channel recording. The other method which is more often used is called bipolar recording which involves connecting rows of electrodes to the EEG machine in a particular montage, so that the channels record from consecutive pairs of electrodes. This has the effect of emphasizing different localized activity under the scalp in the way of deflections in opposite directions, which is called phase reversal phenomena. In the case of monopolar recording this phase reversal phenomena does not happen because the electrodes are not connected to each other but all the electrodes are connected to a common electrode or to a similar electrical connection inside the EEG machine.

**EEG RECORDING**

The placement of the electrodes over the scalp is done according to certain regulations from the International Society on Electroencephalography. One of the most popular montages is based on the so called 10/20 system. The minimum duration of recording of an EEG should be for thirty minutes, during which the recording will be changed over the different montages of electrodes. It is important to compare the background activity with eyes closed and in contrast observe the change of the alpha activity during
opening of eyes. This procedure is called on-and-off-effect which was formally known as Berger-effect particularly in the German speaking countries (Fig. 6.2). For a standard EEG generally two simple provocation methods should be carried out for a proper interpretation of the recording. This includes a hyperventilation for three minutes and at the end of the EEG stimulation through flicker light. The purpose of these provocations is to evaluate the possibility of an epileptogenesis during these procedures. There are different montages of electrodes used in recording EEGs on children and adults, as well as on scalp recording and depth recording.

![Fig. 6.2: EEG. Normal alpha activity blocked by opening of eyes](image-url)
Scalp EEG

The conventional and the frequent method of EEG examination are on scalp recording. Generally an EEG is recorded as interval EEG between the seizures, for the assessment of diagnosis of epileptic seizures or for the evaluation of drug treatment in various kinds of epilepsies. A scalp recording is a comparatively simple procedure and can be carried out ambulatory through a qualified EEG technician. As it is a recording of about thirty minutes, information is available only about the situation of brain activity during this period of time. Some help can be obtained through provocations such as hyperventilation and photic stimulation (Fig. 6.3). The information available particularly during interval of seizures is therefore limited. However, there is no better instrumental substitute for an EEG for the diagnosis of epileptic seizures. In about roughly 50% of the patients with epilepsy an interval EEG may show findings indicative of a focal or generalized epilepsy. In other patients even with frequent epileptic seizures the interval EEG may not show such findings as the origin of seizures could be in the deeper structures of the brain. This is generally the case in respect of certain kinds of cryptogenic epilepsies. In case of idiopathic primary generalized epilepsies the interval EEG may show occurrence of generalized spike and waves during hyperventilation and or photic stimulation (Fig. 6.4). More help can be obtained if the EEG recording in interval is done during sleep. Another alternative is to record an EEG in interval after sleep deprivation which is a further provocation to detect the possibility of an epileptogenic activity.
Fig. 6.3: EEG. Generalized spike wave complexes during Hyperventilation

Fig. 6.4: EEG: Interictal finding in a patient of Lennox-Gastaut syndrome
Ictal EEG

If an EEG recording is done during a seizure as in the case of long-term-monitoring the EEG will always show an ictal activity either indicative of the epileptic phenomena or negating it. It would also give information to further phenomena of an epileptic seizure whether it is a partial or generalised (Fig. 6.5). However, this needs careful observation of the EEG graph if the recording is done without video monitoring. If there is a video monitoring of the patient and simultaneous EEG, then the diagnosis of the seizure becomes much easier. Intensive long-term monitoring of

![EEG: Interictal finding in an adult patient with LGS](image)

epileptic seizures with scalp recording is being practiced in special centres for epilepsy and neurological departments, for the last over thirty years. There are different methods of such recordings.
Recording with 24 Hours Cassette
Ambulatory recording of EEG is done with the help of a cassette which can be worn by the patient on a belt, during a period of 24 hours or longer. The EEG activity is directed to this cassette from the scalp electrodes which store the information. The cassette can be later evaluated through a computer. The advantage of this kind of cassette recording is that the patient is free to move about and can stay at home during the recording. The disadvantage however is the lack of EEG channels, because of which the information available particularly in respect of focal activities is very limited.

Long-term Monitoring with Video and EEG-Telemetry
Much more information can be obtained through long-term monitoring of patients on EEG with video-recording. The EEG-machine here has considerably more channels, somewhere between 16 and 32, which correspondingly gives more information. This needs a laboratory for examination of the patient and the patient has to stay in the hospital for a few days. There are again different technical methods for recording of seizures, particularly two major methods.

Recording with Cable-Telemetry
In the case of cable-telemetry there are long EEG-cables which are connected to the electrodes on the scalp of the patient and to the EEG-machine. Because of the cables, (however long they are) the movement of the patient is limited to the smaller area of EEG-laboratory. The EEG-signals from the scalp electrodes are directed to the EEG-machine and the patient is under observation on a camera with monitoring. There are different techniques of
observation such as the split screen method where the patient is seen on one part of the video screen and the corresponding EEG on the other side. Similar technical methods where the patients may be seen at the corner of the video or in any other formation may be possible. The purpose is to correlate the seizures to the EEG activity to make sure the type of seizure, whether epileptic or of other nature. If the seizure is epileptic, information can be available about the phenomenology of the seizure as focal or generalized.

**Video Monitoring with Radio Telemetry**

This is a better method where the patients have more freedom of movement, however also within the range of the video camera. In the case of radio telemetry the cables from scalp electrodes are directed to a sender which the patient may carry on his / her head or on the waist. From the sender the EEG signals are carried further to the EEG set up so that the video-recording of the patient and the telemetry EEG recording can be seen in the form of a split screen. The purpose of long-term monitoring with simultaneous video-recording is to evaluate the phenomenology of seizure for the purpose of initial diagnosis of epilepsy or for later surgery in case of therapy-resistance epilepsies. It is also useful in therapy-refractory cases for better drug treatment.

**Depth Recording of EEG**

Intracranial depth recording is a partly neurosurgical procedure, as the electrodes must be inserted into the brain through bore holes. This can be done only in the case of a patient being considered for epilepsy surgery because of resistance to conservative antiepileptic drugs. On the whole
between 5 – 10% of the adults with therapy-refractory partial epilepsies are considered suitable for this procedure. It is also necessary that the patient clearly understands the purpose of this examination and should agree for the procedure. A depth recording should be done only after the patient has been examined thoroughly through intensive monitoring of seizures on scalp recording. The idea is to locate the origin of a partial seizure inserting an electrode at the suspected site in brain where the seizure originates. The focal findings of epileptogenic activity in the deeper structures of the brain recorded through depth EEG may sometimes be different from the focal activity of an ictal event recorded on scalp electrodes. Depending on the site of seizures, the possibility of neurosurgical resection of focus is a necessary indication for further treatment procedure. As such only partial epilepsies are indicated. Adult patients who are otherwise socially well integrated with normal intellectual and professional conditions are suitable candidates for such a depth recording. The other kinds of severe epilepsies such as epileptic syndromes which are carried over from childhood or multifocal and secondary generalized epilepsies are generally unsuitable for depth recording. There are however some centres who conduct epilepsy surgery also in such children.

OTHER METHODS

There are some other kinds of simpler depth recordings which can be done in a normal EEG laboratory. Two of these common methods are recording with sphenoidal electrodes and nasopharyngeal electrodes. In the case of sphenoidal electrodes a silver wire chlorided at the tip, can
be introduced through a hypodermic needle around foramen ovale and after insertion the needle is withdrawn leaving the wire electrode in place. This method is used as a simpler alternative to record focal temporo basal activity instead of depth recording. Another method is with the help of nasopharyngeal electrodes which are inserted through the nostrils and are used for recording from the medial and the basal structures.

In case of the EEG examinations the technical recording is done by qualified EEG technicians who must have good training. The evaluation of the EEG needs special training after postgraduation in neurology, neurosurgery or pediatry. For neurologists, neurosurgeons or pediatritions there is a further postgraduate training of minimum six months, only with EEG evaluation whereby each postgraduate must have evaluated minimum 1,500 EEGs before one is in a position to do this work independently. However, long years of experience is needed to make correct judgement of EEG and to differentiate each grapho element from artefacts, specific epileptogenic activity or non-specific activity.

Visual Analysis of the EEG
Reading an EEG and interpretation of the findings require as already mentioned special qualification and experience. It is necessary to recognize and classify EEG waveforms related to the placement of electrodes over different areas on scalp. Thereby it is important to differentiate the background activity from the other focal, diffuse or generalized activity. Under the normality of an EEG waveform, there are several individual variations also related to physiological conditions such as drowsiness, sleep and waking. Moreover,
there are other physiological variations of the normal EEG activity depending on the age of the patient. For clinical purposes it is necessary to classify the EEG signals and describe them from the point of view of topography of electrodes placement, morphology of rhythmical activity and pattern of abnormal waveforms. Two major factors of description of the waveform are the frequency of the signals and the amplitude associated with that. The frequency is measured in the number of cycles per second and abbreviated as Hz/sec. The amplitude is measured from the baseline to the peak of the wave or half to half of peak distance, if the peak below the baseline is also considered. A sine wave can be specified by two measures namely frequency and amplitude.

**Description of EEG**

The analysis of an EEG record begins with the description of the background activity, which is the predominant activity in the posterior area and consists of alpha rhythmic activity from 8-13Hz under normal conditions. There may be variations in the frequency, more so in the amplitude of the background activity. While describing the activity one should mention as a stable or unstable rhythmic activity depending upon the morphology of the EEG signals as shown in the record. The background activity has the additional properties of being stable when the eyes are closed and getting blocked when the eyes are open. A reference of this on-and-off-effect is usual while describing the background activity. The amplitude is generally a little higher in the posterior regions than in the other regions of recording. The description should include the difference in
amplitude and frequency if any, in regard to anterior and posterior areas. Reference should be made to the presence of artefacts from eyelids, muscles or from electrodes (Fig. 6.6). Mention should also be made to the presence of other frequency bands such as theta or delta within the structure of background activity. There may be for example change of frequency and amplitude because of drowsiness. The background alpha activity may be mixed with a faster activity in the range of beta waves, diffuse or spread over only in the frontal areas. Presence of mild beta activity restricted only to the frontal regions may be physiological, whereas diffuse beta activity spread over all regions may be due to intake of medication.

There are some individuals particularly children who may have a beta activity even without medication which may be of constitutional origin. If there is a slowing of the

Fig. 6.6: EEG: artefacts from eye movements
background activity with the mixture of theta waves more or less continuously during the recording, this may mean also the intake of heavy medication or may involve some brain pathology (Fig. 6.7). It must be noted here that intellectual condition of a person cannot be correlated with the background activity in EEG. Some intellectually normal people may have a slightly slower activity in the border of 8/sec. alpha as a physiological activity. On the other hand there are intellectually retarded people who may have normal and symmetrical alpha rhythms as background activity. However, the background activity in EEG has correlation to the state of alertness and consciousness of the person concerned during the recording. The alertness is disturbed when the background activity is very slow in the range of theta and delta. Physiological sleep shows clearly

Fig. 6.7: EEG: slow background activity under medication
slower background activity associated with typical sleep wave pattern (Fig. 6.8).

**Specific Waveforms**

Specific waveforms in EEG are either due to change of vigilance, some normal variations of wave pattern or due to specific pathological activity particularly related to epilepsy. In the case of specific waveforms there is a change in their morphology related to frequency and amplitude and are significant from the point of view of diagnosis. These specific waveforms have names related to topography and morphology of EEG-signals, for example, as spikes, sharp waves, vertex sharp waves, spike and waves, poly spike, and sharp and slow waves.
**K-complex**

This is a paroxysmal waveform arising out of background activity consisting of a slow wave mostly added to a sharp wave like formation and often followed by a spindle like activity. It can occur spontaneously during drowsiness or as a response to stimulus. The amplitude can be as high as 200 uV (Fig. 6.9).

**Lambda Waves**

Lambda waves are characterized by their appearance in the occipital regions as monophasic positive sharp waves with an amplitude of around 50 uV. These are physiological waves related to eye movement.

**Mu Rhythm**

Mu rhythm is an arcade or comb shaped in the range of 7-11Hz with location in the central area with amplitude of...
also 50uV. This activity also has no pathological significance.

**Spike**

Spike as the name suggests is a sharp activity which can be clearly identified as a paroxysmal wave with pointed peak and a duration of 20-70 ms. A spike is more surface negative with a slight deviation below the baseline. A spike remains a very specific grapho element and has a pathological significance particularly as an epileptogenic activity. The only problem is that a spike can be an artefact caused by electrodes or some other movements which must be differentiated (Fig. 6.10).

![EEG: spike and waves](image)
Sharp Wave

A sharp wave is also a paroxysmal wave formation clearly outside the baseline which is slightly wider than a spike in the range of 70-200 ms. A sharp wave is also a pathological EEG activity specific for epilepsy diagnosis (Fig. 6.11).

Spike and Wave Activity

A rhythmic activity of surface negative spikes followed by surface negative slow waves in a frequency of mostly 2.5-3.5/sec. There may be sometimes poly spikes attached to the slow wave also in series. On the other hand there can be bundles of spikes followed by sharp waves in a rhythmic formation (Fig. 6.12).
Sharp and Slow Waves
A similar pattern as mentioned above may show morphologically slightly wider spikes in the form of sharp waves followed by slow waves. This pattern could be rhythmical or even arhythmical as seen in certain kinds of severe epileptic syndromes (Fig. 6.13).

Vertex Sharp Waves
A sharp potential in the form of a sharp wave in a negative formation at the region of vertex occurring spontaneously during sleep or on stimulus. The amplitude may be as high as 300 uV, can also be lesser. The difference to other sharp waves is the location in the vertex region and lack of rhythmical appearance. This is a physiological activity.
Sleep Spindle
Sleep spindle is characterized by a rhythm of 14 Hz over the fronto central regions occurring during sleep. The amplitude is low, can be around 50 µV. This is also a physiological activity.

FIRDA
Definition of FIRDA is “frontal intermittent rhythmic delta activity”. This is a pattern of waves which is seen in the frontal regions and is a reversible activity. Even though it is a paroxysmal waveform, the significance of this activity is not very clear. Generally it is associated with elderly patients who have cerebrovascular disturbances. However, it is not an epileptic activity and the clinical significance is not clear.
This activity must be differentiated from localized delta activity and delta synchronous activity under hyperventilation.

**Interpretation of EEG**

For the clinical purposes the interpretation of EEG must be done particularly in view of epilepsy diagnosis. Until about 1970 the EEG was a broader instrumental method in the neurological diagnosis. Since then we have other technological methods of diagnosis for neurology and neurosurgery such as computer tomography (CT), magneto resonance imaging (MRI), PET and SPECT. As such the EEG though in a much more sophisticated form, is restricted to the diagnosis of epilepsy and sometimes also for the estimation of other neurological disturbances such as coma. An interpretation of EEG is not related to broader pathophysiological changes in brain, but only an analysis of the neuronal electrical activity. During the interpretation we must take care not to make a clinical diagnosis but only to mention the normality or changes in EEG-record depending upon the neurophysiology. Mention can be to the possible epileptogenesis depending upon the focal and paroxysmal activity. It is however generally wrong to pronounce a diagnosis of the presence or absence of an epilepsy as a clinical condition (Fig. 6.14).

**EEG-report**

A classical EEG-report of a conservative scalp EEG should include the following analysis:
Description

Description of the background activity with particular reference to the posterior areas as symmetrical, rhythmic alpha activity or as asymmetrical alpha/theta-activity or as the case may be, with mention to the frequency per second and amplitude. Under description one should mention whether on and affect is positive. The presence of any beta activity in any region should also be described. There should be a reference to the focal or paroxysmal activity in the recording, before the provocations of hyperventilation and photic stimulation are done. Any changes during the hyperventilation carried for three minutes should be mentioned. Usually a generalized or bifrontal epilepsy may get activated during hyperventilation, a partial epilepsy may not be activated. Similar is the case for photic stimulation. A description of any focal activity depending upon the
topography must be mentioned comparing it to different montages of recording. Care must be taken to mention the grapho elements as spikes or sharp waves or as other paroxysms. Any generalized activity without provocation such as spikes, spike and waves or sharp and waves should be mentioned during the entire recording also in comparison with the increased or decreased pattern associated with hyperventilation and photic stimulation.

**Impression**

The total impression of the EEG analysis should be mentioned separately in the end of the EEG report mentioning the changes in the background activity including the presence of beta activity or any other activity. It is generally referred as normal background activity if alpha rhythms are recorded. If there is a mixture of alpha and theta activity it will be a mild disturbance of the background activity. If there is a dominance of theta and delta activity this must be correspondingly reported as major changes of background rhythm. Regarding the focal and generalized paroxysmal grapho elements, special mention must be made about the localization, for example, unitemporal, bitemporal, frontal or other areas and the actual nature of graphic elements whether sharp waves, spikes or sharp waves with phase reversal and their significance in the epileptogenesis. Similarly the generalized spike wave activity should be referred as synchronous or asynchronous with areas of dominance, for example, bifrontal or bilaterally generalised and the epileptogenic potential of this activity, including correlation to clinical phenomena such as absences if any (Fig. 6.15).
The impression of the EEG-analysis must be so clearly formulated as possible however without making reference to the clinical diagnosis. The referring physician should be able to understand the significance of these pathological activities in respect of epileptic or non-epileptic phenomena. The EEG is a laboratory finding, is very useful in diagnose of epilepsy but an EEG-report alone is not sufficient for a complete diagnosis. This fact should be remembered in making an EEG-analysis in a report. The common mistake an inexperienced EEG-specialist can make is an over interpretation of the EEG-record. Certain grapho elements such as sharp waves and spikes can be usually confused with different kinds of muscle and electrode artefacts. A special artefact caused by electrodes during bipolar recording is called “mirror image” which may be easily

![Fig. 6.15: EEG: Repeated sharp waves left temporal](image-url)
confused to the real epileptogenic potential of a phase reversal. Several wave forms during light and deeper sleep may also be confused for real sharp wave activity.

**Further Investigations**

As mentioned in the previous chapters the etiology of epilepsy is mostly of heterogenic origin. From this point of view, we have to classify the epilepsy broadly under three categories:
- Idiopathic
- Cryptogenic
- Symptomatic

In a single patient a combination of these factors particularly idiopathic and symptomatic is possible. Further there are metabolic and neurological degenerative diseases which may also lead to epileptic conditions. Once the diagnosis of epilepsy is made through proper neurological and EEG-examinations, every attempt should be made to evaluate the etiology, which has then consequences for the therapy and long-term prognosis.

**Etiological Clarification**

An idiopathic generalized epilepsy is characterized by certain clear clinical and electroencephalographic features, as also through the age factor when the epilepsy becomes clinically manifest. These patients particularly children and adolescents have generally normal neurological and intellectual findings. In such cases a further investigation through advanced neuroradiological methods may not be necessary, should however be individually evaluated. In other cases of epilepsy, which are not benign, whether
beginning in childhood or in later life, investigations regarding the brain pathology are necessary. This should be the case also in the cryptogenic epilepsies where the etiologies are not known, particularly when the epilepsy begins in adult life. More so in case of symptomatic epilepsies with partial seizures (which generally begin in adult life), the etiology should always be clarified. The method of first choice is the magnetoresonance imaging (MRI) of brain, which can give maximum information regarding the brain pathology. The other investigations are computer tomography (CT) of the brain and in rare cases further sophisticated diagnostic methods such as positron-emissions tomography (PET) and single proton-emissions computer tomography (SPECT). Rarely an investigation by lumbar puncture may be necessary particularly when some brain infection is suspected. The other former methods such as carotid angiography and pneumo-encephalography are largely replaced by MRI.

CT and MRI
The technology of computer tomography is available for physicians in Europe since 30 years and MRI is available since about 25 years. MRI gives maximum information regarding the anatomy of brain under different levels as well as some information regarding the cerebral circulation, trauma or other defects. It is useful to do an MRI examination immediately after the diagnosis of epilepsy is ascertained. Computer tomography is useful for the examination of bony structures.

In case of childhood epilepsies particularly epileptic syndromes, different brain lesions may be responsible for
epilepsy. These include lesions originating during intrauterine life as well as such one’s acquired during birth or later in early childhood. In case of intrauterine disorders there may be placental abnormality, anoxia, results of viral infection, undernutrition of the mother or the influence of alcohol, tobacco or radiation. There may be congenital abnormalities such as tuberosis sclerosis, hydrocephalus, brain cysts and meningio-angiomatosis. Through MRI one could get evidence of these lesions and also of such lesions associated with child birth resulting in cerebral infarct, medial temporal lobe lesions as well as temporomedial occipital lobe infarcts. One could locate lesions arising out of bacterial meningitis, cerebral abscess and lesions associated with any other infections.

Among adults who are otherwise normal and suddenly develop an epilepsy, neoplasms can be ruled out through the help of MRI. Several intracranial tumors may lead to epileptic seizures. A brain tumor must be ruled out in all cases of epilepsy where the etiology remains clinically uncertain; this applies to all age groups from childhood to later adult life. In case of therapy-refractory epilepsies with partial seizures particularly beginning in early adult life attempts must be made through MRI to assess the possibility of atrophic lesions of the temporal lobes particularly in deeper structures in the region of hypocampus. A mesial temporal sclerosis is often a cause for therapy-refractory partial epilepsy in otherwise intellectually normally adults. In such cases further neuroradiological clarification is needed also during the course of the disease to evaluate the possibility of an epilepsy surgery (Figs 6.16 to 6.19).
Fig. 6.16: MRI brain: Normal finding

Figs 6.17A and B: MRI brain: Cortical atrophy

Figs 6.18A and B: MRI brain: Convexity meningioma right temporal
PET and SPECT

These are high cost research oriented cerebral metabolic studies which are rather rarely used in epilepsy diagnosis. The PET-measures biochemical processes of the brain concerning the measurement of cerebral blood flow including oxygen glucose utilization at the time of examination. This may be useful in the study of localized pathophysiology of brain involving further treatment procedures. A PET-examination can, for example, show functional disturbance of the brain involving metabolism, which is otherwise not detected through other methods such as CT and MRI.

SPECT is a similar neuroradiological method with radioactive isotopes for the measurement of cerebral circulation and cerebral metabolism. This is technically somewhat simpler method than PET, gives also lesser information needed for cerebrometabolic clarification.
CHAPTER 7

Treatment of Epilepsy in General
As in any other illness, there are two basic issues in the treatment of epilepsy namely prevention and therapy. Epilepsy is not a very common illness in the general population, but it is one of the most common neurological disorders occurring in about 0.5 to 1% of the population. It is probably the second most common neurological illness, after the group of neurovascular disorders. However, some authors do not consider epilepsy as an illness at all, from the point of view of the definition of a disease. An epileptic seizure is on the one hand, a paroxysmal symptom of a temporary disturbance in brain function, in form of excessive discharge of neurons. On the other hand, it can be a symptom with brain pathology as recurring seizures lead to a chronic condition which may be characterized as an illness. Accordingly the prevention and treatment should be focused on the different aspects of cerebral pathophysiology. In the case of isolated epileptic seizures without definite brain pathology, every attempt should be made to prevent the occurrence of seizures by identification and prevention of the provocative factors which are responsible for a seizure.

In case of febrile convulsions, for example, high fever is a triggerging factor for the convulsion, which must then be controlled through measures to reduce fever. In case of adult seizures where the provocation can be identified, the patient should be advised to avoid provocation factors such as alcohol, sleep deprivation or stress, as the case may be. There is a concept of Gower’s phenomena in the neurophysiology, according to which every epileptic seizure may be the cause for succeeding seizures. Through the animal experiments, we are aware of a phenomena called “Kindling” which has
some similarities to this concept. If the brain of an animal is excited through Penicillin or such other stimulation to a certain extent, the animal may react with an epileptic seizure. The quantity of the drug or the stimulation needed to produce an epileptic seizure for the first time, may not be necessary to produce a second seizure in the same animal. Correspondingly the brain of the animal will react with lesser stimulation or lesser medication during further provocations. After occurrence of several such seizures during stimulation with drugs, the animal may later continue to have seizures even without provocation.

In the clinical practice we come across patients of schizophrenia or other psychosis who are being treated with insulin or electrotherapy for the control of acute psychotic conditions. These patients react with an epileptic seizure of the grand mal type during insulin or electrotherapy, because of which they come out of their acute psychotic conditions. However if these patients get these therapies repeatedly, they may later develop epileptic seizures independent of these provocative therapeutic measures. In case of patients with frequent complex partial seizures from the region of hippocampus, a similar phenomena may be involved in the strategy of seizure occurrence. However for the past 60-70 years we know that epilepsy is certainly a remediable condition particularly where serious brain pathology is not involved. Many patients with epilepsies of the partial or the generalized forms, get free of seizures after some years of medication, a part of them later also without antiepileptic drugs. In such cases we could think of self-regulating phenomena in the brain in the form of a “Reverse Kindling”.

TREATMENT OF EPILEPSY IN GENERAL

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PREVENTION

A general preventive measure related to epilepsy in the population is not possible and not a very sensible approach, as epilepsy is not a common illness like cardiovascular, metabolic disorders or illness of the joints with risk factors. However, once an epileptic seizure is diagnosed, the patient should follow some dietetic measures needed to prevent further seizures. The lifestyle of young people particularly in the age of adolescence and young adult life is characterized by not sleeping for late hours, frequent use of alcohol or stimulating drugs, particularly in the western countries, but increasing also in other countries of the world. It is necessary for people who have a tendency to epilepsy to identify the provocation and to avoid them. The following points should be noted, in such cases where isolated epileptic seizures are known but without the diagnosis of a clear epilepsy.

• Identification of the provocation which was responsible for seizure
• Prevention of the provocation through change of lifestyle.

Such preventive measures should be followed before prescribing antiepileptic drugs. There are however some exceptions such as when the patient involved needs driving for his professional work or when he or she is working with heavy and dangerous machines. In such cases after discussion with the patient a drug treatment may be initiated even without the nosological diagnosis or an epilepsy, as a measure of prevention, however only if the recurrence of seizures is strongly suspected.
Epilepsy as an illness is characterized by recurrence of paroxysmal seizures which appear and disappear. In between the seizures the persons are completely normal except in cases of epileptic syndromes or other kinds of severe epilepsies where the person may have other neurological or psychiatric disorders. Once an epileptic seizure has started in the brain, not much can be done to stop it until it becomes clinically manifest and stops by itself. Accordingly the treatment of epileptic seizures during an attack is not possible excepting in taking care of the patient by moving him to safety during a seizure. During acute attacks treatment is necessary only in the event of recurring seizures leading to a status epilepticus. This condition must be treated through parenteral medication. Otherwise the principle of treatment is basically of a preventive nature. First the epileptic seizures are identified, the form of epilepsy is diagnosed and the drug treatment initiated to prevent further seizures. The patient has to take medication daily so that the occurrence of seizure is prevented. This principle is similar as in the treatment of other diseases such as hypertension, diabetes, asthma, etc. The methods of epilepsy treatment have improved considerably over the past 50 years with the improvement in the diagnosis and drug treatment.

Fifty years ago there were only two potential antiepileptic drugs namely Phenobarbitone and Phenytoin, which though effective against different kinds of seizures, have considerable side effects. With the development of newer and specific antiepileptic drugs, almost 75% of the people with epilepsy can be made free of seizure. The remaining people who do not get seizure free in spite of modern
antiepileptic drugs, are those who either have a serious underlying brain pathology, or such patients who have intractable epilepsies because of a temporal mesial sclerosis. In this second group of patients, improvement is partly possible through epilepsy surgery.

**EMERGENCY CARE DURING EPILEPTIC SEIZURES**

**Grand Mal Seizures**

The most dramatic form of an epileptic seizure is the generalized tonic clonic seizure (GTCS) also called grand mal. When a seizure activity begins in the brain and until it is manifest in other parts of the body, the duration of time is only seconds so that helping a patient to prevent an epileptic attack is generally not possible. Only in such patients who get frequent seizures the relatives may be able to notice the early symptoms, and bring the patient to safety. But once the patient has already fallen to the ground and shows the symptoms of an epileptic seizure in the form of convulsions, the best thing to do is, to bring the patient to safety by moving furniture around so that he or she does not get hurt during a seizure. A generalized tonic clonic seizure can lead to anxiety and even a panic reaction in the people who witness it, because of the dramatic convulsions sometimes associated by froth and blood in the mouth or urine and stool incontinence. However, a grand mal seizures lasts generally one to two minutes or a little longer, even though it makes the impression of lasting much longer. It is then useful to turn the patient to a side so that the saliva can flow freely to prevent aspiration. During the seizures it is not a good thing to put any object in patient’s mouth to prevent tongue biting, as the object may hurt the patient much more...
than the biting of tongue. The tongue biting heals generally within the next few days. After the seizure several patients tend to a postictal sleep, some others become restless and may show a kind of a clouded state of mind. In such cases the patients are in a state of impaired consciousness; having automatic behavior. One should allow them to do that, as they after a short time come to rest by themselves. Because of their clouded state of mind they may otherwise get aggressive if people intervene and try to help them to sit quite or lie down.

Generally a grand mal seizure is an isolated phenomena, where the patient recovers after sleep or clouded state. In certain rare cases the patient may tend to have further seizures of the grand mal type, repeating one after another, without the patient gaining full consciousness. This is a status epilepticus of grand mal seizures and is a serious life threatening condition requiring emergency treatment including hospitalization. The drug treatment of status epilepticus will be discussed in a later chapter.

Complex Partial Seizures
Complex partial seizures have a variety of psychomotor symptoms with a duration of a few seconds up to several minutes. In many cases the patients have a staring gaze, start making automatic movements with their hands and lip smacking movements. There are others who may move about in an automatic robot like manner and may carry out even coordinated movements. There are patients who may automatically manipulate their genitals even to the extent of masturbation. The others may have minor motoric symptoms and more inner experience of hallucination with
a starring look. Cases are known where the patients smoking a cigarette during a seizure go with the burning cigarette to other people, which may be a threatening experience for the environment. There is the risk of patients going into dangerous situations, for example, if they are waiting for a train in a railway station. Fatal accidents are possible during a complex partial or grand mal seizure. It is necessary therefore if a complex partial seizure is recognized, to bring the patient to safety under such conditions. This must however be done with a great care as the patients are in a condition of impaired consciousness and may get aggressive. Cases are known where patients if they had sharp objects like fork and knife in their hands, have attacked people who tried to help them. In other cases, a complex partial seizure may occur with less symptoms and look like an absence of the generalized epilepsy. An emergency treatment is necessary only during status epilepticus of CPS.

Absences

The absences which occur in idiopathic generalized epilepsies are generally void of motoric symptoms. These absences are called typical absences or pyknoleptic absences, formerly they were called petit mal. In case of typical absences the patients may remain silent, have a starring look, may discontinue their activities partly for example if they are writing or eating, only to continue again. Some have blinking of eyelids, the others may not show any motoric symptoms at all. In case of complex absences or myoclonic absences there may be slight motoric phenomena such as jerking of shoulders. The patients may allow the things to fall down if they have any object in their hands.
Sometimes the absences are difficult to differentiate clinically from complex partial seizures. In such cases a differential diagnosis is possible only through an EEG. If the absences continue long in the form of status epilepticus the patients may need a parenteral treatment. This must however be assessed through EEG recording or in the event of doubt, a parenteral treatment for example with Diazepam may be necessary which may be useful in both cases, absences as well as complex partial seizures.

**Tonic, Atonic Drop Seizures**

This kind of seizures with tonic and atonic components are common in patients with the Lennox-Gastaut syndrome. The syndrome has been described in the previous pages, which is a therapy-refractory form of epilepsy. The children and adults having this syndrome continue to have tonic axial spasms, tonic and atonic drop seizures often several times a day. It is not possible to prevent or cure this kind of seizures in Lennox-Gastaut syndrome with drugs available until now. These patients have mixed seizures practically all the forms particularly of the type of generalized seizures. Because of prolonged drug treatment or for reasons not known, the adult patients having this syndrome seem to have lesser grand mal seizures, whereas the tonic and atonic drop seizures continue to occur (Rai et al 1988). Along with epilepsy these patients have also mental retardation because of which, they are either taken care of in long-term hospitals and rehabilitation centres or in their family surroundings. Due to frequent drop seizures they get repeated injuries to the forehead, face and head. In such cases it is useful to make them wear a helmet to prevent frequent injuries.
OTHER ASPECTS OF TREATMENT IN GENERAL

Patients and the dependents often ask the treating physician about the possibilities of treating epilepsy with diet, alternative medical methods, yoga and meditation, Chinese relaxation methods, etc. Even though not many studies have been conducted about the use of such methods, from the information available till now, there are no successful methods to control seizures than through disciplined life style and conservative drug treatment. The problem with epilepsy is, that it is an unpredictable condition regarding the clinical course and prognosis. It is certainly useful to follow a disciplined life style with proper diet, exercise and relaxation. Most important however are, regular hours of sleep and avoiding alcohol excess. All other aspects of healthy living with yoga, relaxation may be useful but these methods cannot substitute the necessity of taking drugs. Herbal medicine may improve the general condition of the patient but their effect on the prevention of seizures has not been properly studied. On the other hand we have thousands of clinical reports and research findings which give us very useful information regarding the treatment of different kinds of seizures with antiepileptic drugs. As such at present, treatment of epilepsies is possible through pharmaceutical preparations. It is generally not possible to take a risk concerning the treatment of epilepsy with other herbal drugs or alternative methods, as every additional seizure can be a disabling factor for the patients involving their psychosocial situations. There are moral and legal implications involving a treatment procedure with dietetic methods. It is an avoidable mistake if a patient, for example, makes an accident because of a seizure, which would have
been otherwise prevented through drug treatment, in many cases of epilepsies however an experienced neurologist would be able to judge the proper treatment and even the possible prognosis under such a treatment, although the responsibility of adequate treatment depends not only on the physician but also on the patient as well.

In some ways epilepsy is comparable to a migraine. Both are paroxysmal disorders, in between the disorder is the patient completely normal. Migraine is a severely painful condition disabling the patients from all their activities during an attack, sometimes for even hours after an attack. Many patients with migraine learn to avoid the risk factors such as chocolates, cheese, red wine and stress. With these measures they are able to prevent many attacks of migraine. The others who rarely get migraine attacks avoid any drug treatment with the conviction that even though an attack is very painful, it is generally over after one hour or so. The difference with epileptic seizures is that, that most of the seizures lead to an impairment or loss of consciousness, which may lead to serious consequences. As such prevention in epilepsy with dietetic methods is possible only in the event of isolated epileptic seizures where the provocation is known. Once the epilepsy has become a recurring condition, prevention through dietetic measures is not possible. Many patients with the diagnosis of epilepsy particularly in adult life, have difficulties to accept a long range drug treatment. Attempts must be made therefore to discuss in detail the pro’s and con’s of a drug treatment so that the patient is convinced about the necessity of such treatment.
CHAPTER 8

Drug Treatment
Even though epilepsy is known as a clinical entity since the time of Hippocrates, for centuries there were no proper drugs for the treatment of this disorder. Scientific papers began to appear in the 18th century, a notable contribution was through a Swiss physician André David Tissaut who published his paper on “petit mal” in 1770. The later important contributions came in 19th century particularly from John Hughlings Jackson and William Gowers. Bromide was introduced as a drug in the treatment of epilepsy in the year 1857 which was then extensively used until the beginning of 20th century. With the advances in neurophysiology, there is now a better understanding of epilepsy, even though the basic neurochemical mechanism related to the influence of drugs is not yet properly understood. However with continuing brain research there is a further understanding of neurotransmitters involved in the occurrence of epileptic phenomena. The earliest antiepileptic drug which is still used even today is Phenobarbitone, which was introduced in 1912. This is a sedative drug which has definite antiepileptic properties.

Over the past fifty years there has been a rational approach to develop more specific antiepileptic drugs. At the same time through newer diagnostic techniques particularly with the telemetry video-recordings, many more kinds of epileptic seizures have been identified. Even though there are many new drugs available in the market today, we are still lacking in specific drugs for treatment of different kinds of seizures particularly where the etiology remains unclear. However, it must be noted that with the development of new drugs about 70-80% of the people with epilepsy
remain free of seizures today compared to the situation fifty years ago. On the other hand there are some basic difficulties in treating epileptic seizures because of their heterogenic origin. The drug to be effective should be available with a maximum concentration at the site of seizure occurrence namely in the brain, with minimal side effects to the other somatic organs and systems. With occurrence of every epileptic seizure, there is a disturbed stability at the neuronal level concerning excitation and inhibition. The purpose of an antiepileptic drug is to establish stability in the bioelectrical field.

An epileptic drug, like any other drug has to be absorbed through the gastrointestinal system and then reach the blood circulation. Accordingly the drug will be distributed in the whole body mostly through protein binding. That part of the drug which is free and without protein binding can reach the brain and other organs and show its effect. Most of the antiepileptic drugs will be metabolized in the liver, only some of them will be excreted without change through urine and stool. During the metabolization and the biotransformation there may be new products namely metabolites which along with the parent drug show antiepileptic properties of different effectivity. Depending on various factors, the metabolization of the drug may be too fast, so that the bioavailability of antiepileptic properties of the drug is reduced. On the other hand if the metabolization is very slow, the antiepileptic properties available to the body may be more than planned, leading to side effects. The excretion of antiepileptic drugs is carried mostly through the kidneys, which can, however, be influenced by the use of other drugs. Depending upon these
factors, the dosage of an antiepileptic drug should be planned carefully in order to get the maximum benefits in the range of therapeutic effect. Too much of a drug made available is contraproductive and may lead even to increase of seizures and side effects. Too less may be insufficient and may not control the seizures. The spectrum of effectiveness must be based on the pharmacokinetic and pharmacodynamic properties of the drug concerned.

It is therefore essential to know the properties of an antiepileptic drug regarding the indication in different kinds of epilepsies based on symptomatology and nosology. Further the basic aspects of the pharmacokinetic and pharmacodynamic of the drug based on half life, steady state and interactions with other drugs must be understood. In the following chapters mention will be made to the general properties of important antiepileptic drugs, in respect of their pharmacological properties and indications. The following table shows a list of antiepileptic drugs and the year of their introduction in the market.

<table>
<thead>
<tr>
<th>Year</th>
<th>Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>1857</td>
<td>Bromide</td>
</tr>
<tr>
<td>1912</td>
<td>Phenobarbitone</td>
</tr>
<tr>
<td>1938</td>
<td>Phenytoin</td>
</tr>
<tr>
<td>1945</td>
<td>Trimethadion</td>
</tr>
<tr>
<td>1958</td>
<td>Ethosuximide</td>
</tr>
<tr>
<td>1963</td>
<td>Carbamazepine</td>
</tr>
<tr>
<td>1964</td>
<td>Sodium valproate</td>
</tr>
<tr>
<td>1965</td>
<td>Diazepam</td>
</tr>
</tbody>
</table>

The next table shows the newer antiepileptic drugs which were introduced in the European Market after 1990.

<table>
<thead>
<tr>
<th>Year</th>
<th>Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>1991</td>
<td>Vigabatrin</td>
</tr>
<tr>
<td>1993</td>
<td>Lamotrigine</td>
</tr>
</tbody>
</table>
1995 Gabapentin  
1995 Felbamat  
1996 Oxcarbazepine  
1997 Tiagabin  
1998 Topiramat  
2000 Levetiracetam

In addition to these basic drugs mentioned above, there are some other preparations which are further developments or changes in the basic components of a drug. Some of them are Primidone, Clobazam, Clonazepam, Midazolam, Sultiam. Reference will be made separately to major drugs which are commonly used in the treatment of epilepsy today. The other recent drugs are Pregabalin and Zonisamide.

**PHENOBARBITONE**

Phenobarbitone is an old drug, one of the first drugs to be introduced in the treatment of epilepsy as early as 1912. It is a substituted barbituric acid, the free acid of which is somewhat water soluble, the sodium salt is freely soluble. It is a sedative but with considerable anticonvulsant effect. Phenobarbitone is effective mostly on generalized tonic clonic seizures of grand mal type and less effective on partial seizures and absences. Some other barbiturates such as Pentabarbitone produces strong sedation under higher dosage. Phenobarbitone given in clinical dosage has good antiepileptic property without causing over sedation. The mode of action may be in modification of postsynaptic neurotransmitter responses to enhance GABA mediated inhibition and to diminish glutaminergic and cholinergic excitation (Rimmer and Richens 1988).
Pharmacokinetics of Phenobarbitone

- Daily dosage for adults 50-200 mg (300 mg), children 2-6 mg / kg body weight
- Elimination half-life adults 50-160 hours
- Children 30-70 hours
- Time to reach steady state up to 30 days
- Percentage of protein binding 45%
- Effective serum level 40-130 mmol/l

Phenobarbitone can be theoretically given in all kinds of epilepsies, generalized and the partial forms with grand mal seizures. The advantages are that the drug can be given only once daily, mostly in the evenings in the dosage of 50-150 mg, sometimes up to 200 mg as a monotherapy. The dosage should be adjusted properly if it is given with other drugs particularly Sodium valproate, as there may be interactions. Interactions are also known with Warfarine, oral contraceptives and some other substances. Inhibition of Phenobarbitone’s own metabolism is possible through other drugs such as Sodium valproate leading to clinical toxicity. Phenobarbitone is a sedative drug and causes side-effects particularly leading to cognitive and behaviored problems. In adults higher dosage of the drug may lead to general psychomotor slowing with reduced dynamic. In children it is rather disadvantages to give this drug particularly in the school age as it may cause learning problems as well as behavioral disturbances. Mood alterations including depressive tendencies are possible in all age groups. Abrupt removal of the drug may lead to withdrawal symptoms in the form of recurrence of seizures, insomnia and anxiety. Discontinuation of the drug should
be done carefully in a tapering dosage extending over several weeks. Most of the side effects of the drug are reversible. Even though Phenobarbitone is a dependable antiepileptic drug, it is not advisable to use this as a drug of first choice because of several side effects. Particularly in children it should be avoided to the extent possible as there are today several other specific drugs available in the market. The indications are in the first place grand mal seizures. Like other antiepileptic drugs Phenobarbitone can also cause various side reactions and hematological toxicity. Clinical and laboratory controls are needed during the early month’s treatment. The teratogenic properties of Phenobarbitone seem to be considerably lower than that of Phenytoin and some other antiepileptic drugs.

PRIMIDONE

Primidone is a desoxybarbiturate which was introduced in the early 1950s as an antiepileptic drug. The main components of Primidone are its two major metabolites namely Phenobarbitone and Phenyletylmalonamide (PEMA). Primidone is metabolised to a short acting PEMA and long acting Phenobarbitone. Both Phenobarbitone and PEMA seem to be effective against epileptic seizures. The drug has side effects particularly during the beginning of treatment and has only a few advantages regarding the spectrum of indication. In addition to the properties against grand mal seizures which is due to the major metabolite Phenobarbitone, Primidone seems to be effective against complex partial seizures and some form of myoclonic absences.
Pharmacokinetics of Primidone

- Daily dosage for adults 250-750 mg (1000 mg), children 15 to 30 mg / kg body weight
- Frequency of daily dosage 2-3 times
- Major active metabolites Phenobarbitone and PEMA
- Elimination half life Primidone 4-12 hours, Phenobarbitone 50-160 hours, PEMA 29-36 hours
- Time to reach steady state up to 30 days for Phenobarbitone

The drug is generally not so well tolerated by many patients and accordingly is being used far less these days. Other indication for Primidone is in the case of essential tremor. On the whole Primidone has only a corner place in the group of present day antiepileptics.

PHENYTOIN

Phenytoin is a major antiepileptic drug, which has been used extensively worldwide since its introduction in 1938. It is an effective drug in the treatment of grand mal seizures and partial seizures but it is contraindicated in the case of absences as this drug may clearly increase absences. Therefore, the drug is less suitable in the treatment of grand mal seizures occurring in primary generalized epilepsies, as these epilepsies are characterized by the presence of absences and grand mal seizures. Even though Phenytoin is a long-standing drug and has been extensively used and put to clinical studies, the mechanisms of action of this drug is not completely understood. Like some other antiepileptic drugs Phenytoin could improve the mechanism of GABA inhibition with reduction of excitatory synaptic potentials.
Pharmacokinetics of Phenytoin

- The daily dosage adults 150-300 mg (400 mg), children 5-15 mg/kg body weight
- Dosage frequency twice daily (sometimes once daily)
- Elimination half-life 10-140 hours
- Time to reach steady state 7-21 days
- Serum concentration 20-80 mmol / l
- Percentage of plasma protein binding 85-90%

Because of high percentage of plasma protein binding, there may be sometimes problems with the absorption of Phenytoin particularly if the patients are taking other drugs. As in cases of all plasma protein binding drugs, only the free portion of the drug is available as antiepileptic at the site of action. Phenytoin is metabolised mostly in the liver.

There is variability in the rate of Phenytoin metabolism between different individuals and as such the dosage must be done carefully to reach the required therapeutic range of antiepileptic effect. Even though a daily dose of 200-300 mg is generally sufficient, some individuals may need higher doses even up to 400 mg/day. On the other hand slight difference in the dosage of the drug may lead to quick changes in the serum concentration level, varying between sub-therapeutic and toxic proportions. Increase of the dosage should be therefore done very carefully in small doses of 25-50 mg of the drug, as a small change in the dosage may lead to fluctuations in the bioavailability of Phenytoin. At the same time one should consider the possibility of drug interactions if Phenytoin is given in a combination therapy. Because of these problems the dosage of Phenytoin is considerably more difficult to be handled than in the case of many other antiepileptic drugs.
Even though Phenytoin is a potential antiepileptic drug against grand mal seizures particularly in cryptogenic or partial epilepsies, its use has been reduced over the years partly because of the severe side effects and partly because of the availability of other drugs of newer generation. One of the most common side effects is the gingival hyperplasia under long range medication, which is a disturbing feature in most of the patients under Phenytoin. There are other side effects as well under Phenytoin which include increase of body hair particularly in woman, several central nervous system side effects such as nystagmus, vertigo, ataxia, tremor and headache. Some of the side effects are reversible but some others such as gingival hyperplasia and hypertricosis are not reversible and must be corrected through surgical or physical methods. Acute toxicity with Phenytoin may lead to cerebellar symptoms with severe ataxia and disarthria. In addition there are other side effects which involve the cognitive functions both in adults and children. Consequently use of Phenytoin is not suitable for children, as it may lead to learning problems.

Phenytoin is a difficult drug for long range treatment of epilepsies particularly because of irregular nonlinear pharmacokinetics and due to several serious side effects. The advantages of the treatment is that the drug can be given as a monotherapy and on a dosage of twice daily sometimes even once daily. In addition to these side effects mentioned above the drug has also teratogenic side effects and as such not indicated in woman in childbearing age. On the whole, the use of the drug as a first choice has reduced over the past 15 years because of the development of new line specific antiepileptic drugs.
TRIMETHADION

Trimethadion was an antiepileptic drug which was rarely used in some countries of the world in the sixties and seventies. The drug was given in therapy-refractory epilepsies as an add-on-medication. It has serious side effects and considerably less antiepileptic properties and accordingly it has been removed from the market in most of the countries.

ETHOSUXIMIDE

Ethosuximide is also a fairly old drug which has effectiveness against absences particularly the type of pyknoleptic absences. The drug is not useful in grand mal seizures or partial seizures. This drug is also not suitable as a monotherapy but mostly as an add-on-therapy in cases of generalized epilepsies. It is still used in some countries in childhood syndromes such as Lennox-Gastaut syndrome and similar epileptic encephalopathies in combination with other antiepileptic drugs.

Pharmacokinetics of Ethosuximide

- Daily dosage in adults 500-1000 mg, children 10-15 mg/kg body weight
- Frequency of dosage twice daily
- Time to reach steady state about 14 days
- Serum concentration 280-700 mmol/l
- Percentage of protein binding is very small

The use of this drug has reduced considerably after the development of newer drugs particularly Sodium valproate which has similar and additional properties in the treatment of generalized epilepsies. However in combination, the drug
may find a place in the treatment of childhood generalized idiopathic epilepsies where other drugs are contraindicated because of tolerance difficulties. On the whole the use of Ethosuximide is declining over the past twenty years.

CARBAMAZEPINE

Carbamazepine was introduced as an antiepileptic drug in 1963 and since then has been used extensively world over in the treatment of partial epilepsies with complex partial and simple partial seizures and also in cases of secondary generalization leading to grand mal. It is however not a good drug for the treatment of absences occurring in idiopathic generalized epilepsies. Even though the drug may not provoke so much of absences as Phenytoin, it may still lead to worsening of EEG in respect of generalized spike wave activity. Carbamazepine is structurally similar to the tricyclic antidepressant drug Imipramine. Probably during the course of drug development the anticonvulsant properties of Carbamazepine were recognized and further developed into an antiepileptic drug. The actual mechanism of antiepileptic properties on the neuronal activity is not properly understood. The clinical effectiveness however is very well documented in hundreds of studies throughout the word, even after the drug has been in market for over 40 years, Carbamazepine is still used as a basic drug in the partial epilepsies.

Pharmacokinetics of Carbamazepine

- Daily dosage for adults 400-1600 mg/day (1800 mg)
  children 10-30 mg per kg bodyweight
- Frequency of dosage in retard form twice daily
• Elimination half-life beginning of therapy 20-50 hours, in steady state 10-30 hours for adults, 8-20 hours for children
• Time to reach steady state up to 10 days
• Serum concentration 15-50 umol / l
• Percentage of protein binding 75%

Carbamazepine is available only in the oral form as tablets and some companies make syrup for children but the drug is not available for parenteral administration. The exact bioavailability of Carbamazepine in oral form is not clearly known but it is expected to be in a higher range of 75-85%. There is a major metabolite of Carbamazepine the 10,11 epoxide which also has anticonvulsant properties. Carbamazepine has a regular kinetic so that the therapeutic dosage can be adjusted properly. The plasma half-life is around 55 hours which however decreases consequently into the range of 8-30 hours because of the mechanism of auto-induction. Accordingly under chronic therapy an increase of dosage is necessary to arrive at the therapeutic effect. Even though generally a well tolerated drug, Carbamazepine can have disturbing side effects particularly in the beginning of medication. Most common side effects are an allergic reaction causing skin rashes, blood picture changes and central nervous system symptoms. As such, it is necessary to initiate the medication in a very small dosage and increase the dosage slowly over a period of several weeks to get a good tolerability. In adults it is useful to start with a small dosage of 100 mg/day and increase in intervals of 2-3 days at the rate of 100 mg further until a therapeutic dosage is reached. Frequent clinical examinations of the patient to exclude central nervous system side effects and
allergic reactions followed by hematological controls are necessary. Generally one has to make a monthly control of hematology 2-3 times in the beginning of medication. Under monotherapy the adults require a dosage of generally 800-1200 mg/day divided in two doses of retard form of tablets, the children need considerably lesser dosage. Once the preliminary dosage has been adjusted properly, the tolerance is generally good under long range medication.

Interactions and Side Effects
Carbamazepine can interfere in the pharmacokinetic of other drugs such as Sodium valproate, Phenytoin and Ethosuximide. On the other hand, these drugs can also reduce the serum concentration levels of Carbamazepine. Carbamazepine can reduce the effectiveness of some hormonal preparations including anti-baby pills. The central nervous system side effect consists of nystagmus, diplopia, dizziness and ataxia. Most of these side reactions are associated with too fast introduction of the medication during the beginning of therapy or under over-dosage during a chronic medication. These side reactions are reversible. It is also a useful drug in the concomitant treatment of psychiatric problems particularly in depressive disorders. Carbamazepine seems to have lesser side effects on the cognitive functioning and as such, is useful both in adults and children.

Even though a good drug, a long range medication of Carbamazepine needs frequent monitoring clinical and with blood examinations. One of the common problems encountered in practice is the hyponatremia under chronic medication of carbamazepine. Hyponatremia may lead to
weight gain and irritability. The teratogenicity of Carbamazepine seems to be minimal, must however be considered under the medication in pregnant women. The women taking oral contraceptive should be informed accordingly about the increased metabolism of oral contraceptives under the influence of Carbamazepine, which may lead to unwanted pregnancies. Even though a drug with several side effects Carbamazepine is one of the most useful antiepileptics particularly in the treatment of partial and cryptogenic epilepsies.

Carbamazepine is also being used quite often for the treatment of neuralgias particularly of the type of trigeminal-neuralgia, post herpes-neuralgia and poly-neuropathies of the type of diabetic poly-neuropathy. It is used in the psychiatric practice for the treatment of unipolar, bipolar affective disorders and also in conditions of psychosis. In case of epilepsy one must try to keep Carbamazepine under monotherapy to the extent possible. If a combination is required, the other suitable drugs for combination are Sodium valproate, Lamotrigine, Topiramat and Phenobarbitone, depending upon the type of epilepsy.

**SODIUM VALPROATE**

Sodium valproate was introduced as an antiepileptic drug in the European countries around 1964. Sodium valproate is the sodium salt of valproic acid. Structurally this is a somewhat different drug in comparison to other antiepileptic drugs. There are different theories regarding the mechanism of action in brain. Sodium valproate seems to increase the brain concentration of the inhibitory neurotransmitter GABA. Further there could be a selective
enhancement of postsynaptic response to GABA as well as a direct effect on neuronal membrane in regard to reduction of brain concentration of excitatory amino acid neurotransmitter.

Pharmacokinetic of Sodium Valproate

- Daily maintenance dosage adult 900-2400 mg (3000 mg), children 20-30 mg per kg body weight
- Minimum dose frequency twice daily (enteric tablets)
- Elimination half-life 9-21 hours
- Time to reach steady state 4 days
- Serum concentration 350-700 mmol/l
- Percentage of protein binding to plasma nearly 90%

Sodium valproate is a widely used antiepileptic drug throughout the world. It has a wide spectrum of antiepileptic effect and can be given in practically all the kinds of epilepsies, even though it is a specific drug in the case of idiopathic generalized epilepsies with absences and grand mal seizures. It can be effective also in partial seizures in the group of partial epilepsies or cryptogenic epilepsies. Further Sodium valproate is used in many kinds of epileptic syndromes of childhood. Sodium valproate can be given as a monotherapy in most of the generalized epilepsies including juvenile absence epilepsy, juvenile myoclonic epilepsy and similar syndromes. Under polytherapy it can be combined with several other preparations such as Carbamazepine, Lamotrigine, Phenytoin, Topiramat and Phenobarbital. In case of Phenobarbital however it could sometimes cause severe interactions leading to clinical toxicity.

Sodium valproate can be effective in smaller dosage of 600 mg per day, sometimes however higher dosage is needed
particularly in complex form of epilepsies. The effect of antiepileptic action can be seen clinically as well as in the EEG particularly in such EEGs with generalized spike wave activity. In certain cases of primary generalized epilepsies there may be a dramatic response to monotherapy of Sodium valproate with rapid improvement in the clinical course associated with EEG improvement.

**Interactions and Side Effects**

There are however some disturbing side effects during the treatment of Sodium valproate. One of the serious one’s is in case of children in the way of hepatotoxicity, very rarely with fatal consequences. The most common side effects are seen particularly in young women by increase of body weight and loss of hair. These side effects can be sometimes so disturbing that the drug must be discontinued in spite of very beneficial antiepileptic effects. The side effects related to the central nervous system are mild and mostly reversible. Occasionally one sees tremor of the hands in patients who take Sodium valproate in higher dosage, which is also a reversible condition. Cases of mild gingiva hyperplasia is seen also under long range intake of Sodium valproate. There may be certain amount of teratogenic effect, which must be considered in case of childbearing women. For the past 10-15 years there have been further indications for the use of Sodium valproate. These are in case of affective bipolar disturbances and certain forms of psychosis. However, the drug is a basic and very useful antiepileptic particularly in generalized epilepsies. There is no clear contraindication for the use of this drug in any kind of epilepsy. An important factor is the necessity to use enteric coated tablets, because
of the gastric irritation caused by the substance. The drug should be given with care in people suffering from renal or liver disease. There may be interactions and serum level changes if the drug is used with Phenobarbitone, Phenytoin, Carbamazepine. In such cases frequent clinical and laboratory controls are then needed.

**BENZODIAZEPINES**

The Benzodiazepines are synthesized around 1930 and they are in the market since 1965. The Benzodiazepines are primarily tranquillizers and are being used worldwide because of this property. In addition to the tranquillising properties of Benzodiazepines, they have potential anticonvulsant effect particularly in the parenteral form and as such are important drugs for the treatment of status epilepticus. Their effect in the long range treatment of epilepsy is however limited as they develop tolerance after some months of treatment. Moreover, the Benzodiazepines have sedating side effects and severe withdrawal reactions. Some drugs from the group of Benzodiazepines have however found a place also in the long range treatment of epilepsy, particularly in refractory epilepsies of the childhood syndromes. The Benzodiazepines are not suitable for monotherapy in any kind of epilepsy. The value in the polytherapy must be carefully and individually estimated. A reference will be made here about the common drugs which are used in the management of epilepsy.

**DIAZEPAM**

Diazepam is a useful drug in the treatment of status epilepticus of different varieties namely grand mal status,
status of partial seizures and absence status. It should be given intravenously in the dosage of 10-20 mg for adults during a status epilepticus. The injection should be administered slowly as there may be sometimes side effects such as depression of respiration. Rarely an intravenous injection given during a status epilepticus may even provoke tonic seizures. Diazepam can be given also in an infusion, the action of which however is slower than the direct use of Diazepam as an intravenous injection. If it is given intramuscularly the effect is not satisfactory and is not a proper way of treatment for status epilepticus. During intravenous injection Diazepam will be absorbed fast and concentrations are reached in the brain within 5 minutes. The elimination half-life during a long range medication is 20-60 hours. In addition to the intravenous usage, Diazepam can be given in the form of rectioles particularly in children to control epileptic seizures. Generally rectioles for adults and children are available which can be used correspondingly for older children and younger children and infants. They are not suitable for the treatment of a status epilepticus.

**CLONAZEPAM**

Clonazepam is available as parenteral preparation and also as oral preparation. The drug can be given as an add-on-therapy in certain kinds of childhood epilepsies for a definite length of time to improve the control of seizures. Orally they are given in a dosage of 1-3 mg/day divided in two to three doses. The drug is useful in myoclonic absences and other forms of complex absences. As an intravenous drug Clonazepam can be used for the treatment of status epilepticus in all the forms including grand mal status.
long range use of the drug can lead to sedation and other central nervous system side effects which are however reversible.

**CLOBAZAM**

Clobazam is available as tablets and are being used more often in the management of epilepsy however as an add-on drug for both, children and adults. The dosage for adults is 10-20 mg/day in two divided doses. This drug is useful particularly to prevent withdrawal seizures when a major change of medication of the basic drugs is being done. The drug helps also to improve seizures in therapy-refractory epilepsies both of the generalized form as well as the partial form. However, Clobazam can develop tolerance after some time and there may be difficulty to stop the drug because of withdrawal reactions.

On the whole Benzodiazepines are not very useful in the long range treatment of epilepsies but two of the drugs namely Diazepam and Clonazepam are very useful in the treatment of status epilepticus particularly with intravenous usage. Under chronic medication side reactions are marked particularly in the form of central nervous system, leading sometimes to severe sedation. Tolerance develops in the Benzodiazepines under long range medication with reduction of antiepileptic effect.

**NEW GENERATION DRUGS**

In the following pages reference will be made to new generation of antiepileptic drugs which have been introduced in the market since 1990. Some of the newer drugs such as Lamotrigine, Oxcarbazepine, Topiramat and
Levetiracetam have made useful contribution in the treatment of different kinds of epilepsies. They can be used in the same way as Sodium valproate, Carbamazepine, Phenytoin and Phenobarbitone as monotherapy or in combination. Some other newer drugs such as Vigabatrin, Pregabalin, Zonisamide, Felbamat and Gabapentin have made limited contributions as antiepileptic drugs but are used for other indications such as severe neuralgias, neuropathies and other pain syndromes. Some of these drugs have shown considerable side effects but others again have made definite contributions and help in the control of seizures with improvement in quality of life for epilepsy patients.

**VIGABATRIN**

Vigabatrin was introduced as an add-on drug for the treatment of epilepsy particularly the partial epilepsy. Even though the drug has some antiepileptic properties, it has also severe side effects. The antiepileptic action of the drug seems to be dependant on its effect on the modification of GABA. In the clinical trials and later in the treatment of epilepsy the drug was found useful as an add-on-therapy for the control of partial seizures particularly complex partial seizures. However because of several central nervous system side effects and also such side effects related to mood changes leading to depression, this drug is being used rarely in the long-term management of epilepsy.

**LAMOTRIGINE**

Lamotrigine is a useful antiepileptic drug which was introduced in the market in European countries in 1993.
Since then it has been used in different kinds of epilepsies partial and generalized both in children and adults quite extensively throughout the world. Its action seems to be the inhibition of excitatory neurotransmitters. The pharmacokinetic of Lamotrigine is dependable in respect of bioavailability, regular kinetic and fairly long plasma half-life of around 25 hours. It has however interaction with other antiepileptic drugs as well as with oral contraceptives. Oral contraceptives can, for example, decrease the level of Lamotrigine serum concentration. However, there is no contraindication for a combination of Lamotrigine with other drugs if proper serum concentration levels are estimated from time to time. The serum concentration level of Lamotrigine is 10-50 mmol/l under therapeutic effect. As with other antiepileptic drugs side effects are known in higher dosage particularly central nervous system disturbances and sometimes also hematological changes. In combination with other drugs, for example, in higher dosages of Sodium valproate there may be significant risk of hematological and liver function changes. Skin rashes are known particularly during the earlier periods of medication. The dosage for adults is 150-400 (500) mg in two divided doses per day, for children correspondingly less between 50-100 (150) mg per day.

Lamotrigine is a useful antiepileptic drug in the treatment of practically all kinds of epilepsies and epileptic syndromes. It seems to have clinical effects somewhere in the range of two earlier drugs namely Carbamazepine and Sodium valproate. Like Carbamazepine it is indicated in partial epilepsies with partial and secondary generalized seizures. At the same time it can also be given in generalized
epilepsies of the idiopathic forms with generalized spike waves in EEG. Whereas Carbamazepine can provoke the spike wave activity in EEG, Lamotrigine does not seem to do this. According to the experience until now, Lamotrigine does not cause two major side effects caused by Sodium valproate namely increase of body weight and loss of hair particularly in young women. Lamotrigine can completely replace Carbamazepine in case of partial epilepsies. In case of generalized epilepsies even though it is equally effective like Sodium valproate, the suppression of spike and waves seems to be better with Sodium Valproate. Lamotrigine can be given as monotherapy in children and adults, but it can also be combined with practically all of the other antiepileptic drugs. It is however necessary to start with a small dosage of 50 mg/day per adults and increase the dosage as required up to a daily dosage of 300 - 400 mg under monotherapy. For children the dosage must be individually adjusted from 50-100 mg or 150 mg per day. The estimation of serum concentration is useful for the purpose of effectiveness as well as to avoid side reactions and interactions when given in a combination therapy. A further indication for Lamotrigine is in the treatment of bipolar affective disorders, however with a lesser dosage of maximum 200 mg/day.

**GABAPENTIN**

Gabapentin was introduced as an antiepileptic drug in the European market in the year 1995. It is available in the form of capsules and tablets of 100 mg, 300 mg and 600 mg. The drug is indicated mostly as an add-on-therapy in the treatment of partial epilepsies. For a monotherapy Gabapentin seems to be not very suitable. Like other antiepileptic...
drugs it acts on the regulation of neurotransmitters involving excitation and inhibition. In a combination treatment Gabapentin may be useful in the treatment of chronic therapy-refractory partial epilepsies. However, over the past years it has lost some of its importance in the treatment of epilepsy but has found effectiveness in management of different kinds of neuralgias particularly postherpes neuralgia, diabetic polyneuropathy, other neuralgias and in undetermined pain syndromes. In these cases the drug seems to have definite benefits in comparison to the other drugs. The dosage varies from 600-1800 mg/day in adults. Its indication in case of children has not been properly estimated. The serum concentration of Gabapentin in the effective therapeutic level ranges between 30-90 mmol/l. There are some disturbing side effects particularly in the way of sedation during the early stages of treatment. Most of the adults tolerate the drug after an intake of around two weeks. The other side effects are related to central nervous system and hematology as in case of different antiepileptics.

**FELBAMAT**

Felbamat was introduced as an antiepileptic drug in the year 1995 for restricted treatment of epileptic syndromes particularly of the type of Lennox-Gastaut syndrome. It is available in the form of tablets and syrup and has found very restricted indication as an antiepileptic drug. The dosage should be individual in children and it is given only in combination. There are several side effects particularly related to hematology and liver function. The use of the drug with other kinds of epilepsies has not been
properly evaluated. The recommended dosage is 7-15 mg per kg body weight.

**OXCARBAZEPINE**

Oxcarbazepine was introduced in the European countries in the year 1996. It is a further development of the drug Carbamazepine with a ketoderivative. The main drug Oxcarbazepine is rapidly converted in the humans into a metabolite, which has definite antiepileptic properties. The metabolite has a much longer plasma half-life than the main drug. Oxcarbazepine has considerably lower central nervous system side effects and is on the whole better tolerated than Carbamazepine. However, Oxcarbazepine requires higher doses than Carbamazepine for effective antiepileptic action. In one of the early studies of Rai and Rai et al 1978 and 1979, the drug showed advantages over Carbamazepine in regard to better tolerance. The indications are the same as in the case of Carbamazepine, which are partial epilepsies with simple partial and complex partial seizures also with tendency to secondary generalization. Regarding the effectiveness, the drug does not have much advantage over Carbamazepine. The side effects particularly skin rashes, hematological changes and central nervous system disturbances are less in comparison to Carbamazepine, even in a dosage 30-50% higher than that of Carbamazepine. Oxcarbazepine can cause often hyponatremia, which needs frequent laboratory controls. The effect on the EEG seems to be less provocative in respect of generalized spike and waves when compared to Carbamazepine. The EEG changes however do not correlate with clinical effectiveness, as also in the case of Carbamazepine.
The daily dosage for adults ranges between 900 and 2,400 mg. The serum concentration in the effective dosage ranges between 30 and 80 mmol/l. Oxcarbazepine has somewhat broader indication including secondary generalized epilepsies, however it is not suitable for the treatment of primary generalized epilepsies. In case of partial epilepsies and cryptogenic epilepsies with partial and secondary generalized seizures the drug can be given as a monotherapy, needs however a higher dosage. It can be given in combination with practically all other antiepileptic drugs. The advantage of Oxcarbazepine is on the whole its better tolerance. In addition to antiepileptic properties the drug is given also in the treatment of depression and neuralgias.

**TIAGABIN**

Tiagabin is available in the European market since 1997. The drug has been allowed for the use as an antiepileptic in persons above the age of 12 years as an add-on-therapy for the treatment of partial epilepsies. Tiagabin has the properties like several other antiepileptic drugs to improve the GABA stabilization at the level of neurotransmitters. The bioavailability is fairly high up to the level of 89%. The recommended dosage of Tiagabin for adults is between 30-50 mg/day in divided doses of two or three times. This dosage is recommended particularly in combination medication where patients may be taking other enzyme induction drugs. If the drug is given alone, a considerably lesser dosage may be sufficient in the range of 15-30 mg/day. However, the drug has not been allowed for use as a monotherapy.
Tiagabin has side effects involving central nervous system disturbances as well as hematological and liver function changes.

**TOPIRAMAT**

Topiramat was introduced in Europe as an antiepileptic in 1998 and since then has been used fairly extensively in different types of epilepsies. This drug seems to have a broader spectrum of action in different kinds of epilepsies mostly of the partial form but it can be effective also in generalized epilepsies, particularly such generalized epilepsies with predominantly grand mal seizures. Depending upon information available until now, Topiramat does not seem to provoke absences in case of primary or secondary generalized epilepsies. As in case of many other antiepileptic drugs the actual mechanism of action at the level of neurotransmitters is not clearly understood, but the drug seems to improve the inhibitory qualities of GABA. The dosage in monotherapy ranges between 100-400 mg/day/adults and for children comparatively lower. The effective serum concentration ranges in the level of 12-36 mmol/l. As in case of other antiepileptic drugs, there are some serious side effects involving the central nervous system, particularly speech disturbances and liver function. One of the known side effects of Topiramat is a reduction of body weight, which however is rarely a contraindication for its use, except in case of very thin persons. The drug is useful also in case of therapy-refractory partial epilepsies and epileptic syndrome of childhood and adolescence. In case of women taking oral contraceptives a faster metabolism of contraceptive can be
expected with decreased efficacy of contraception. Interaction with other anticonvulsants particularly Sodium valproate must be considered during the long range usage of Topiramate. Along with its antiepileptic properties, Topiramate has effectiveness in the management of pain syndromes particularly neuralgic pains.

**LEVETIRACETAM**

Levetiracetam is one of the latest drugs available for the treatment of epilepsy, which is available in the European market since the year 2000. It is a very water soluble product and is available in the form of tablets in different dosages. The exact mechanism of antiepileptic action is not known even in the case of Levetiracetam. In animal experiments Levetiracetam showed considerable inhibitory properties in the pattern related to Kindling. In humans it is expected that Levetiracetam may modulate the GABA neurotransmitter, even though a direct inhibitory action was not significant. Levetiracetam is rapidly absorbed after oral administration and the pharmacokinetics seems to be linear. Levetiracetam is less than 10% protein bound and the bioavailability is good. Brain concentrations are reached in about one hour following oral administration. The plasma half-life in adults is 7-8 hours. The drug is effective in partial epilepsies with partial seizures and with secondary generalization. The recommended daily dosage for adults ranges in combination therapy between 500-2000 mg/day. The effectiveness of the drug in case of generalized epilepsies as well as its action on the reduction of generalized spike wave activity in EEG has not been properly documented. In
case of therapy-refractory epilepsies and epileptic syndromes Levetiracetam can be given both for children and adults. The side effects are usual central nervous system sedation and liver function as well as hematological changes. On the whole the drug has proved useful in epilepsies which are otherwise difficult to manage.

**ZONISAMIDE**

Zonisamide is one of the recent additions to the group of antiepileptic medication. This drug has been allowed for restricted use as an add-on-therapy in the treatment of adults only with partial epilepsies having partial seizures also with secondary generalization. The drug is available in the form of capsules in dosages of 25 mg, 50 mg and 100 mg. The daily dosage has been recommended between 300 mg and 500 mg. The drug should be added on with a small dosage of 50 mg/day to begin with once or twice daily, the dosage should be slowly increased depending on tolerance and effectiveness until the adequate dosage has been reached. There does not seem to be additional advantages in using this drug in comparison to the already established antiepileptic drugs. The probable indications are therapy-refractory partial epilepsies with complex partial seizures with a tendency also for secondary generalization. The side effects mentioned in the literature are mostly liver- and kidney-function disturbances as well as hematological changes; central nervous system side effects such as ataxia, vertigo, drowsiness and headache have been reported. Probably over the next years we will hear more about the indications and contraindications about this drug in the field of epileptology.
PREGABALIN

Pregabalin is also a new drug recently introduced allowed as an add-on medication for the treatment of partial epilepsies. The drug is available in different dosages of 50 mg, 150 mg, 300 mg and 600 mg tablets. Along with the antiepileptic properties the drug has been found useful in the treatment of neuropathic pain syndromes and the neuralgias. In a study published recently, fairly good results have been recorded as an add-on-therapy in the treatment of refractory partial epilepsies on a daily dosage of 150 mg-300 mg. It can be combined with other conventional drugs used in the treatment of partial or generalized epilepsies. As a monotherapy Pregabalin is indicated in the treatment of migraine, diabetic polyneuropathy, herpes-neuropathy and other forms of neuralgias. The side effects mentioned are mostly related to central nervous system such as vertigo, sleepiness and cognitive disturbances particularly in the higher dosage.

From the different antiepileptic drugs mentioned so far, the following drugs are widely used in the clinical neurological or neuropediatric practice depending upon various indications.

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium valproate</td>
<td>- Generalized epilepsies, primary and secondary, in adults and children</td>
</tr>
<tr>
<td></td>
<td>- Partial epilepsies, epileptic syndromes</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>- Partial epilepsies with or without secondary generalization, in adults and children</td>
</tr>
</tbody>
</table>

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Contd...

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lamotrigine</td>
<td>- Partial and generalized epilepsies in adults and children, epileptic syndromes</td>
</tr>
<tr>
<td>Topiramat</td>
<td>- Partial epilepsies also with secondary generalization</td>
</tr>
<tr>
<td></td>
<td>- Secondary generalized epilepsies, epileptic syndromes</td>
</tr>
<tr>
<td>Oxcarbazepine</td>
<td>- Partial epilepsies also with secondary generalization</td>
</tr>
<tr>
<td>Levetiracetam</td>
<td>- Partial epilepsies with or without secondary generalization, epileptic syndromes, generalized epilepsies</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>- Grand mal epilepsy, partial or cryptogenic forms. Not suitable in primary generalized epilepsies with absences</td>
</tr>
<tr>
<td>Phenobarbitone</td>
<td>- Grand mal epilepsy, cryptogenic form, eventually generalized epilepsies with grand mal. Not suitable in partial epilepsies with predominantly complex partial seizures</td>
</tr>
</tbody>
</table>

GENERAL PRINCIPLES OF DRUG TREATMENT

Epilepsy is a heterogenic condition manifesting as a clinical entity with seizures, due to various causes known and unknown. Even though the diagnosis of epilepsy has to be evaluated as rationally as possible depending upon the phenomenology of seizures, EEG findings and nosology, the principal of drug treatment is rather empirical. However, several clinical and laboratory diagnostic factors must be evaluated properly before a drug treatment is considered. First of all it should be very clear whether the seizure is of an epileptic nature, that means whether it is really a clear
cerebral phenomena. As already mentioned in the previous pages there are many other seizure types and conditions which may simulate an epileptic seizure but of entirely different origin. Some of the common non epileptic seizures are vago-vasal syncopes, cardiac syncopes, positional vertigo, certain types of migraine, psychogenic seizures and several other seizures like phenomena. These non-epileptic seizures must be excluded through proper history-taking and general examination of the patient. Some epileptic seizures such as grand mal can be often diagnosed as epileptic. The other seizures of the complex partial type and absences need further investigations before a diagnosis of the epileptic phenomena is established. Once the seizure has been diagnosed as epileptic, attempts must be made to evaluate the possibility of a nosological diagnosis as epilepsy. Such a diagnosis is never possible under one clinical sitting, as further examinations particularly with EEG and sometimes neuroradiology is necessary.

**Isolated Seizures**

One of the important aspects is to differentiate an isolated epileptic seizure from the possibility of an epilepsy becoming a chronic condition. An isolated seizure in adults is associated with certain provocations particularly in the form of excessive alcohol, sleep deprivation and severe stress. If the provocations are clear and the interval EEG does not show a positive finding for epilepsy, then a drug treatment is generally not indicated. There is however no general agreement among neurologists anywhere as to when one should start with a drug treatment and with what kind of drug for a newly diagnosed seizure. If however two isolated
seizures occur in a short interval even due to provocations, then there is already the doubt of epilepsy becoming a chronic condition and as such, the necessity of initiating a drug must be individually assessed. Similar is the case in respect of *febrile convulsions* in children. Generally the occurrence of one or two febrile convulsions in children in the age group of one to five years is not an indication for initiation of an antiepileptic drug. On the other hand if a child has more than around five febrile convulsions, then the matter has to be considered individually depending upon other clinical and laboratory factors to find out whether an antiepileptic drug as a prevention of further seizures is to be given. The initiation of a drug treatment must always be carefully considered also in discussion with the patient or dependents and under consideration of long range prognosis.

**Procedure of Drug Initiation**

Before a drug treatment is commenced, it is necessary to discuss the pro’s and con’s of treatment with the patient. Every drug treatment to control epileptic seizures is basically of a preventive nature, except in the case of parenteral treatment of status like seizures. As such, it is necessary to select a drug which is most effective for the treatment of seizures. In selecting a drug we have to consider primarily the phenomena of seizure and secondarily the EEG findings, which might give us an information about the nature of epilepsy as an nosological entity. There are other considerations as well, particularly the social situation of the patient. Generally as mentioned before, it is not advisable to start with a drug treatment after only one
epileptic seizure, even if the seizure can be classified clearly as an epileptic phenomena. The clinical judgement should depend upon other factors such as the EEG findings and professional and social situation of the patient. If after one epileptic seizures the EEG shows a clear epileptic activity in interval such as generalized spike and waves or a temporal lobe focus of sharp waves, then it may be justifiable to start a drug treatment. Accordingly if a patient is entirely dependant on driving for his professional purposes and / or if he or she is working on heavy machines, even then it may be justifiable to start a treatment even after one epileptic seizure. In the event of an EEG finding as mentioned before, after even a single epileptic seizure, we could be fairly certain that there is a risk of an epilepsy becoming chronic and as such there may not be much meaning in waiting longer before starting the drug treatment. As mentioned in the earlier pages the diagnosis of single seizures as epileptic or otherwise is in some cases extremely difficult as shown by the studies of Rai et al 1988.

Febrile convulsions as a principle do not require drug treatment. It must however be considered that severe febrile convulsions can lead to structural damage in the temporal lobes, which may later be a cause for chronic and even therapy-refractory epilepsy. Moreover the repeated occurrence of febrile convulsions is a distressing condition for the child and the parents. Even though there are no clearly defined rules regarding the initiation of drug prophylaxis in febrile convulsions, it is useful to instruct the parents to use Diazepam rectioles as a prophylaxis during high fever in children, who already had more than one or two febrile convulsions. In addition the child must be treated with fever
reducing measures such as applications of cold water packs and intake of Aspirin or Paracetomol.

**Strategy of Drug Treatment**

Before a drug treatment is considered to treat a person with suspected epilepsy, the following points must be taken into consideration.

- Assessment of the seizure as epileptic through proper history-taking from the patient and the dependents
- Exclusion of an isolated epileptic seizure depending upon the provocation factors
- At least one interval EEG examination with standard requirements such as hyperventilation and photic stimulation
- Assessment of the possible etiological factors, and the classification of epilepsy as idiopathic, cryptogenic or partial
- Selecting one antiepileptic drug suitable for seizure type considering however also the nosological diagnosis
- Discussion with the patient about the need for anti-epileptic medication and the possible duration of intake
- Selection of the drug for the use of once or twice daily intake.

**Monotherapy**

As a principle one must select a single drug for the treatment of epilepsy. The drug must be selected on the basis of available standard preparations which have been found suitable in different kinds of seizures and epileptic syndromes. The use of a single drug treatment is advantageous because of different factors. The efficacy and
the side effects of a single drug can be much better estimated than a combination of drugs. Certain antiepileptic drugs are suitable for monotherapy, the others are less suitable. There have been several international studies regarding the efficacy and side effects of single drugs in different kinds of epilepsies. Even though some basic factors regarding the mechanism of action of some drugs are known such as in the case of Sodium valproate which stabilises the GABA neurotransmitter, much is unknown regarding the mechanism of action of several other useful antiepileptic drugs. Some drugs such as Carbamazepine have been found effective in the treatment of partial epilepsies with simple partial, complex partial and secondary generalized seizures. However, Carbamazepine is not a suitable drug in the treatment of primary generalized epilepsies of idiopathic nature with absences and generalized tonic clonic seizures. A careful estimation of the efficacy and possible side effects of a mono preparation must be thoroughly considered before the drug is given to a patient. The practice of giving a single preparation can be carried out in the following manner.

- Starting the drug in a small dosage to begin with preferably evenings
- Increasing the dosage of the drug in intervals of 3-5 days until a tolerable dosage is reached.
- The interval of drug intake per day must be considered depending upon the plasma half-life of the drug, preferably twice daily
- The patient must be informed about the procedure of drug effectiveness, and the possible side reactions before the final dosage is reached
- At the end of the final dosage depending upon the steady state of the drug a serum concentration level must be ascertained
• The patient must be examined during the titration of the drug for possible side effects.
• Depending upon the preparation hematological and liver function tests must be done in intervals of 4-6 weeks on the whole 2-3 times when a new drug is given.
• Depending upon the type of the epilepsy an EEG examination may be necessary after the steady state of the drug is reached.

The effect of drug can be estimated only after the steady state is reached, in some cases much later. Many patients have problems in accepting a higher dose of the antiepileptic drug, which must be discussed with them from time to time. Even if there is no sufficient effect of the drug, which means, if the seizures continue, the drug must be carried to the maximal level until the patient reacts with side effects. Generally this takes a period of 4 to 6 weeks after the drug has been introduced. A hasty clinical judgement regarding the effectiveness or the decision to change the drug or make a combination of drugs should be avoided.

Some thirty years ago it was an usual practice to combine antiepileptic drugs for the treatment of various kinds of epilepsies. This practice has been abandoned to a great extent over the past two to three decades. Those days when a combination was given the antiepileptic drugs were called as basic drugs and as secondary drugs. In the clinical practice today we do not need this nomenclature, because most of the drugs taken for monotherapy must be considered as basic drugs in respect of seizure classification and epilepsy diagnosis. The developments in long-term EEG monitoring with video have enabled this kind of better diagnosis of seizures and epilepsies. In case of epilepsies diagnosed in adults, around 50% of patients can be
successfully treated with single drugs, if the drugs are properly selected and the procedure of treatment is carried out with counselling of patients. A monotherapy is always superior to a combination of drugs for the reasons which have already been discussed. However, there are patients with other kinds of epilepsies who cannot be treated with single drugs only, but sometimes during the course of their illness need a second drug. Before starting a second drug, the monotherapy should be carried out with different preparations. For example in a patient with partial epilepsy if a monotherapy with Carbamazepine is not successful, the next attempt should be to give another monotherapy, for example Lamotrigine. This procedure is rather delicate as the patients may suspect that the physician is experimenting with them. Such a procedure therefore needs frequent counselling of the patients and explaining them the long-term usefulness of having a single drug therapy. If Lamotrigine is not successful there may be the possibility of a third alternative for example of trying somewhat a unconventional drug Sodium Valproate in the treatment of partial epilepsy. Changing over from one drug to another is however difficult and the patient may lose confidence in the physician. Generally it is not possible to try consequently more than three preparations, one after another, as monotherapy because of the time needed for such a change over. If however a change over is possible for example from Carbamazepine to Lamotrigine, the second drug must be introduced in a small dosage as cross over with slow increase of dosage up to the maximum dosage planned. Parallely the dosage of the first drug should be slowly decreased in order not to provoke withdrawal seizures. It is known that
even if an antiepileptic drug has not shown sufficient effect in controlling seizures, it could provoke withdrawal seizures if it is abruptly removed.

**Combination of Two Drugs**

In spite of the many advantages of a monotherapy, in patients where the seizures cannot be controlled, the combination of a second drug is necessary. Sometimes a smaller dosage of the second drug is sufficient to enhance the antiepileptic properties of the first drug in the way of a synergetic action. An example for such a combination is the addition of a smaller dosage of Sodium valproate or Lamotrigine to an existing monotherapy of Carbamazepine, in difficult cases of temporal lobe or frontal lobe epilepsy. The other example is the juvenile myoclonic epilepsy which almost up to 80% can be treated only with a single drug Sodium valproate. However, some patients develop during the course of the disease in spite of Sodium valproate generalized tonic clonic seizures. In such cases they need an addition of a second drug such as Lamotrigine or even small dosage of Phenobarbitone. The unclassified grand mal epilepsies in adult life require sometimes during the course of illness a second drug. The combination should be done also with great care taking into account different factors involved in the classification of seizures, epilepsies and epileptic syndromes. There are patients who have a genetic predisposition to generalized epilepsies in the form of idiopathic epilepsy but also with a minimal brain damage which may result in the manifestation of partial seizures. Even such patients generally need a combination to be free of seizures. An important step in this procedure is that one
does not hurriedly introduce a second drug. Under monotherapy it is essential to reach the maximum drug tolerance clinically as well as in serum concentration. In combination however it is the clinical improvement which is necessary sometimes associated with EEG finding than the other laboratory parameters. In the succeeding pages reference will be made to monotherapy corresponding to epileptic seizures and epilepsies and the guidelines for combination of a second drug.

Polytherapy

In about 75% of the cases the control of seizures can be reached with an adequate monotherapy or with a combination of two drugs if careful analysis of the diagnosis and selection of drugs are made. If a seizure freedom can not be attained under these conditions of monotherapy or combination of two drugs, the epilepsy must be considered as therapy-refractory, however after considerable period of time generally a duration of one to two years. There are cases where even in a combination therapy, seizures cannot be controlled. In such cases one has to consider if the second drug introduced is a proper drug or if this drug has to be replaced again through some other drug. The other alternative will be to replace the first drug and keeping the second drug with optimal dosage. According to experience available from different sources worldwide a combination of more than two antiepileptic drugs for the treatment of seizures in adults is not useful. Somewhat different is the case regarding serious childhood syndromes. Patients of Lennox-Gastaut syndrome or similar secondary generalized epilepsies which begin in early childhood may need even
three antiepileptic drugs which is then generally termed as polytherapy. The assessment of such a therapy must be done individually with careful monitoring of clinical side effects and laboratory-findings. There is a justification in giving a third drug, for example, in Lennox-Gastaut syndrome as this may help control at least grand mal seizures as shown by Rai et al 1988 in institutionalised adult patients with Lennox-Gastaut syndrome. Rarely a polytherapy may be tried even in the case of severe partial epilepsies with temporal mesial sclerosis. Sometimes a third drug has to be introduced if the patient is already on two drugs without much help. However, attempt must be made to withdraw the “unwanted” drug.

Selection of Antiepileptic Drugs

Over the past forty years two aspects in the management of epilepsies have contributed very much for the control of seizures. They are the identification of epileptic seizures and classification of epilepsies according to the international guidelines through intensive long-term EEG monitoring accompanied by video-recording and the introduction of newer antiepileptic drugs, based on the developments in neurophysiology. With this additional knowledge resulting out of basic research and clinical practice epileptology has become a specialized field in neurology. These two factors have enabled the medical profession to control epileptic seizures in about 75% of the patients. The other nearly 25% of patients who cannot be made seizure free, have mostly severe brain pathology of various kinds from childhood brain damage up to different encephalopathies. The table above shows the indication of
**Epileptic seizures and corresponding drugs of choice for monotherapy**

<table>
<thead>
<tr>
<th>Epileptic seizures / Epilepsies</th>
<th>Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Partial epilepsies with simple partial, complex partial and secondary generalized seizures</td>
<td>Carbamazepine, Lamotrigine, Oxcarbazepine, Phenytoin, Primidone, Topiramat, Sodium valproate</td>
</tr>
<tr>
<td>- Generalized epilepsies with simple absences, complex absences, tonic, clonic, myoclonic and generalised tonic clonic seizures (grand mal)</td>
<td>Sodium valproate, Lamotrigine, Topiramat, Levetiracetam</td>
</tr>
<tr>
<td>- Cryptogenic epilepsies with partial seizures and with secondary generalized seizures (grand mal)</td>
<td>Lamotrigine, Carbamazepine, Phenytoin, Oxcarbazepine, Topiramat, Levetiracetam, Sodium valproate</td>
</tr>
<tr>
<td>- Childhood epileptic syndromes with secondary generalised and partial epilepsy forms (Lennox-Gastaut syndrome)</td>
<td>Sodium valproate, Lamotrigine, Levetiracetam, Carbamazepine, Oxcarbazepine, Phenytoin, Phenobarbitone, Clonazepam, Clobazam, Ethosuximide</td>
</tr>
<tr>
<td>Infantile epilepsies (West syndrome)</td>
<td>ACTH, Clonazepam, Sodium valproate, Lamotrigine, Levetiracetam</td>
</tr>
<tr>
<td>Status epilepticus (grand mal, partial seizures, absences)</td>
<td>Diazepam intravenous, Clonazepam intravenous, Phenytoin intravenous, sodium valproate IV</td>
</tr>
</tbody>
</table>

drugs in regard to the international classification of epileptic seizures and epilepsies.

The drugs in the above mentioned table are more or less in the order of preference as single drugs. The combination
should be done however individually according to the diagnosis of seizures and epilepsies. Among adults one has to deal with mainly partial seizures with simple partial (SPS) and complex partial (CPS) symptomatic. Other than that the adults have generalized tonic clonic seizures of the grand mal type (GTCS), which must be classified as primary generalized or secondary generalized. In case of primary generalized tonic clonic seizures the diagnosis is mostly an idiopathic generalized epilepsy may be with absences also and associated with generalized spike wave complexes occurring during hyperventilation. In this case Sodium valproate is certainly the drug of choice and Phenytoin is contraindicated because of its provocation of absences and spike waves in EEG. Relatively contraindicated is also Carbamazepine. Very often however the generalized tonic clonic seizures of the grand mal type occurring in adulthood are because of partial epilepsy which cannot be properly estimated in an interval EEG.

The patients who do not have a focal finding in EEG or no evidence of neurological abnormality including MRI, we have to consider them as having cryptogenic epilepsy where the etiology is not known. Such adults have sometimes grand mal seizures only in sleep where the proceeding aura cannot be clinically assessed. The seizures may be provoked through sleep deprivation and alcohol or stress. These patients react well to such drugs like Carbamazepine, Lamotrigine and Phenytoin. On the other hand there are adult patients who have grand mal seizures mostly on awakening on early morning in which cases one should suspect the possibility of primary generalized epilepsies. Some reasons for drug failures can be related to
a difficulty in this diagnosis. It was a practice in earlier years to give Phenytoin and Phenobarbitone in all cases of grand mal seizures irrespective of the origin of primary generalized, partial or cryptogenic epilepsies. A differentiated selection of drugs after analysis of seizures and epilepsies is therefore very useful for effective drug treatment.

The two drugs of the newer generation Lamotrigine and Topiramat seem to be effective in both generalized and partial epilepsies. However in cases of primary generalized epilepsies Sodium valproate is still a better drug and in case of clear partial epilepsies Carbamazepine is equally good as the newer products. The use of Phenytoin and Phenobarbitone should be reduced to the extent possible particularly in school going children and young adults. Even though both are still effective against grand mal seizures and partial seizures, they may lead to comparatively serious side effects. Another new drug, Levetiracetam, is effective against partial and generalized seizures.

The international classification of epileptic seizures, epilepsies and epileptic syndromes give us guidelines for the diagnosis of the heterogenic forms of epilepsy. The evaluation of a differentiated diagnosis is not an easy matter in the clinical practice. The basic factors in epilepsy diagnosis however are the clinical phenomena, the EEG findings and the possible etiology. Depending upon these factors, the selection of a drug is generally possible.
Absence Epilepsy in Childhood

The childhood absence epilepsy is characterized by the occurrence of simple and complex absences associated with generalized and bilateral synchronous spike wave complexes in EEG particularly occurring during hyperventilation. These are generally idiopathic primary generalized epilepsies with the possibility of a genetic predisposition. Along with absences the children may have rarely generalized tonic clonic seizures. Other than epilepsy, the children show no abnormality related to neurological and psychological findings.

The treatment in cases of childhood absence epilepsy should start with Sodium valproate as monotherapy. The drug of second choice may be Lamotrigine. The parameters for clinical judgement are the reduction of absences with reduction of spike wave activity in EEG. If there is no control of seizures under an optimal monotherapy a combination can be tried with Lamotrigine and Sodium Valproate. An addition of Phenobarbitone to the existing monotherapy of Sodium valproate is possible but not a good combination considering the side effects of Phenobarbitone particularly in the school going children.

Idiopathic Generalized Epilepsy in Adolescence

The idiopathic form of generalized epilepsy in adolescents and young adults is either a continuation of the absence epilepsy of childhood or an independent phenomena characterized by absences and generalized tonic clonic seizures. The patients have very indicative EEG findings in the form of bilateral synchronous generalized spike wave complexes particularly provicable under hyperventilation.
In this age group the clinical manifestation of absences is lesser than in the case of absence epilepsy of children. The epilepsy is characterized by occasional occurrence of generalized tonic clonic seizures of the type of grand mal particularly upon awakening early mornings. The EEG shows a characteristic diagnosis by the presence of longer duration of spike wave complexes where a clinical absence may be registered during hyperventilation. The patients come for treatment however mostly because of the occasional grand mal seizures. Even in this case of generalized epilepsy the first drug of choice is Sodium valproate and the second drug is Lamotrigine. Lamotrigine does not seem to provoke spike wave complexes and gives protection against grand mal seizures and probably also against absences. Nearly half of such patients can be seizures free under a fairly high dosed monotherapy of Sodium valproate. But the others require during the course of epilepsy a second drug which can be Lamotrigine. As an alternative to Lamotrigine the newer drug Topiramat can also be given. As mentioned already, Sodium valproate can lead to increase of body weight particularly among young women. Topiramat on the other hand seems to reduce body weight, but has other CNS side effects, particularly of speech.

Grand Mal Epilepsy in Adults
The epilepsy characterized by the occurrence of only grand mal seizures can be of different etiology namely idiopathic generalized, partial with secondary generalization or cryptogenic epilepsy. Before a drug is initiated in these cases, a differential diagnosis of the epilepsy classification is necessary to make sure about the indication of a particular
drug. If the grand mal epilepsy is of the generalized and idiopathic form as can be assessed through EEG, then the drug of choice is Sodium valproate or Lamotrigine as monotherapy. In these cases the grand mal seizures occur often in the early mornings after awakening, the patients may or may not have absences. In cases of partial epilepsies with secondary generalization leading into grand mal seizures, the drug of first choice would be Carbamazepine or Phenytoin followed by Lamotrigine, as monotherapy. The diagnosis of a partial epilepsy with secondary generalized seizures is based on history-taking and EEG findings where an occasional focus in temporal or frontal lobes can be registered. Most of these patients have grand mal seizures in sleep later also during day. The other drugs which can be used here are Oxcarbazepine, Topiramat and rarely Sodium valproate.

If the grand mal seizures cannot be correlated to generalized or partial epilepsy forms, then we have to consider the epilepsy as cryptogenic which means the etiology is unknown. The drugs of choice are the same as mentioned for partial epilepsies with grand mal seizures. The terminological use of cryptogenic epilepsy means mostly our inability to reach a proper etiological diagnosis. However, attempts must be made to estimate to the extent possible the etiological factors involved. One of the most important aspects is to rule out the possibility of a neoplasma in all adult epilepsies.

**Juvenile Myoclonic Epilepsy**

The juvenile myoclonic epilepsy of young adolescence is an idiopathic form of generalized epilepsy with myoclonic jerks
and occasional grand mal seizures. The EEG shows generalized spike wave complexes with poly spikes sometimes with bundles however not so synchronous as in the case of idiopathic absences. The patients have myoclonic jerks on awakening or also during day which sometimes lead to generalized tonic clonic seizures. The drug of choice in case of juvenile myoclonic epilepsy is Sodium valproate which is sufficient to control seizures in almost around 70 to 80% of patients. In some patients however the grand mal seizures persist in spite of high dosage of Sodium valproate. In such cases the drug may be combined with Lamotrigine which may result in total control of seizures. The prognosis of juvenile myoclonic epilepsy under medication is good, a high percent of patients however react with recurrence of seizures in the event of drug withdrawal, even if they were seizures free for a period of over five years. Because of this factor, withdrawal of medication even after long duration of seizure freedom is very difficult in patients with juvenile myoclonic epilepsy.

**Partial Epilepsy (Temporal Lobe Epilepsy)**

The partial epilepsy with simple partial, complex partial and secondary generalized seizures is one of the most difficult forms of epilepsy for drug treatment in adult life. Several of these patients have temporomesial sclerosis or lesions in temporobasal or frontobasal structures. A majority of these adult patients who are therapy-refractory have normal intellectual faculties. One must begin with a monotherapy of Carbamazepine or Lamotrigine. The other alternatives for monotherapy are Phenytoin and Oxcarbazepine. Very often however the patients need a second drug
which may be a combination of Carbamazepine and Lamictal, Oxcarbazepine and Lamictal, Phenytoin and Lamictal or Carbamazepine and Sodium valproate. A good number of patients however continue with seizures in spite of high doses of combination drugs. Depending upon the etiological factors based on MRI and long-term EEG recordings the patients should be considered for epilepsy surgery. In case of partial epilepsies arising out of fronto basal structures a combination of Sodium valproate and Carbamazepine or Lamotrigine is effective. In long-term EEG one can record in such cases a frontal or fronto-temporal focus with extension to bifrontal regions. Sometimes one gets an interval EEG with findings similar to generalized epilepsies, however with a difference of focal dominance in one hemisphere. As an alternative to the combination of Carbamazepine and Sodium valproate, similar combinations with other drugs such as Oxcarbazepine, Lamotrigine, Topiramat or Levetiracetam with Sodium valproate can be tried.

Lennox-Gastaut Syndrome

Lennox-Gastaut syndrome is characterized by a therapy-refractory epileptic encephalopathy. In addition to practically all kinds of epileptic seizures the children have mental retardation. The majority of seizures occurring in Lennox-Gastaut syndrome are tonic axial spasms followed by tonic, atonic, complex partial and generalized tonic clonic seizures. It is necessary to start with drugs such as Sodium valproate, Lamotrigine, to begin with as monotherapy but which must be soon combined with other drugs such as Carbamazepine, Phenytoin, Topiramat, Felbamat,
Levetiracetam, Clobazam and Clonazepam. The patients cannot be made free of seizures, the attempt should be made however to make them free as far as possible from grand mal seizures and the frequent drop seizures. Even though the syndrome has general characteristics, the clinical course of the disease is somewhat variable. The patients need a combination of two to three drugs in order to reach some betterment in the clinical condition. They should be taught to wear an helmet for prevention of frequent injuries to forehead and face resulting from drop seizures.

Treatment of Status Epilepticus

As already mentioned in previous pages, a status epilepticus of generalized tonic clonic seizures (grand mal) is a life-threatening emergency condition. A status epilepticus can be defined as a condition of repeated seizures for a period of 5 to 30 minutes longer. The seizures may occur continuously or one after another without the patient regaining consciousness, which is the case in grand mal seizures. The diagnosis of a status epilepticus with grand mal is clinically clear because of the phenomenology of tonic clonic components and the loss of consciousness. In case of absence seizures the condition is difficult to diagnose as it is a non-convulsive phenomena. Partial seizures with simple partial symptomatic and motoric phenomena can be noticed where the patients may be generally not unconscious. The status epilepticus in case of complex partial seizures can be to a good extent clinically diagnosed because of the automatisms of the patients with impairment of consciousness. Sometimes however a differentiation of status epilepticus of complex partial seizures from absences is difficult and
may need EEG monitoring for a differential diagnosis. In case of non-convulsive status epilepticus with absences some patients may have a secondary generalized grand mal seizure, when the absence status is ended. Similar is the case in partial seizures which can terminate in a grand mal seizure. Both these conditions of absence status or status of partial seizures are generally not such emergency conditions as a status of grand mal seizures.

**Grand Mal Status Epilepticus**

A status of generalized tonic clonic seizures of the type of grand mal must be treated with the utmost emergency under a Hospital set up. Even though a status epilepticus is more common among patients who have an epilepsy, it can start also as the first symptom in about 30% of patients who do not have epilepsy. The reasons for a status epilepticus in patients without epilepsy may be metabolic disturbances such as sever hypoglycaemia particularly in patients with type I diabetes, other kinds of electrolyte disturbances and intoxications particularly alcohol. There may be direct cerebral causes as in the case of a cerebral tumor, cerebral stroke or other serious brain pathology. In case of patients with epilepsy the most common reason is the sudden withdrawal of antiepileptic drugs or severe infections particularly in children. In all cases it is useful to make a fast blood examination to rule out metabolic disturbances. Parallely and without waiting the treatment should be commenced as intravenous injections or infusions. Intramuscular route for management of status epilepticus is not suitable because of slow absorption of drugs. Benzodiazepine in two to three forms is a good drug for the
treatment of status epilepticus, followed by Phenytoin and Sodium valproate. In adults an intravenous injection of Diazepam 10 mg in 2 ml is sufficient to control status epilepticus in about 50 - 60% of the cases. Some patients may need double the dosage also per intravenous route. The injection should be given slowly as it may cause respiratory depression in certain patients. The other drugs are Clonazepam or Lorazepam in a dosage of 2-4 mg injected also slowly in adults with correspondingly lesser dosage for children amounting to roughly 1/3-1/2 of the adult dosage. Clonazepam is on the whole more effective in controlling status like seizures than Diazepam.

The other potential drug particularly in the treatment of grand mal status is Phenytoin given intravenously in a dosage of 500 to 1000 mg in adults also per slow intravenous injection. It is important in case of Diazepam, Clonazepam and Phenytoin to inject as slowly as possible. As a first choice it is better to start with Benzodiazepam and in the event of uncontrolled seizures to switch on to Phenytoin. If the seizures are not controlled with one drug, there is not much use in giving the same drug in larger doses. A second drug or even a third drug may be used to control seizures. One of the drugs which can be given per intramuscular injection is Midazolam which is effective in status epilepticus of different forms, if given as the first drug.

A status epilepticus with repeated grand mal seizures without recovery of consciousness can cause several complications leading to anoxia, hypoglycemia, pyrexia which may lead to irreversible brain damage and death if not treated immediately. In case of children a severe grand mal status even when controlled after adequate treatment,
may led to certain degree of permanent brain damage, which again can complicate an existing epilepsy. During the emergency treatment of a status epilepticus with grand mal seizures, the danger of subsequent complications must be considered and handled accordingly. The patient should receive according to necessity intravenous infusions of glucose and saline under intensive observation. At least 24 hours of observation even after the recession of status epilepticus is generally necessary. Every attempt should be made to evaluate the factors which have led to a status epilepticus. In case of patients with epilepsy the main cause is sudden withdrawal of drugs which can be assessed through the monitoring of drug serum concentration. Any infection before or consequent to status epilepticus must be evaluated and treated accordingly. The use of oxygen is generally not indicated in case of status epilepticus as it may lead to provocation of seizures. An EEG examination during a status of grand mal seizures is generally not possible and also is of not much help. However, a postictal EEG is helpful for the evaluation of etiology and classification of epilepsy. In spite of all the facilities of present emergency medical treatment, some cases of status epilepticus with repeated grand mal seizures are difficult to control with the conventional intravenous treatment of Diazepam, Phenytoin or Sodium valproate, particularly such cases which are the result of severe brain pathology. In such cases the last possibility is to treat them with a barbiturate narcosis.

**AMBULATORY TREATMENT OF EPILEPSY PATIENTS**

Epilepsy is a paroxysmal disorder, which can occur in any person at any age group irrespective of intellectual condition.
and social situation. There are however two main groups of patients from the point of view of the psychosocial aspects. The majority of people who get epileptic seizures have no brain damage and no intellectual deficits. As such these people are well integrated in their social, professional and family set up. The other group, a smaller group of people, who get epilepsy, particularly in the early years of life may have different degrees of brain damage, which prevent them from a proper professional and social integration. The first larger group of people react generally well to drug treatment and become free of seizures under mono- or combination therapy. Approximately 70-80% of the epilepsy patients belong to this group, out of which in nearly half of the people antiepileptic drugs can be withdrawn at some stage of life. These people can be then considered as cured of epilepsy, as they remain free of seizures even without medication. It is possible, that such patients remain free of seizures the whole life without medication, or they may get an isolated seizure sometimes due to some provocations as also in the case of general population. The situation is much different in the case of people with brain damage. In spite of advances in the drug treatment these people cannot be made free of seizures even with a polytherapy because of the underlying brain damage. Generally such patients during childhood or later in adult life have epileptic syndromes with different kinds of seizures, both of the generalized and partial forms. The most common example for such patients is the Lennox-Gastaut syndrome which begins in childhood and may be carried further into adult life. The other group of adult patients who have therapy-refractory epilepsies of the temporal lobe have generally a mesial temporal sclerosis
which makes the epilepsy resistant to drug treatment. However, these patients have generally normal intelligence and are more or less integrated in their professional and family spheres.

The management of these heterogeneous groups of epilepsy patients under a single set up in a neurological practice, seizure clinics in the neurological centres or pediatric hospitals is not a easy matter. As epilepsy is a common neurological disorder, probably the second most common after neurovascular disorders, most of the practising neurologists have special experience in handling epilepsy patients. The specialized knowledge for neurologists would mean sufficient clinical experience in the classification of epileptic seizures, epilepsies and epileptic syndromes with additional training in electroencephalography and pharmacology. Along with neurologists, pediatricians with experience in neuropediatry particularly in epileptology are competent to treat children also with different kinds of epileptic syndromes.

**MANAGEMENT OF EPILEPSY PATIENTS UNDER VARIOUS CONDITIONS**

There are several possibilities for epilepsy management in industrially developed countries but the facilities are increasing also in the developing countries. In some of the European countries such as United Kingdom, Germany, Netherlands, Scandinavian countries and Switzerland there are traditional epilepsy centers which were started more than hundred years ago. These centers have developed into modern epilepsy hospitals with facilities for diagnosis and treatment, as also for long-term care and rehabilitation. The
急性医院在这些中心的建立类似于癫痫单位在教学医院，然而与传统癫痫中心多学科设施用于管理具有各种心理社会问题的患者的区别在于，这些中心起初更像照顾和管理癫痫患者的殖民地，当时几乎不可能有效控制癫痫发作。不仅有用药难治性癫痫如Lennox-Gastaut综合征和其它类型继发性全面性癫痫以及各种程度的脑损伤的患者，因为社会原因在这些中心停留了更长的时间。情况发生了很大变化，随着现代抗癫痫药物的可用性，这些中心的患者占用率在过去三十年中显著减少。然而，大多数的中心已经适应了癫痫学条件的变化（Rai 1990）。

在组织一个特殊的单位用于诊断和治疗癫痫时，存在一些心理社会问题。一方面这样的专门单位应该能够用常规EEG、带测传和视频监测的EEG、现代实验室设施及其它神经生理学领域设施对癫痫及相关的障碍进行正确的诊断。另一方面，这些单位也应当专业化于各种类型的癫痫综合征，包括儿童和成年人的智力功能差异。因此，在特殊的癫痫单位，患者可以是正常人。

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intelligent and well integrated in their professional and social spheres, as also with such patients with various degrees of mental retardation and disabilities.

In a common ambulatory unit, the experience could be uneasy and anxious for a patient who comes for a first diagnosis when he has to share the unit with severely disabled people who also have the same disease. Such confrontation is unavoidable in larger epilepsy units belonging to a neurological department, pediatric section or an epilepsy center. Ethically and medicolegally it is not possible to divide the units according to the intellectual status of patients but the facilities should be directed for the scientific evaluation and management of the clinical condition epilepsy. However, one has to accept the anxiety of the patients who were never confronted with similar situations and offer them counselling if needed.

The majority of epilepsy patients are being treated today by neurologists, pediatricians and general practitioners. Whatever be the set up of an epilepsy unit a thorough counselling of the patients and the dependents is always necessary. Before starting a drug treatment the pro’s and con’s of short or long range drug treatment must be carefully considered by the treating physician and should be discussed with the patients. The patient should be made clear why he or she has to take medicine also in the interval during seizures and what are the clinical and social consequences in the event of not taking the medication properly. It must be noted that in principle every drug treatment against epilepsy other than in the case of ictal conditions such as status epilepticus, is of a preventive nature. One assumes the possibility of further seizures
without medication and tries to give the drug to prevent the recurrence of seizures. Many patients, even educated ones, have some difficulty in understanding the necessity of long range medication if the seizures are occurring in long intervals of months only. There are patients with different mental make up, as also is the case in the general population. Some of the patients are very careful and would not like to discontinue the medication even if they remain free of seizures over years. The others, the larger group of patients, want to reduce the drug as early as possible. These individual aspects must be considered under a long range drug treatment.

The side effects occurring due to medication cannot be underestimated. Some effective drugs such as Carbamazepine can create several side effects if a larger dose is introduced in the beginning. It is useful to begin with a small dosage, for example, 50-100 mg Carbamazepine or 150-300 mg Valproate or 50 mg of Lamotrigine as the case may be, and to increase the dosage in intervals of 3-4 days until the optimal dosage is reached. This improves considerably the patient compliance and gives time for clinical observation regarding the effectiveness and side effects. Irrespective of the drug given in the initial stages, fairly frequent clinical controls followed by some laboratory examinations are necessary. Depending on the drug introduced it may be necessary to see the patient initially every month for a period of three months. At least one to two blood examinations should be done to rule out hematological or other biochemical side effects. A serum concentration of the drug can be estimated depending upon half-life and steady state earliest in 4-8 weeks after the
optimal dosage has been reached. Similar is the situation concerning EEG examination. In case of generalized epilepsy where spike and waves were registered during the first examination, second EEG may be necessary within a period of 2-3 months. In case of partial epilepsies where interval EEG findings were negative, further EEGs are necessary only depending upon individual variations. In all cases of adult epilepsies particularly of the partial form but also in some generalized epilepsies a neuroradiological examination with Computer tomography or MRI of brain is necessary also in the early stages. In several partial epilepsies of adult life the first symptom of a neoplasm is generally an epileptic seizure, sometimes even before the brain pathology has been properly established.
Surgical Treatment
INTRODUCTION

Surgical treatment of epilepsy is possible in a very small percentage of chronic epilepsy patients mostly in adult life. The epilepsy surgery has been practised almost since about 6–7 decades. The pioneers were Penfield and Jasper at the Montreal Neurological Institute in Canada. Over the last decades many countries world over have specialized units for epilepsy surgery. During the previous years the concept of surgical operation for the treatment of epilepsy was mostly in the form of lobectomy particularly temporal lobectomy. The situation has improved considerably over the years but also has become complicated in the procedure.

Wilder Penfield made pioneer work in the field of epilepsy surgery already during the 1960s by identifying the possible epileptogenic areas in cerebral cortex, which could then be removed in epilepsy patients. However, over the past decades it was found that resection of cortical areas was not the best solution for treating epilepsies arising from limbic system. The animal experiments which showed the phenomena of Kindling did further help for the assessment of epileptogenesis in the deeper structures. With such additional knowledge in the neurophysiology, further operative techniques involving stereotactic methods were developed in human neurosurgery. Improved methods of presurgical assessment were developed as well, in several centers world over. The main purpose of presurgical evaluation is to determine the focus of epileptogenesis in the cortical or deeper structures in patients who have remained drug resistant to all the available antiepileptic drugs. These patients belong to the group of chronic partial epilepsies mostly of temporal lobes or of the deeper
structures. The criteria for the selection of patients should be considered very carefully, in order to avoid further disappointments for the patients and their dependants. In the selection of patients the following clinical aspects must be considered:

- The epilepsy is properly diagnosed clinically and with ictal EEG as a partial form belonging to the broader classification of symptomatic (or cryptogenic) epilepsy
- The epilepsy must be established as therapy-refractory after drug treatment with suitable antiepileptic medication under monotherapy, combination or polytherapy
- The focus of epileptogenesis in the cortical or deeper structures of cerebrum has been established
- The patient has average intelligence to understand the procedure of operation and the possible complications due to operation
- The reduction of seizures after the neurosurgery would help the patient for better psychosocial integration
- The epilepsy surgery does not cause the patient further serious neurological or neuropsychological deficits
- The focus of epileptogenesis is preferably not situated in the dominant cerebral hemisphere.

As an invasive method the application of neurosurgery in the treatment of epilepsy must be very carefully considered from different medical and medico-social aspects. Only in about 5% of the patients having epilepsy a neurosurgical treatment is possible. As such the patient must undergo a thorough evaluation through clinical neurology, electroencephalography, neuroradiology and neuropsychology. An ideal patient for consideration of neurosurgery should have partial epilepsy with disabling
complex partial seizures which are resistance to such drugs as Carbamazepine, Oxcarbazepine, Lamotrigine, Topiramat and further preparations such as Phenytoin, Levetiracetam and Valproate. The patient must have an average education and is professionally integrated. The patient finds the epileptic seizures as disabling him/her in professional and social life. The focus of epileptogenesis has been established through long-term EEG- and video-monitoring. If the focus has not been established clearly, then the patient has to undergo invasive methods with depth electrodes. The hemispheric dominance has been established through neuropsychological tests and WADA-test. The patient has undergone a counselling through the neurologists, if necessary also through neurosurgeons and neuropsychologists. The patient has agreed to undergo the operation, even in the event of operation not becoming successful for the complete control of seizures.

**CLINICAL OBSERVATION AND HISTORY-TAKING FOR EPILEPSY SURGERY**

In preparing a patient for epilepsy surgery, the physician has to get convinced that the patient needs surgical treatment for the control of therapy-refractory seizures. During the history-taking it is necessary to classify the seizures and the epilepsy according to the international classification of epileptic seizures and epilepsies. Seizure being mentioned as grand mal or petit mal or psychomotor is totally insufficient for a proper classification. The patient must be encouraged to describe repeatedly about his experience before a seizure occurs. Many patients mention the occurrence of aura as a distinct phenomena of abnormal
subjective experience located in the head or in the epigastric region. It is necessary to understand whether during the aura there was an impairment of consciousness or the patient realized most of what happened. Other experiences involving motor symptoms, special sensory and somatosensory symptoms, as well as psychomotor symptoms with or without impairment of consciousness must be evaluated. Already at the clinical stages attempts should be made to assess the origin of seizures in regard to cerebral lateralization.

The clinical examination must be followed by EEG studies. Quite often an epileptogenic focus recorded in the ictal and interval EEG is not the location in the deeper structures of the brain. This is particularly the case in case of partial seizures arising in the limbic system. There may be a lateralization of focus in surface EEG, but the location of epileptogenic activity may be in the contralateral hemisphere. This happens mostly in patients who have alternating epileptogenic focus in interval EEG. The EEG examination should include the recording of one or more epileptic seizures, which must be then verified with the patient and dependents to correlate the seizure experience of the patient. The ictal EEG may show the origin of epileptic activity in a different region than generally recorded through interval EEG. These patients need further examinations through depth electrodes implanted through stereo tactic methods. With the improvement in monitoring surface EEG coupled with video-recording, several patients may satisfy the requirements for neurosurgery even without depth recording. However in such patients who do not have very frequent seizures or who have seizures in clusters with
periods of seizure freedom, the seizures may have to be activated during long-term-monitoring by withdrawal of drugs. Such a procedure must be carried out carefully in view of not provoking a status epilepticus. Any intensive monitoring either with surface recording or depth EEG must be done under a clinical set up, so that any emergency can be handled without delay. A long-term-monitoring of the patients to register an ictal activity must include such measures as EEG recording during sleep, sleep deprivation or with such methods which usually provoke the seizures in a particular patient. Provoking seizures with drugs has not been considered to be a suitable method as shown by Wieser et al 1979, who described that chemically induced seizures do not have the same correlation to spontaneously occurring seizures and accordingly may lead to a false finding. Alternatively Wieser et al 1985 showed good results with recording seizures through electrodes inserted in the foramen ovale.

A very important aspect of recording an epileptogenic focus in EEG is to make sure that the focus actually correlates to the origin of seizure. In a patient who is suitable for epilepsy surgery the seizure should originate from one single focus possibly from the non-dominant hemisphere. If there are two separate epileptogenic foci in both hemispheres or a “mirror focus”, the patient is generally unsuitable for surgery. In such patients it is possible that after the resection of epileptogenic tissues, the mirror focus may be involved in the production of further seizures. Attempts must be made to correlate the clinical phenomena of seizures with the ictal findings in electroencephalography recorded with surface or depth electrodes. In addition to this, information must be
obtained through neuroradiological methods such as MRI, SPECT and PET.

Methods of Epilepsy Surgery

During the previous years as already mentioned, epilepsy surgery was mostly restricted to temporal lobectomy in case of therapy-refractory temporal lobe epilepsies. With the advancement of diagnostic and operative techniques, today there are several other methods of surgery for epileptic seizures. Even though epilepsy surgery is a complicated, time consuming and expensive method, it can, however, considerably help such patients where the indication has been properly estimated. The statistics available from different major centres worldwide show that in successful cases almost 70% of patients remain free of seizures, which was otherwise not possible through any kind of drug treatment. Proper preparation of a patient for epilepsy surgery must be done through a team work of specialists namely neurologists, neurosurgeons, neurophysiologists and neuropsychologists. It may be necessary to treat a patient for a period of at least 1 – 2 years with conservative drug treatment before a decision is made for the consideration of epilepsy surgery.

The information given in the following pages about the operative methods in epilepsy surgery is primarily a global orientation of the presently practiced methods but without going into the details of operative procedure. For many years and even now, temporal lobectomy seems to be the most practiced neurosurgery in epilepsy. In rare cases of epilepsia partialis continua almost complete lobectomy was done particularly the method followed by Rasmussen and
associates at the Montreal Centre for Neurosurgery. Over the past decades however newer methods have been introduced in epilepsy surgery particularly the selective resections of amygdala and hippocampus. In addition further methods of partial lobectomy, functional hemispherectomy, multiple lobectomy and colosiotomy have been practiced. The most common indication in chronic temporal lobe epilepsies is a mesial temporal sclerosis. This brain lesion consists of a loss of neurons in the sector of hippocampus. These lesions could be unilateral or may be predominantly one-sided and may involve the structures of hippocampus and amygdala.

**The Selective Amygdala-Hippocampectomy**

This method is being practiced in many neurosurgical centers for the treatment of chronic mesial temporal lobe epilepsies. It has the advantages of removing only the pathological lesions with minimum injury to the neighboring tissues of brain. These operations are conducted by experienced neurosurgeons after careful preparation of the patient with long-term EEG monitoring using surface and depth electrodes. The selective amygdala-hippocampectomy has the advantage of avoiding neuropsychological deficits after the operation, with most of the patients having considerably less memory and concentration difficulties. The chances of patients becoming free of seizures have been mentioned to be as good as 70%. Yasargil in Zurich (Wieser & Yasargil 1982) adopted amygdala and hippocampectomy using a microsurgical technique in such patients who had unilateral epileptogenic activity of the medial temporal structures. These operations
were done after presurgical evaluation of the patients through depth EEG recordings.

Stereotactic procedures are known in epilepsy surgery since several decades. Narabayashi reported stereotactic amygdalactomy in children and adults with considerable success (Narabayashi & Shima 1973, Narabayashi 1979). Balasubramanian & Kanaka (1976) reported stereotactic operations of limbic lesions with seizure freedom in over 50% of patients.

Other Kinds of Operations
Resection of partial or total temporal lobes as well as partial (even total) hemispherectomy has been used in the epilepsy surgery also for a fairly long time. Such operations are necessary in serious cases where more cortical areas are involved in the epileptogenesis in the temporal lobes, in the limbic system or in other areas. To this group of operations belong such techniques as isolated lobectomy and multiple lobectomies in different regions of the brain. With these techniques one is also trying to block the pathways which lead to formation of epileptogenic activity. About 50 – 60% success in relation to freedom of seizures have been reported through such operative techniques. Another less commonly practiced method is the colosiotomy to dissociate the connection between the two hemispheres for the blocking and reducing the epileptogenesis. This method is practiced mostly in severe cases of therapy-refractory syndromes such as Lennox-Gastaut syndrome.

Major Cortical Resections
With the advance in epilepsy surgery, the necessity for major cortical resections has reduced considerably. However,
such surgery is performed in certain difficult cases in epilepsy, both in adults and children, including such patients who have mental retardation. The methods involved are partial resection of frontal lobe and sometimes parietal lobe. There are other rare cases of subtotal or total hemispherectomy, as has been practiced in the Montreal Neurological Institute by Rasmussen and associates. The indication for subtotal resection of frontal lobe is similar, as in the case of temporal lobes but much more difficult to decide for a operation. A further difficulty arises because many patients may have bilateral focus in the frontallobes or in the fronto basal structures which factor must be carefully evaluated. From the studies of Rasmussen (1975) the results of partial frontal lobectomy are less favorable than in the case of temporal lobe resections.

The indication for major resections involving subtotal or total hemispherectomy is even rarer than lobectomy. The patients who are selected for this group have intractable epilepsies associated with hemiplegia and with or without mental retardation. One of the main indication for such a surgery is the severe form of continues partialis epilepsy of the type of Kozhevnikov. These patients cannot be treated with the available antiepileptic drugs, also not through parenteral routes. Very often they need barbiturate narcosis just to help them to be free of seizures for a short time. Such patients may benefit from operative procedures as the partial or total hemispherectomy with significant reduction of seizures and improvement of their psycho-motoric functions.

In conclusion the indications for epilepsy surgery can only be partly planned in a neurological practice, even when the concerned neurologist has advanced knowledge in epileptology. The preparation of the patient and dependents
including further investigations may have to be carried out in a specialized unit for long-term-monitoring with newest methods in electroencephalography. This unit has to work in close collaboration with the neurosurgeons and further multidisciplinary staff. With the availability of present range of antiepileptic drugs, a considerable freedom of seizures can be reached even in the case of partial epilepsies with complex partial seizures or frontal lobe seizures, which were earlier totally therapy-resistant. A judgement has to be made about the psychosocial necessity of the patient involving complete or partial freedom of seizures. If a quality of life is maintained with freedom of grand mal and complex partial seizures with drug therapy, one should be careful in attempting invasive methods of epilepsy surgery. On the other hand if a therapy-resistance is established in spite of intensive medication, the patient may be considered for epilepsy surgery for all-round improvement of medico-social situation. In such cases it is undesirable to wait for many years, but to evaluate the indication for the performance of epilepsy surgery. However, this procedure must be carried out in close collaboration with the patients and their dependents.

**Vagus Nerve Stimulation**

One of the new methods in the surgical treatment of epilepsy is the vagus nerve stimulation. In this partly surgical procedure a special shunt connected to the vagus nerve is attached to the left side of neck, which again is in connection with a battery implanted in the sternal region. Through this battery the vagus nerve is stimulated from time to time. This
method is indicated in patients with therapy-refractory epilepsies, who are not suitable candidates for a more conventional surgical operation such as amygdala hippocampectomy.
CHAPTER 10

Complementary Methods of Treatment
INTRODUCTION

Even though almost 70-80% of patients with epilepsy can be made free of seizures with the available antiepileptic drugs, several patients in course of their illness seek other methods of treatment. The main reasons are that some patients have psychological problems in taking antiepileptic drugs continuously during interval between the seizures. Others have problems with the side effects associated with an antiepileptic medication. Still another group of patients have difficulty to accept the diagnosis of epilepsy and the necessity of a long range medication. In epilepsies which begin in adult life, the patients have in general to change certain aspects of their lifestyle. This involves mainly keeping regular hours of sleep, reducing alcohol intake and avoiding excessive stress, mental and physical. Most of the patients seem to have no difficulty in changing their lifestyle, but a minority persists in continuing their previous way of living. Getting the first diagnosis of epilepsy is for many patients a shocking experience, partly because of the lack of knowledge involving epilepsy and partly because of the prejudice associated with this neurological condition.

Even though much information is available through thousands of scientific studies involving the standard antiepileptic drugs, there is very little information regarding the advantages or disadvantages involved in the practice of complementary methods for the treatment of epilepsy. However, complementary medicine and lifestyle methods have become popular over the last 2-3 decades worldwide. The common methods practiced are the following:

- Traditional Chinese medicine including acupuncture
- Homeopathy
• Ayurveda
• Phytotherapy
• Bio-feedback
• Other methods

In the medical management of people with epilepsy, there are primarily two aspects. As an epileptic seizure is the main symptom of epilepsy, attempts should be made to control the seizures even when the etiology is not clearly known. This is being done by the use of standard antiepileptic drugs based on over half a century of fundamental and clinical research. As has been described elsewhere in this book, the seizure classification is important for selecting the drug of choice. In case of alternative methods we are somewhat in the darkness regarding the possibility of treating epileptic seizures. It can be inferred that certain herbal preparations may be effective in controlling seizures but there are no clinical studies to help us for selecting a drug. Moreover there are problems involving medico-social and medicolegal aspects, when we have to select an unconventional method for treating epilepsy. As a paroxysmal disorder epileptic seizure is an unpredictable symptom which may occur under variable circumstances.

After the diagnosis of epilepsy on the basis of clinical judgement and EEG examination, a single antiepileptic drug is introduced for the treatment. If the patient remains free of seizures under this drug, then there is no question of changing the drug or treating the patient with other alternative methods. With the freedom of seizures the patients acquire security of life including in such conditions as driving and working. Accordingly the drug cannot be changed without proper reasoning, as any change may lead...
to withdrawal seizures or the occurrence of further seizures. Such a condition would totally imbalance the psychosocial stability of the patient. In other cases where a patient does not get seizure freedom on the first drug, the usual clinical practice is to change the drug depending on second and third priorities, also under monotherapy. In the failure of such a monotherapy, it is the conventional practice to try a combination of two drugs which can make many patients free of seizures. The eventual use of an alternative drug from phytotherapy can be tried only in case of therapy-refractory epilepsies. Even then we have no information as to which drug from the phytotherapy may be combined with standard antiepileptic drugs. The experiences available from such systems as TCM, Homeopathy, Ayurveda are restricted only for the treatment of isolated epileptic seizures, which do not give us sufficient information for long range treatment of epilepsy.

At the present stage of advancement in epileptology, we know that majority of patients remain free of seizures under standard antiepileptic drugs. The mechanism of seizure freedom can be evaluated at least partly depending upon the clinical, EEG and laboratory-findings, which may be correlated to the effectiveness of a given antiepileptic medication. In case of therapy-refractory epilepsies such as temporal lobe or frontal lobe epilepsies and childhood syndromes the reasons for therapy-resistance can also be understood. It is therefore not possible to substitute a standard medication through a clinically not standardized phytotherapy in the treatment of any kind of epilepsies. However if the patients strongly desire an alternative treatment, in case of therapy-refractory epilepsies after
discussion with adult patients or with the parents of children, an additional medication through some suitable phytotherapy may be possible. The physician initiating such a phytotherapy must be in a position to justify the reasons for introducing a particular drug from phytopharmacy. Even though patients have the freedom to use whatever drug or method for their health benefits, the physician should be able to justify the necessity of treatment given, conventional or unconventional. It is therefore not possible for a physician to treat epilepsy exclusively on phytotherapy or with other complementary methods, as there are no studies available about such drugs and methods of treatment.

The situation however is different regarding the change of lifestyle through several methods of complementary medicine. Lifestyle leading to self discipline in such daily activities as sleep regulation, diet, alcohol intake and stress management is useful for every patient with epilepsy. Like any other individual, an epilepsy patient must be encouraged to lead a healthy life regarding nutrition, physical and mental training. Many patients have difficulties in accepting an epilepsy and accordingly they develop a secondary neurosis. For such people practices such as yoga, meditation and autogenes training are useful. The impact of social prejudice on a person with epilepsy can be damaging in all cultures. Psychological therapies may be useful in such situations. As prejudices cannot be changed, it is necessary for the patients to cope up with this situation through the help of psychological therapy. A special mention has to be made in case of yoga practices such as pranayama. If not practiced properly, pranayama
can lead to hyperventilation which might have negative effect in people with epilepsy leading to provocation of seizures. However, a correct practice of yoga and related methods may be useful for all people with epilepsy. In matter of nutrition no special diet is necessary, the only restriction being the over consumption of alcohol. Even in the matter of alcohol consumption and provocation of epilepsy, there are not sufficient studies to give clear information. It is known that overuse of alcohol will provoke seizures particularly in the withdrawal phase. Even though a clear guidance in this respect is not possible, it seems better for people with epilepsy to avoid alcohol or to restrict the quantity to one glass of Bier, wine or one small hard drink a day.
Chapter 11

Psychosocial Aspects of Epilepsy
INTRODUCTION

Even though epilepsy is clearly a neurological disease, the patients are often confronted with other medical specialties particularly psychiatry. Epileptic seizures originate in the brain with or without traceable brain pathology. In some patients an epileptic seizure may be the symptom of a severe brain damage or disease; in others the brain may be completely normal between the seizures. Epilepsy, particularly the chronic ones may change certain personality trends in a patient. In the medical literature on epilepsy from the antic until the beginning of modern neurology, much has been mentioned about the personality changes seen in people with epilepsy. Description of such personality changes have been made also in the general literature such as from Dostoevsky’s “Idiot”. In many situations since the antic epilepsy has been associated with “genius and madness”. Whereas as a genius always had a proper place in the society, the common person with epilepsy suffered his or her reputation because of this illness. This prejudice has lasted until today almost in all the cultures. Epidemiological studies carried out in different countries have shown that a certain percentage of general population even in the twentieth century lacked information about the nature of epilepsy as a neurological disease. These studies also show that some people have difficulty to differentiate epilepsy from real psychiatric diseases such as schizophrenia and psychosis. The others are simply intolerant to any kind of disease leading to disability mental or physical. Some of the studies show that people in the general population who are intolerant to other races or cultures, are also intolerant to people with epilepsy.
The earlier textbooks on neurology and psychiatry mention about epileptic personality disorders and epilepsy psychosis. The development in neurophysiology and neuroradiology over the past 5-6 decades has contributed considerably to clarify the situation involving the neuropsychological and neuropsychiatric aspects in patients with epilepsy. As a chronic illness, one can understand that epilepsy may lead to some complications. This is similar as in case of other chronic disease such as diabetes, rheumatic disease, asthma, diseases of heart and circulation, etc. A patient with uncontrolled diabetes may develop over the years such complications as heart disease, eye troubles or neuropathic problems. Similar is the case with other chronic diseases which begin around mid-life. Most of these patients do not suffer from social prejudice, even though their health problems are of considerably severe nature than of those people with epilepsy. In clinical practice, one sees that even patients with Parkinson syndrome face less prejudice in the society than those with epilepsy. The reasons may be that Parkinson syndrome begins generally after midlife where some kind of social tolerance may be expected. The intolerance against people with epilepsy seems to be associated with some kind of suspected mental disability. Disability is a phenomena which is not properly defined and as such seems to cause fear and anxiety in the people who witness disabled people which consequently lead to refusal, even though as high as 8-9% of the general population worldwide seems to have some kind of “disability” mental, physical or age related dependency to others.

In case of people with epilepsy there are some other clinical factors. The sight of a sudden epileptic seizure in
the form of grand mal may lead to anxiety and helplessness among people who witness the seizure. A patient with complex partial seizures can sometimes walk around with automatisms in the way of a robot causing even more anxiety among people who witness him. Such phenomena can happen sometimes also as a postictal “clouded state” where the patient is not fully conscious and may tend to show unusual automatisms. Further a certain percentage of people with epilepsy particularly with childhood syndromes have concomitant brain damage or brain diseases leading to mental retardation. These are handicaps, however, only in a small percentage of the people with epilepsy which may however be the cause for prejudice under the general population.

From the subjective side, the major problem people with epilepsy have is in the unpredictability of seizures. Many patients during the clinical consultations mention this aspect as a main problem, living in constant fear of getting an epileptic attack at any time of day or night. Patients mention with agony how they awaken after an epileptic seizure in disorientation, not knowing what has happened to them or where they are. A dynamic business man who was getting occasional grand mal seizures of once or twice a year only at night, mentioned about his totally helpless condition after a grand mal seizure in a hotel room in a different country. He had gone on a business tour and in the previous evening had taken several alcoholic drinks with this partners which probably provoked a severe grand mal seizures early morning still in sleep. For nearly 15-20 minutes or longer after the seizure he was partly conscious but without orientation in respect of place and time.
Amnesia after grand mal and complex partial seizures is a common phenomena experienced by most of the patients. Considering this aspect it is necessary for a physician to analyse the psychosocial aspects of epilepsy both from the subjective situation of patients as well as from the objective social surroundings. Some major problems involving the psychosocial aspects among children and adults with epilepsy are as follows:

1. Schooling
2. Education
3. Job, promotion at work
4. Driving licence
5. Social contacts
6. Partnership, marriage
7. Child bearing
8. Self-confidence

SCHOOLING

Broadly there are two kinds of epilepsies which affect children around school age. The serious forms of epileptic syndromes generally start before the school age, mostly within the first three years of life. These epilepsies are caused by serious brain pathology with or without additional hereditary factors. Epileptic syndromes such as West syndrome, Lennox-Gastaut syndrome and other forms of epileptic encephalopathies begin at this early age group. The children have serious therapy-refractory epilepsies with frequent drop seizures, myoclonic astatic seizures and also grand mal seizures. There is an underlying brain damage or metabolic disease which is responsible for the epilepsy. The children have handicaps on the one hand because of
learning difficulties due to brain damage but on the other hand also because of frequent epileptic seizures which cause further disability. In addition they have problems due to complicated antiepileptic medication. These children are unable to go to normal schools and therefore require special remedial schooling facilities. However, every attempt must be made to individually evaluate the capabilities of such a child for adequate schooling. Some children improve during the course of treatment and may be able to join better schools. But a normal schooling is on the whole not possible for children with severe epileptic encephalopathies.

The second group of children where the epilepsy begins, around school age between four and six years, has generally no signs of brain damage. These epilepsies belong to the idiopathic forms often with genetic predisposition and are generally of a benign nature. The children may have absences but have no learning difficulties or reduced intelligence. Some children may have mild neuropsychological deficits also due to frequent absences or sometimes due to wrong medication. These children have however no handicaps and can go to normal schools. Some of them may have absences in the school, which factor should be discussed with the teachers and school authorities. Even in such cases an individual assessment of the child is necessary before schooling and during the course of further schooling. The problems can occur due to some prejudice associated with epilepsies and intolerance showed by other children and teachers. Epidemiological studies show that even in western countries some parents are reluctant to send their children to the same class where children with epilepsy are being taught. These aspects should be handled with the
concerned authorities to improve awareness about the mostly benign nature of epilepsy.

In the event of schooling difficulties it is necessary to test children with epilepsy for any kind of possible neuropsychological deficits. Depending upon the results the treating physician should hold counseling with the parents and the teachers as well as with the children themselves. It must be made clear that not epilepsy as a single phenomena which creates learning or behavior difficulties if any, but an association of several other factors such as cerebral, drugs and social impact due to negative reaction from the environment. On the other hand it should be accepted that the children with epilepsy whether of benign or serious forms can face some difficulties during the schooling, which needs additional management.

The figures available from different epidemiological studies about children attending school in different countries are somewhat variable. It is believed that between five and eight children for every 1,000 children in the school age have epilepsy. According to studies of Ross and Peckham (1983) 67% of the children with epilepsy were attending normal schools at the age of eleven in United Kingdom. This figure reduced to 58% at the age of fifteen when the children were attending the secondary school education. The performance of the children at school depends on several factors mainly cerebral, seizures and the drugs. For children in the school going age it is advisable not to prescribe such drugs as Phenobarbitone and Phenytin. Both drugs even though having potential antiepileptic properties, are known to create learning difficulties. It is better to use the later generation antiepileptic
drugs such as Oxcarbazepine, Lamotrigine and Valproate. Attempt should be made as far as possible to treat children under monotherapy with one of these drugs or make careful combination of two drugs depending upon the classification of seizures. If the seizure freedom is reached with lower dosage of drugs, it is not necessary to increase the dosage for improving the EEG or to bring the serum concentration of drugs to the optimal level. In some cases of generalized epilepsies where children have often spike wave complexes in EEG, the absences may correlate to the EEG findings. In such cases an individual assessment is needed with neuropsychological tests to find out the negative influence of spike wave activity on learning and behavior of the child.

In case of remedial schooling the situation is different, as these children have serious forms of epileptic syndromes and need main attention for the control of epileptic seizures even with multiple drugs. Because of the epileptic encephalopathies, these children are rarely in a position to manage even remedial schooling properly. Even in cases of such children, one should try to keep the combination maximum to the extent of three drugs. All children with epilepsy must be encouraged to the normal style of living to the extent possible. Particularly in case of children going to normal school, attempts should be made not to restrict them from such activities as sports, cycling, swimming, etc. However, individual assessment is necessary before advising the parents in view of these activities. There is no doubt that children with frequent epileptic seizures are in the danger of having more accidents in all activities of sport particularly swimming.
Adolescents with epilepsy who have finished normal schooling are generally in a position to continue their professional careers. It is important to advise these youngsters about the kind of professions which are suitable for them. Even in these cases an individual assessment is necessary to evaluate the professional risks involved. Several professions are suitable for people with epilepsy, some are however unsuitable. In case of idiopathic primary generalized epilepsies where the prognosis is good, the professional situations are fairly encouraging and comparable to general population. In other cases of partial or generalized epilepsies where the prognosis of becoming seizures free is uncertain, the professions must be properly selected right from the beginning of education in order to avoid later disappointments. People who tend to get epileptic seizures with a poor long-term prognosis are unsuitable for learning such professions dealing with heavy machines, requiring regular driving or working in higher levels, for example in the field of construction. A counselling of such patients needs an intensive study of their case records in view of short and long-term prognosis of epilepsy, which may have an impact on their social and professional lives.

In spite of several epidemiological studies, no clear data is available about the people with epilepsy who are properly integrated in their professional and social spheres. In a neurological practice with emphasis on epileptology, one comes across people who are well integrated in their professional and family lives if they have remained free of seizures with the diagnoses of benign epilepsies such as primary generalized epilepsy. These people have no
intellectual deficits or neuro-psychological problems so that excepting for the need of intake of antiepileptic medication, they do not differ from the other general population. The situation is somewhat different in case of people who are integrated in the professional and family lives but who tend to get occasional complex partial or simple partial seizures. The psychological problems then arise once an epileptic seizure is noticed in their working place. Several people with partial epilepsies particularly temporal lobe epilepsies also have some neuropsychological deficits because of cerebral dysfunction but also due to the side effects of the long-term antiepileptic drugs. The people who have rare attacks of grand mal seizures in sleep, also seem to be well integrated in their psycho-social field, as they mostly become seizure free under medication. On the whole it must be recognized that people with epilepsy have more problems of integration than, for example, people with other chronic diseases such as diabetes, bronchial asthma or even depression.

It is therefore necessary to advise young people with epilepsy about their selection of proper professional training or studies. Over the last thirty years of practice in epileptology in two industrialized countries namely Switzerland and Germany, the author has come across, several young people who came with the desire of becoming pilots, railway drivers, police men, medical nurses, medical doctors and such other professions. Some professions such as pilot or railway driver are basically unsuitable for people who had epilepsy even if they become free of seizures. The local laws prohibit such people from doing work as a pilot or a train or a bus driver even if a person had only one
epileptic attack in his or her life time. On the other hand professions such as medical nurses and practically all the academic disciplines can be suitable for people with epilepsy depending upon their cognitive abilities and on the basis of their getting free of seizures. It is important to consider some factors before an advice is given regarding a particular profession.

- Classification of the epilepsy with long-term prognosis
- The required antiepileptic drug treatment and the duration of treatment
- Cognitive functioning of the patient
- The personality structure of the patient.

A patient with benign epilepsy of idiopathic generalized form which starts in school age or adolescence has a good prognosis of becoming free of seizures with or without medication. Such patients generally do not have cognitive problems, and they are suitable for most of the professions the exceptions being such ones as pilot or driver of heavy vehicles. If these patients need medication over a period of five to ten years, they can be mostly treated with a monotherapy. In case of juvenile myoclonic epilepsy even though the prognosis of becoming free of seizures is good, the withdrawal of medication may not be possible for many years or even for life time. Even though most of the patients with a JME do not have cognitive problems, the necessity of long range medication mostly on a combination of two drugs must be considered before starting a profession. A further aspect is related to the neuropsychological deficits which many patients of partial epilepsies may have in various degrees. Some of the patients with temporal lobe epilepsies with temporomesial sclerosis may be normal intelligent and
in a position to take up several professions depending upon their cognitive performance. Most of them however have some neuropsychological deficits which they compensate with some kind of so called secondary neurosis. These personality problems can give them some difficulties during professional training, studies and during the actual professional activities. This situation is however not much different from the general population who may also have such problems even without epilepsy. However, the people with epilepsy are in a rather difficult situation because of this health problem whereas by the normality of general population such problems may go unnoticed or accepted. It is therefore necessary to advise a young person with epilepsy by a multi-disciplinary team consisting of neurologist, psychologist and social worker. Some of the professions such as working in an office, stores, schools and hospitals are on the whole good professions for a person with epilepsy if the seizure freedom is reached. For some particular people who have photo sensitive epilepsy working long hours on computers is rather unsuitable. Professions where driving is involved as a part of the job, are generally unsuitable. Working on heavy and dangerous machines is also not suitable.

**JOB, PROMOTION AT WORK**

For the majority of people with epilepsy an important question while seeking a new job is to declare the epilepsy or not. It is not customary to mention a health problem while applying for a job, unless specially asked for, as in the case of professions involving risks such as driving heavy vehicles. People for example with diabetes who have to take daily
doses of insulin or others who have to take drugs because of high blood pressure or bronchial asthma do not declare their illness while seeking a job. How does the situation concerning epilepsy become different? The occurrence of an epileptic seizure particularly with loss of consciousness as in case of grand mal or with impaired consciousness as in complex partial seizures, may lead to an uneasy environment where the patient works. It is a situation where the people do not know how to help the patient, or where they feel themselves awkward because of working with such a person who has this health problem. Very few people take the trouble of informing themselves about the real situations involving epilepsy but develop prejudice. Accordingly even if the job performance of a person with epilepsy is above the average level, the people may develop an unfriendly relation to the person. This in turn, can create an environment where the patient may not know how to cop up with the circumstances. Some of them react with aggression and the others with more depressive mood changes. The situation in such cases can be embarrassing if the epilepsy of patient was not declared at the working place.

On the other hand if the patient declares an epilepsy even with detailed mentioning of control of seizures under medication, he or she may be denied the job without giving proper reason for the denial. How should then the attending physician advise the patients regarding the necessity to declare epilepsy or not? There is no definite answer to this question. It is necessary to analyse the individual variations concerning the job, the tendency to epileptic seizures, neuropsychological deficits and the side-effects of medication. In an environment where a patient, for example,
goes to work as a specialist in software or hardware, there is not much problem involved through the occurrence of rare epileptic attacks. In other cases for example where the patient has to serve customers directly as in the case of a bank or other offices, even a single epileptic attack could lead to social consequences.

In dealing with counselling of a patient in respect of job, both the physician and the patient must reach a particular understanding about the need to declare the illness or not. Generally it may be useful to mention the illness in the event of the patient joining a small undertaking as in the case of a family venture. In such a situation an emotional understanding between the employer and the employee may be useful. Depending upon the situation the patient may ask the employer to seek advice of his or her physician. In case of larger organizations where the atmosphere is less familial, it may not be necessary to mention the illness, as in such a condition performance of the individual is more important than the confidence he or she creates in the employer. However there cannot be a general agreement in dealing with this problem but individual solutions should be found from time to time.

Most of the people with epilepsy complain of injustice regarding the promotion at work. It requires a broad minded employer to promote an employee with epilepsy for higher job levels, because of the competition found in many enterprises. Even though the promotion of an individual is based mostly on the merits of his or her performance, the personality of the individual plays a definite role. In evaluation of the personality there are no actual parameters generally available. As such a person with epilepsy, in spite
of good performance and intact personality structure may be left behind for promotion. The qualification of a person for promotion of job is not always based on rational factors but decided also on the basis of empirical and emotional grounds. It is however necessary to evaluate the situations involving each incidence of denial of promotion in job, analysing the reasons for such a denial. The physicians cannot always share the opinion of the patient who may complain that he or she has been denied a promotion because of epilepsy, but must go deeper to find out the reasons for denial and possible solutions.

**DRIVING LICENCE**

One of the most time consuming consultations in a special center for epilepsy, a seizure clinic or a neurological practice with specialization in epileptology, involves the question of driving licence. Acquiring and maintaining a driving licence has become a necessity for adult patients with epilepsy. The law regarding the driving licence for people with epilepsy varies from country to country, even among the industrially developed countries. However during the past decades there seem to be a tendency in most of the Western countries for a more or less standardized regulation of the requirements for a driving licence. In some countries such as India, the laws regulating driving licence for people with epilepsy have remained unchanged for fifty years or longer. A person who had epileptic seizures at some time or other in life, is not eligible for a driving licence. This is the law in theory, but the practice seems to be entirely different. The people who apply for driving licence for example in India have to sign a questionnaire stating whether they had
epileptic seizures or not. It is assumed that even people with uncontrolled epilepsies deny the illness, as otherwise they are not eligible for a driving licence. In spite of the efforts of the Indian Epilepsy Association, the laws have not been relaxed so far.

Even in the Western countries there is no general conformity about the regulations involved in the driving licence for people with epilepsy. However, there seems to be some uniformity in the countries belonging to European Union as also in other European countries such as Switzerland. In Switzerland the recommendations for the regulation of driving licence for epilepsy patients are done by the Swiss League against Epilepsy in collaboration with the Swiss Neurological Society and the Swiss Society for Neurophysiology. The recommendations are generally accepted by the traffic control authorities of federal states (cantons) which then become a part of the law.

The epidemiological studies in countries like Switzerland and Germany have shown that the traffic accidents caused because of an epileptic seizure make only 0.3% of all the accidents which means that only one in 5000 traffic accidents is due to an epileptic seizure, out of which almost 20% accidents happen because of the first occurrence of a seizure in otherwise healthy patients. The majority of traffic accidents occur due to human mistake, alcohol and drug intake or because of other factors. However at least a small number of accidents do occur during epileptic seizures and as such there has to be a regulation for people with epilepsy.

In forming the regulations for driving licence one has to differentiate between lighter vehicles such as motor cars,
motor bikes and much heavier vehicles like transport lorries, buses, which need further professional driving regulations.

**GENERAL REGULATIONS**

1. In the case of an active epilepsy with uncontrolled seizures, with or without medication, a driving licence cannot be granted.

2. The issue of a driving licence is only possible after a minimum of one year of freedom of seizures, with or without medication.

   A relaxation of this time interval is possible under the following conditions:
   - Occurrence of only simple partial seizures without impairment of consciousness and without sensorimotoric phenomena
   - Rare occurrence of seizures only in sleep under observation for over a period of three years
   - Reflex epilepsies which occur only under definite provocations

3. Stringent controls are needed under following conditions:
   - Misuse of alcohol and drugs
   - Reduced patient compliance
   - Seizures occurring because of a progressive cerebral lesion
   - Severe metabolic disturbances which are uncontrolled in spite of medication
   - Excessive tendency to sleep during day with or without drugs

4. After the first occurrence of an provoked seizure even if the epilepsy is diagnosed the issue of a driving licence
is possible after six months, if the other conditions are favorable.

5. After the first occurrence of a provoked seizure due to trauma or operation, the duration of licence withdrawal may reduce to three months.

6. Similar is the regulation in case of good controlled epilepsy with a minimum of two years of seizures freedom. If a seizure residue occurs due to provocation the driving licence can be withdrawn for a period of about three months only.

7. The EEG finding should be compatible for driving, that means the interval EEG should not show active occurrence of longer duration of generalized spike and waves or similar focal findings.

8. In the event of the withdrawal of an antiepileptic medication for any reason, the issue of driving licence should be denied for the entire period of withdrawal of medication as well as for a further period of at least three months. Some individual variations are necessary in such cases depending upon the prognosis of epilepsy, personality structure of the patient including patient compliance. These regulations hold good mostly in the event of driving a motor car for personal purposes. There have to be special considerations if a driving licence has to be issued for driving heavier vehicles and or for professional purposes.

The physician treating a patient with epilepsy must hold efficient counselling in regard to the regulations of issue of a driving licence. It is necessary to explain about the risk involved due to epileptic seizures which is generally unpredictable. The responsibility of holding a driving
licence must be shared by the physician and the patient. The discussions held with the patient must be registered in the case records, which then become a legal document in the event of any litigation. It is, however, important to consider the necessity of driving a vehicle for the patient for his job and private requirements and the risk involved in such a procedure for the general public in the traffic.

It should be obligatory for the patient to inform the occurrence of any epileptic seizure during the period of his holding a driving licence. There should be regulations regarding the intake of alcohol as well as of sleeping hours. Even though it is not possible to prohibit the patient from drinking alcohol, intake of alcohol during driving should be totally avoided. It is also good to mention that driving should be avoided on such days when the patient had excessive sleep deprivation or stress.

The certification of holding a driving licence must be renewed from time to time depending upon the personal and clinical condition of the patient, namely in intervals of six months, one year or two years.

Even though it is not obligatory to consider the interval EEG findings and the drug levels in serum, it is generally useful to carry out these examinations in certain intervals for the evaluation or epilepsy prognosis and patient compliance. The counselling should be held in a relaxed atmosphere creating confidence in the patient. However in difficult patients the regulations should be made clear and there should not be much hesitation to deny the driving licence under unfavorable circumstances.
Special Considerations

The above mentioned regulations apply for majority people with epilepsy who use a motor car for personal needs. In case of professional drivers for transport lorries, buses and taxis, the regulations are individual. Generally a very good prognosis of epilepsy as well as a minimum period of five years of seizure freedom under medication or without medication is necessary to reissue a driving licence for such patients, if they were already holding a driving licence. For new cases such licence cannot be granted under normal conditions.

Further in case of professional driving licence for larger personal transportation of people with such vehicles as buses or tram or railway, driving licence cannot be granted after an epilepsy is diagnosed, as the risk involved is very high. Special consideration could be done only under individual evaluation and after minimum five years of freedom of seizures. In countries like Switzerland driving licence cannot be issued for aeroplane pilots, railway drivers and drivers of public transportation such as tram or bus, once an epileptic seizure has been diagnosed.

SOCIAL CONTACTS

Problems arising out of reduced social contacts are not specific for people with epilepsy only. However, situations may arise right from school days because of over protection by the parents at home and somewhat rejection from the school mates due to epileptic seizures. These children and young adults have to compensate this problem in their own way. They may develop a secondary neurosis in the way of
an inferiority complex. Several patients develop extreme sensitiveness and avoid social contacts; others may develop a sense of over confidence and even idealize their epilepsies. Both these aspects may have impact on the social contacts and lead to some isolation. In such situations the occurrence of seizures, neuropsychological deficits and the side effects of medication play a role in the personality development which then eventually leads to disturbed social contacts. Epidemiological studies show that the incidence of depression and mood changes are somewhat increased in people with epilepsy when compared to the general population. Depending upon their cognitive abilities many people with epilepsy however find proper compensation when they reach adult life. For younger people avoiding alcoholic drinks or driving a vehicle may create problems leading to reduced social contacts. This in turn may have consequences in their psychosocial integration, also in respect of finding a proper partner and a job.

These problems seem to be less pronounced in people who get epilepsy in adult life, as they are already under proper integration in respect of family and professional lives. The illness seems to be then accepted in the family and profession as in the case of any other illness which may begin in midlife or later. Counselling wherever required should be individual, taking note of the impact of epilepsy on psychosocial problems. Corrections can be made in matter of medication to ensure better seizure freedom and lesser sedation and other side effects through medication. Counselling based on supportive psycho-therapy is useful in most of the cases.
People who get epilepsy during adolescence or earlier, do have some problems in getting a proper partner and getting married. During the nineteen fifties when the epileptic seizures were poorly controlled through antiepileptic drugs and when the drugs had often side effects, much was written about the personality changes in people with epilepsy. There was often mention of organic personality changes and even of “epileptic psychosis”. This situation has changed for better during the past decades with the advancement of drug treatment and with the better understanding of epilepsy as a cerebral disease. Clinically one does come across certain personality changes in some percentage people with epilepsy even today, however in a much milder form than described in the earlier literature. The frequent occurrence of seizures may lead to some organic personality changes over a period of several years in the way of psychomotor slowing, reduced flexibility, cognitive and affective disturbances. Severe epilepsies with uncontrolled seizures need also generally a much higher medication which results again in side effects. Various studies have shown that people with temporal lobe epilepsies may have sexual disturbances in the way of a reduced libido or hyper sexuality. Some of these problems may even today be associated with side effects of the medication.

These factors may lead to difficulties in finding a proper partner and developing a long-term relationship. However, the majority of people with epilepsy, who are under controlled seizures, find partners and settle down in married life. It is important to mention here that the declaration of epilepsy in a personal relationship is very useful and even
necessary to maintain confidence in the partner. In case of young people who enter into partnership or marriage, it is also necessary for the patients to make clear about the nature of epileptic seizures and the methods adopted to control seizures for example in the way of medication, as well as any action the partner has to undertake during the occurrence of a seizure. In patients who get grand mal seizures with total loss of consciousness, it is the partner who realizes the total seizure and the anxiety associated with this situation as well as the helplessness during a seizure. The patients have no subjective experience of a grand mal seizure other than a feeling of embarrassment during the phase of awakening. Similar is the situation in respect of complex partial seizures with impairment of consciousness. It is known from different cases that during the discussion with a partner or television seeing, the patient with a complex partial seizure may suddenly stand up, move with automatisms around like a robot. If one is smoking a cigarette, for example, may go threateningly near the partner or other persons. Such patients may also show fearful staring during a seizure which may cause anxiety for the partner. In some cases the partner may live in constant anxiety that the patient of epilepsy may suddenly die during an attack and he or she may have to stay completely helpless. Counselling of partners is therefore very useful in all these situations. Further they should be encouraged to read literature about epilepsy or see video films of epileptic seizures for general information. However from clinical experience and from the studies available, the rate of divorce among people with epilepsy does not seem to be higher than it is the case in the general population.
The situation for women patients in child bearing age is, somewhat a difficult matter and must be properly considered before the onset of pregnancy. There are two main factors namely the risk involved for the fetus through the occurrence of epileptic seizures during pregnancy and the teratogenic side effects of antiepileptic drugs. In spite of several studies, a proper estimation of the teratogenic influence on the foetus through antiepileptic drugs is not available. On the one hand there is certain prevalence of congenital malformations in the general population irrespective of epilepsy or the intake of medication. On the other hand it has been found that the risk through certain antiepileptic drugs is considerably higher for malformation in the offspring. Certain congenital abnormalities such as spina bifida, cleft lip, congenital heart lesion and malformations of skeletal and central nervous systems are known with such drugs as Phenytoin, Sodium valproate and lesser also in other drugs like Carbamazepine. It is however difficult to evaluate whether these congenital defects are definitely caused by antiepileptic drugs or incidentally occurred due to multiple factors. Studies however show that the rate of congenital defects in women taking antiepileptic drugs is 2 - 3 times higher than in the general population.

Individual management of these situations is necessary. The young women wishing to have children under the intake of antiepileptic medication must be advised to plan the pregnancies properly. If it is clinically possible depending on the occurrence of seizures, the first trimester of pregnancy the patients should avoid the antiepileptic medication. If however the risk through grand mal seizures
or frequent complex partial seizures is higher, then they should be advised to take a single drug where considerably less teratogenic side effects are known such as Lamotrigine. A monitoring of the antiepileptic drug is necessary during the pregnancy as also the monitoring of the entire clinical situation concerning epilepsy. The ideal solution is to keep the pregnant women with epilepsy free of seizures with lowest monotherapy medication possible which is also known for less risk of teratogenic side effect. In cases of idiopathic generalized epilepsies or such epilepsies occurring because of genetic predisposition a genetic counselling is useful. If only one partner has an epilepsy which is generalized or partial but not strongly genetic, the risk of transmission to offspring is considerably low. A proper assessment of the situation is useful for avoiding later marriage conflicts.

**SELF-CONFIDENCE**

Self-confidence is a psychological problem which can involve any individual with or without epilepsy. But the occurrence of epileptic seizures and the prejudice associated with this illness may cause additional problems for a youngster during the personality development. As already mentioned such youngsters may develop severe inferiority complex during schooling and further education. The problem can begin right within the family where sufficient tolerance is not found through the siblings or the other members of the family. The duty of a neurologist or physician handling people with epilepsy therefore is not only the proper control of seizures with adequate antiepileptic drugs but also the comprehensive management of the patient.
involving psychosocial problems as well. Counselling a patient at any age, particularly in the school going and adolescent age is a necessary part of epilepsy management. A realistic approach must be adopted making it clear that the individual has this health problem but it is not a problem which cannot be solved. Guidance should be given based on the medical facts but with optimistic psychological supporting therapy. It may be useful for the patient to learn complementary methods such as autogenic training, meditation, yoga or similar techniques to develop self confidence. The situation must be analysed however depending upon the ratio of brain organic component and the compensation through secondary components. It is useful to adopt a multidisciplinary approach taking the help of psychologists, teachers including remedial healing and social workers. This multidisciplinary management is necessary in many cases of other chronic diseases but much more in case of a cerebral illness like epilepsy which may affect the patient not only because of his or her seizures but also due to the various negative influences from the society around.
CHAPTER 12

Special Case Histories of Epilepsy Patients
INTRODUCTION

In the succeeding pages case histories of epilepsy patients will be presented under following subtitles:

- Diagnostic clarification
- Brain tumor and epilepsy
- Traffic accidents caused by seizure
- Drug and alcohol provocation.

DIAGNOSTIC CLARIFICATION

Epilepsy is generally caused by multiple etiological factors and as such a diagnostic clarification of epilepsy as a nosological entity, is difficult even for an experienced neurologist. The phenomenology of epilepsy in form of an epileptic seizure is not sufficient for a clear diagnosis, as this needs further clarification of possible etiological findings and localization of the epileptogenesis in cerebrum. For example, a grand mal seizure can occur practically in all forms of epilepsy whether generalized or partial. It is then necessary to find out if a grand mal occurs as primary generalized tonic clonic seizure without a focal onset, or whether a grand mal seizure is a secondary manifestation of a focal beginning. The possibility of a focal beginning cannot be estimated in many cases of grand mal seizures particularly such one’s which occur during sleep, as patients are not capable of mentioning their focal experience because of sleepiness. In spite of exhaustive history taking from the patients and relatives it may sometimes not be possible to evaluate the beginning of a seizure. The EEG which is generally done during interval may not help in the further assessment of localization. In case of primary generalized epilepsy the EEG may show spike wave activity
particularly during hyperventilation which is then conclusive for a diagnosis. In case of clear temporal lobe epilepsies the EEG may show in interval focal findings in temporal regions unilateral or bilateral. In case of several so called cryptogenic epilepsies the interval EEG may not be contributory for the diagnosis. An ictal recording of EEG is hardly possible in patients who have occasional seizures. But without a proper classification, it is not possible to select a proper medication as for example, a grand mal in generalized epilepsy may be well treated with a drug like Sodium valproate, whereas a grand mal in partial or cryptogenic epilepsy could be better treated with a drug like Carbamazepine or Lamotrigine. In several cases the failure of drug treatment may be due to the insufficient clarification of nosological diagnosis.

Case History 1
This 37-year-old woman was referred for a clarification of two seizures with impairment of consciousness which occurred as isolated phenomena first at the age of 36 and the second a month before the consultation. The patient had no history of epilepsy or other neurological disorders in the family. She was the 4th of 6 children; the mother had diabetes type II and died at the age of 65 due to complications of diabetes. The patient was involved in a car accident at the age of 10 years with a mild brain concussion, she was not hospitalized and recovered fast after mild impairment of consciousness. At the age of 15 years she had an episode of dizziness as she was in the bathroom. After finishing the toilet, she felt dizziness and was disorientated so that she could not open the door of the
bathroom from inside. Only after a few minutes she regained the orientation and could open the door and come out. She ignored this incident and lead a normal life completing her professional training, joining a job and getting married. After 20 years she had a seizure again at home while she was preparing food in the kitchen. Shortly before the seizure occurred she felt an aura in the form of unfamiliar sensation in the head, followed by a fall, convulsions of the arms and legs and loss of consciousness for a few minutes. The patient went to a general physician for check up, a diagnosis was not made and she did not receive a medication.

Around two months before the first neurological consultation the patient had one more seizure, this time in a restaurant during dinner. In the middle of eating she had rotation of eyes side wards, had convulsions of arms and legs with impairment of consciousness. During the driving back home with her husband she had vomiting and later also a few loose motions of stool. A few days after this incident the patient saw her general physician, who then referred her for the neurological diagnosis of the seizures.

This patient had actually three episodes of seizures, whereas the first one without any convulsive phenomena but probably with mild impairment of consciousness. The second and third seizures can be clinically diagnosed as epileptic; the clinical description speaks for focal beginning and secondary generalization in the form of a grand mal. The neurological status of the patient was normal, there were no neuropsychological deficits. The EEG done after the first neurological examination showed a focal disturbance at the right temporal lobe without clear epileptogenesis. A MRI of brain showed normal findings.
Considering the clarity of seizures as epileptic and after discussion with the patient a monotherapy was started with Carbamazepine 400 mg/day, under which the patient remained free of seizures. The medication was started under medical and social considerations. On the one hand even though the patient had only two seizures there was the risk of chronification. On the other hand she was professionally active and needed driving of a motor car for her job.

She came for yearly neurological controls when an EEG was also recorded. The EEG in interval was sometimes normal, sometimes showed focal findings bitemporal without evidence for epileptogenesis. Almost five years after the last seizure and medication with Carbamazepine, the patient came again for a routine neurological check up with EEG. This time she looked tired and stressful because of her job and family problems, but she had remained free of seizures. Astonishingly the EEG recorded showed this time a remarkable finding during hyperventilation in the form of irregular generalized sharp and slow wave complexes for a duration of over thirty seconds. The drug was changed slowly as cross over from Carbamazepine to Sodium Valproate which the patient also tolerated quite well. The later EEG recording did not show the appearance of generalized sharp and slow wave complexes even under hyperventilation. The drug change was necessary to correct the paroxysmal generalized sharp wave activity during hyperventilation which might be a problem for the patient during driving because of prolonged reaction time.

This case history shows that a differentiation of the epilepsy as partial or generalized is not always possible. Attempts should be made however to determine the
classification for the purpose of proper medication. It is better in cases where the diagnosis is not clear to choose such drugs which have a broader spectrum of effectiveness in undifferentiated forms of epilepsies. The question of giving a long-term medication must be decided on the basis of various medical and medico social factors which must be however initiated after proper counselling of patients.

**Case History 2**

This man, aged 25, came for a neurological examination because of persisting epileptic seizures in irregular intervals. He gave a history of having seizures from the age of about fourteen years and having treatment for epilepsy since then. His girl friend who was living with him for around two years reported that the patient had during day and also at night (in sleep) seizures with the following symptomatic: He would suddenly turn his head to the left side, his eyes moving extremely to the left, then he would have convulsions of both sides, which terminated sometimes with biting of tongue, frothy saliva and then sleep for about half an hour. During the earlier neurological consultations elsewhere, an epileptogenic focus was recorded in EEG over right fronto temporal areas. A partial epilepsy with simple focal seizures and with secondary generalization was diagnosed. The patient received a monotherapy with Carbamazepine which did not improve his seizures to the desired extent. There was no history of complex partial seizures.

The epilepsy was considered as therapy refractory in a young patient who was fairly well integrated in the professional and family life. There were two aspects in the
clinical and EEG findings. The phenomenology of seizures beginning with a focal component of head turning to the left followed by grand mal as well as a interictal EEG finding of right fronto temporal focus could speak for a partial form of epilepsy. On the other hand the patient had mostly seizures in sleep and mornings on awakening, however without clear history of absences. During the course of treatment EEGs were recorded twice with forced hyperventilation. Both the EEGs showed during hyperventilation the occurrence of bilateral synchronous and generalized spike wave complexes which lasted for ten to twenty seconds. This made the diagnosis of epilepsy as a generalized form clear in spite of the focal components found in the phenomenology of seizure and interictal EEG recordings. The drug was changed to a combination of Sodium Valproate and Lamotrigine, under which the patient remained free of seizures for the last seven years, and the EEG did not show spike wave activity. This is a clear case of generalized epilepsy of the primary generalized form, probably with an additional slight focal component. Clarity in the diagnosis in such cases is necessary particularly from the point of view of medication. Carbamazepine is known to provoke spike wave complexes in generalized epilepsies particularly of the primary generalized form. Even though the patient was repeatedly asked about the occurrence of absences, he denied any such phenomena. Perhaps the epilepsy began in this patient around the age of fourteen years with absences which later under medication disappeared with the occurrence of grand mal seizures only. The grand mal seizures in the early mornings speak mostly for a generalized form of epilepsy.
Epileptic seizure is a common symptom in brain tumors particularly tumors of the cerebral cortex. In case of otherwise healthy people, it is obligatory to rule out cerebral tumors after an unprovoked occurrence of epileptic seizures. With the development in neuroradiology particularly with magnetoresonance imaging (MRI) it has become much easier to diagnose a brain tumor than it was the case in earlier days. Formerly the diagnosis had to be made through rather inaccurate methods such as X-ray skull, pneumoencephalography, EEG and carotis angiography. The diagnosis can be delayed in certain cases even today if the symptoms of tumor are not clear, or in such cases where extra cerebral conditions are suspected with psychiatric or other problems. The following two cases show how the possibility of a brain tumor can be masked because of predominantly different psychosomatic symptoms.

Case History 1
This 37-year-old woman with acute history of frontal headache, nausea sometimes followed by vomiting, sleeplessness, and extreme tiredness came directly for a neurological examination. She was under treatment of her house physician for sometime because of these problems. The patient was a working woman, had two school going children and was divorced around two years before the consultation. She had difficulty in managing her work and the two children as the father of the children did not support them properly. For nearly a year she was depressed and had several psychosomatic problems including headache. The house physician treated her with painkillers,
antidepressants and supportive psychotherapy. The condition however did not improve and with the appearance of nausea and vomiting she got into an acute condition.

The patient reported that as a child around the school age she had epileptic seizures and received for several years antiepileptic medication. After puberty the seizures completely disappeared and the antiepileptic drugs were withdrawn, even then the patient remained free of seizures. She completed her schooling and professional training, married and got two children. Until the age of 36 years she had no health problems. According to her opinion the problems started after the divorce because of the difficulties of management of her work and two children. There was a court case against the former husband as he was not paying the maintenance for his children. She got slowly into a depression and then the other symptoms such as headache started.

On examination the patient was found in a totally reduced condition, the neurological examination did not show pathological findings. An EEG was recorded which however showed a practically continuous delta activity left frontotemporal accompanied by diffuse epileptogenic activity in this region which showed a tendency for generalization in the form of sharp and slow waves. Considering the possibility of a brain tumor, in spite of her several psychiatric problems, the patient was started on a medication of cortisone 60 mg/day and also an antiepileptic drug in the form of Carbamazepine 800 mg / day. MRI done after two days showed a brain tumor left temporo-occipital region which the neuroradiologist suspected as a cystic meningeoma. The patient was admitted in the neurosurgical
hospital and underwent surgery. The neurosurgeons operated the tumor and classified it as glioblastoma in the region left temporo-occipital extending to the basal structures. The tumor could be operated almost completely however leaving behind a thin structure. The patient underwent a series of radiotherapy and later also chemotherapy. Her acute symptoms disappeared almost completely, however she started getting complex partial seizures sometimes with secondary generalization, in spite of high doses of Carbamazepine. The antiepileptic drug had to be supplemented with Lamotrigine, the seizures reduced but she did not become completely free of seizures. Though the prognosis of glioblastoma was found unfavorable, the patient continued to live without a tumor recedive. The neurosurgeons later corrected the diagnosis and thought of a lower grade astrocytoma considering the better prognosis, even though after the operation the histological findings showed the possibility of a glioblastoma.

This is a rather unusual case where psychiatric and social factors were involved in the history of the patient which somewhat masked the neurological symptoms. In all suspected cases it is always useful to rule out the possibility of a brain tumor through cranio-cerebral MRI.

**Case History 2**

Woman 62 years, was referred for a neurological evaluation of multiple problems. Her mother and elder sister, both had tremors of the hands, the mother died at the age of 84 years. The patient was married for over three decades and divorced about two years before the consultation. The patient was mother of five grown up children. After the divorce she
became nervous, irritable and suffered from sleeplessness. Her complaints were multiple symptoms such as headache, tremors of the hands particularly on intention, backache, joint pains and dizziness. Because of these complaints she was going to several doctors, some of them did not like to treat her because of her character with psychosomatic and psychological problems. For about one year before the first consultation she had a tendency to nausea and vomiting, both troubles appeared and disappeared in irregular intervals. She complained of memory and concentration difficulties. A few times she had an orientation disturbance while walking in a well known place. She reported that she went in a wrong direction and did not know why she did it. Similar experience she had also during driving a car so that she drove for one to two kilometres entirely in a different direction. The main problem for which she came to the neurologist was her tremors of the hands which were increasing, so that some doctors suspected a Parkinson syndrome. The people known to her thought that she might be under the influence of alcohol even though she was not regularly drinking and if at all, she took only one glass of wine for dinner. Some doctors diagnosed depression and gave her antidepressive medication, which did not help her.

During the examination the patient was found slightly obese but her general condition was good. She had a hypertonia which was being treated with anti-hypertonic drugs. In the neurological examination she had a tremor of both hands which increased on intention. Otherwise there were soft neurological findings without further significance. She was nervous and somewhat depressive, had a tendency
to exaggerate her problems. The personality structure showed brain organic components. After the exhaustive history-taking and clinical examination the following points were evaluated for diagnosis:

- A Parkinson syndrome could be ruled out because of bilateral tremor of hands without other symptoms of rigor or akinesis
- There was a suspected diagnosis of essential tremor
- The paroxysmal disturbance of orientation could be of epileptic nature particularly in form of complex partial seizures
- In the differential diagnosis, transient ischecidal attacks could be ruled out
- The etiology of late onset epilepsy must be ascertained, particularly in view of brain tumor.

The EEG showed in interval a focal epileptogenic activity right temporal sometimes also bitemporal. MRI of brain brought the finding of a meningeoma in the right temporal area. The patient was placed on a medication of Primidon 500 mg /day which helped her against the essential tremor and also for the control of complex partial seizures. The patient underwent a neurosurgical operation with complete removal of the convexity menigioma right temporal. Under a long-term medication of Primidon 500 mg /day the patient remained free of seizures and her tremor disappeared completely. However, she continued to have memory and concentration difficulties but her quality of life improved. Almost ten years after the neurosurgical operation and drug initiation the patient has remained free of the earlier symptoms. Her somatic problems such as joint pains, sleeplessness and sometimes headache however persist.
This is a case where at least two neurological problems were parallelly present namely brain tumor associated with epilepsy and essential tremor. Whereas a diagnosis of tremor was clinically possible, the diagnosis of disturbed orientation had to be clarified through EEG and MRI of brain.

**TRAFFIC ACCIDENTS CAUSED BY SEIZURE**

People with epilepsy are prone to accidents because of unpredictable epileptic seizures particularly grand mal seizures and complex partial seizures. Traffic accidents caused by people with epilepsy are however a small number compared to the other accidents caused by people with different conditions such as psychotic behavior, human problems, alcohol and drug intake. Accidents do happen in epilepsy patients not only while driving but in other situations as well. Every attempt should be made to make the situation clear to the patients. It is not possible to prohibit a patient from doing all things which involve a certain amount of risk because of epileptic seizures. There is however increased risk of accidents under different circumstances such as mountaineering, driving, cycling, swimming, working with heavy machines and even in household. One must try to estimate the risks involved but without jeopardizing the quality of life of the patient. Most of the accidents happen in cases of therapy refractory partial epilepsies with complex partial seizures and/or seizures with secondary generalization in the form of grand mal. In adult life the grand mal seizures in generalized epilepsies occur mostly early mornings as in the case of grand mal epilepsy on awakening or at night in sleep. The rhythm of
this epilepsy can however change during the course of treatment and also due to other provocations such as stress, sleep deprivation and alcohol intake. However, the people with epilepsy seem to be less worried about the risk of accidents but the partners or other close relatives are more concerned. The following examples refer to the circumstances of traffic accidents caused because of epileptic seizures, sometimes also with fatal consequences.

Case History 1

Boy, thirteen years, comes for the treatment of epilepsy which was diagnosed at the age of twelve years. The patient was the first of two children, there was no history of epilepsy in the family. The pregnancy of the mother was normal, the birth was somewhat complicated and delayed, there were also some feeding difficulties. Later mile stones were normal. The patient had three febrile convulsions between the age of two and four years. The further development psycho-motoric as well as schooling was normal. Seizures started at the age of twelve years in the form of simple partial seizures and complex partial seizures with secondary generalization. The EEG showed epileptogenic focus bitemporal with a left sided dominance. Right from the beginning the epilepsy was found to be therapy refractory even though there were remission for weeks or months under the medication of Carbamazepine, later also in combination with Phenytoin and Sodium Valproate. However, the patient did not become free of seizures for longer than three months, in spite of intensive medication. His intellectual development and school performance was good and around the age of sixteen he was an ambitious
boy wanting to become a professional pilot. The father of the patient was a flight engineer and the mother was for many years a stewardess in an airline.

In the long-term monitoring of seizures there was a bitemporal focus with left sided dominance going up to left temporal basal areas. The Computer tomography of brain did not show pathological findings. The case history goes back to a time when MRI was not available. The patient was referred for epilepsy surgery and was found unsuitable because of bilateral temporal focus particularly of dominant hemisphere. Practically all the antiepileptic drugs available in the 1970s were used in different combinations which did not make the patient free of seizures. However, he was a very dynamic type of a young man and managed to continue his professional studies as an engineer. At the age of eighteen he wanted to acquire a driving licence which could not be granted because he was not free of seizures for the required period of one year. There was the risk of accidents because of unpredictable complex partial seizures which would sometimes appear in clusters. At the age of nineteen a tragic accident happened when the patient was waiting at the railway station for his train connection. Probably he had a sudden grand mal seizure and fell on the rails loosing his life. With the drugs available as of now, the patient would have had a slightly better prognosis of his complex partial seizures than in the 1970s when such drugs like Lamotrigine, Topiramat, Gabapentin and Levetiracetam were not available. However, one sees such therapy refractory cases in temporal lobe epilepsies even today. Neurosurgery must be attempted wherever possible in such therapy refractory partial epilepsies.
Case History 2

Man 25 years gives a history of epileptic seizures since the age of twelve years. There is no family history of epilepsy; one younger sister has a tendency to vaso-vagal syncopes. As far as the history is available: normal pregnancy of the mother, normal birth and milestones. The patient completed normal schooling and a training in the field of building construction and masonry work. Epileptic seizures occurred for the first time at the age of twelve years in the form of grand mal. Absences were not noticed however the patient had a tendency to get the seizures particularly in the early morning hours. The interval EEG did not show proper findings in the beginning but later a clear generalized bilateral synchronous spike wave activity during hyper-ventilation. He was treated with a monotherapy of Sodium Valproate with which he became free of seizures until the age of about sixteen years. During the period of his professional training he started drinking beer and other alcoholic drinks and the seizures reappeared particularly on weekends after consumption of alcoholic drinks. Sometimes he felt headache and muscle pain early mornings on awakening which could be the symptom of a nocturnal grand mal. The treatment was intensified with the addition of Phenobarbital to existing medication of Sodium Valproate under which the patient again remained free of seizures for three years. The patient had some psychosocial problems particularly in choosing a proper partner. He changed his girlfriends often and was probably irregular in the intake of medication or avoiding other provocations such as alcohol intake and sleep deprivation. Gradually however he became cooperative and tried to discipline his lifestyle in the intake
of medication. Accordingly he remained free of seizures for
two to three years and satisfied the conditions for acquiring
a driving licence. The EEGs showed no abnormality of spike
wave activity even during forced hyperventilation and the
serum-concentration of the drugs was within normal limits.

After the age of nineteen years he started driving a motor
vehicle, and the driving licence was given according to the
regulations in Switzerland.

After nearly three years of freedom of seizures and normal
interval EEG findings as well as the serum-concentration of
the drugs being within the normal limits, the patient had an
epileptic seizure during driving which resulted in a serious
accident. As usual he was driving to his working place at
five o’clock in the early morning when he suffered a grand
mal seizure. His car was totally smashed, he had a cerebral
concussion and some injuries when the car hit a huge tree
before it came to a stop. According to his information he
could manage to drive the car away to the roadside avoiding
a major catastrophic accident. The bypassers called the
ambulance and the police brought him to intensive care
unit. His driving licence had to be cancelled for one year.

An EEG recorded a day after the accident showed under
hyperventilation continuous activity of generalized spike
and waves for a duration of thirty seconds. The serum-
concentrations of the drugs were in the lower level than
usually the case was. During the further neurological
consultations his drug was changed to a combination of
Sodium Valproate and Lamotrigine. The later controls in
intervals of about three months showed normal EEG
findings even during hyperventilation and the serum levels
of both drugs namely Sodium Valproate and Lamotrigine.
in therapeutic levels. The driving licence was granted under the
type of somewhat frequent neurological controls
in three to four months with EEG recording and estimation
of drug levels in serum.

After the accident even though a proper history was not
available the increased epileptogenic activity in EEG as well
as reduced serum levels of the drugs are suggestive of a
provoked grand mal seizure. The patient reported of certain
amount of sleeplessness because of his emotional problems
with the partner.

Case History 3

This thirty-one-year-old man gives a history of epilepsy since
childhood. There is some history of epilepsy in the family.
One uncle and younger brother of the patient had probably
epileptic seizures and were treated for some years with
antiepileptic medication. The patient is the second of three
children and had no complications during pregnancy of
the mother and at birth. Already at the age of two to four
years he had two or three epileptic seizures, without a proper
history whether the seizures were febrile convulsions or
unprovoked seizures. He remained free of seizures almost
until the age of eighteen years. He finished the school and
learned a simple profession as mechanic. After the age of
eighteen years he was getting complex partial seizures and
migraine attacks in irregular intervals. He was treated with
Phenytoin and later the drug was changed to
Carbamazepine. The EEG showed focal epileptogenesis
bitemporal mostly left temporal. Under a regular intake of
Carbamazepine the patient remained mostly free of seizures,
his migraine attacks reduced to a good extent.
The patient had less than average verbal intelligence but had sufficient practical capacities to cope up with the different situations in life. He got married to a working woman, had three children before the age of thirty years, was driving a car. He worked in his profession as a mechanic for sometime and later lost the job partly because of epilepsy and partly because of his character structure with reduced cognitive abilities. The patient decided to remain at home and take care of children, his wife was working 100%. After the birth of the third child the patient and his wife developed family problems, as the wife fell in love with another man. The patient had no personal earnings but the family was living through the earnings of the wife.

A day before the pair had to go to a court for settling divorce the patient was involved in a car accident. In the morning hours when he was driving he suddenly felt dizzy and hit the car to a cement barrier, where he was found unconscious. Even though the actual cause of the accident could not be estimated, most probably the patient had a complex partial seizure before hitting the cement barrier. He had remained free of seizures for over one year and the serum-concentration of the medication Carbamazepine was in the therapeutic range. The patient reported that he could not sleep sufficiently over the previous two to three nights and had great stress because of his divorce and was worried concerning his financial situation. He had to surrender the driving licence for the next six months, when his drug was intensified by increasing the dosage. The further neurological controls showed that he remained free of seizures over the following years under a combination of Carbamazepine and Lamotrigine. The EEG showed,
however, in interval focal findings in the temporal regions. This is a case of partial epilepsy in the form of a temporal lobe epilepsy with simple partial and complex partial seizures probably because of a mild degree of childhood brain damage. Sometimes such cases have a familial predisposition to epilepsy. The prognosis of this epilepsy is on the whole fairly good.

Case History 4

This man, aged twenty one, came with a history of epileptic seizures which started at the age of nineteen years. There was no family history of epilepsy or other neurological diseases. The patient completed normal schooling and a profession as technical worker, migrated from former Yugoslavia to Switzerland. At the age of nineteen years the patient suddenly got a grand mal seizure. The neurological examination showed the possibility of further seizures and the patient was put on a long term antiepileptic drug Carbamazepine. Nearly one year he remained free of seizures under the medication. After that a series of grand mal seizures occurred, nearly nine to ten seizures in a period of about six months. On examination the neurological condition of the patient was normal, the EEG showed however clear epileptogenesis right temporal as a focal finding. The patient reported of getting an Aura before grand mal seizures, the Aura being a diffuse feeling of unfamiliarity in the head. The Carbamazepine dosage was in the optimal range of serum-concentration, but the patient had further seizures. Because of that he was given a second drug Lamotrigine to the existing Carbamazepine. Under this medication the patient remained free of seizures for over
one year, the EEG showed in interval however a focal finding in the right or left temporal regions mostly on the right side. MRI of brain did not show any abnormalities.

The patient was cooperative in that, he was coming regularly for neurological examinations in periods of three to four months; the serum-concentration of the drugs taken was in the normal limits. After over one year of seizure freedom he was given a driving licence for motor car. Six months after this, still with the history of seizure freedom and good compliance, the patient caused a severe traffic accident. He came from a discothèque where he had taken a couple of alcoholic drinks particularly beer. Around three O’clock in the morning he hit against a big tree and went into unconsciousness. The emergency hospitalization showed that he had a fracture of the jaw on the right side and cerebral concussion. He had also facial injuries and had to undergo surgery. The driving licence was cancelled for one year but the antiepileptic drugs were kept unchanged in proper dosage. After one year of seizure freedom after the accident, the patient was granted driving licence again under stringent conditions of four monthly neurological controls with EEG and serum-concentration of antiepileptic drugs. The patient had to undergo a parallel program for alcohol abstinence before the driving licence could be granted to him again.

This is a case of partial epilepsy which began rather in late adolescence but was treatable with antiepileptic drugs. The seizure during accident which probably started as a partial one went into a secondary generalization as grand mal was certainly provoked because of alcohol misuse. It is seen that a good number of such cases particularly in young
men the epileptic seizures are provoked through alcohol and sometimes by sleep deprivation and stress. A patient such as this one must be considered as a potential risk in matter of traffic accidents and needs special counseling.

**DRUG AND ALCOHOL PROVOCATION**

Several drugs can increase the risk for epileptic seizures in general and particularly in people who are prone to epilepsy. In patients with epilepsy who are being treated with antiepileptic drugs this aspect of seizures provocation must be considered before prescribing a drug for any other illness. The common drugs given during the course of treatment for longer periods are antidepressants and neuroleptics. Antidepressants particularly of the group of tricyclic drugs are known to reduce the threshold for epileptic seizures. The following case shows that even in people who do not have a clinical epilepsy, a provocation of seizures is possible particularly with higher dose of antidepressants.

**Case History 1**

This 56-year-old woman is an inhabitant of a home for moderately mentally retarded people. She is the first of three children. A mild intellectual retardation was noticed during the school age and her normal school had to be changed to a school for children with learning disabilities. There she finished her schooling and underwent a program for managing household work. She was living with her mother until the age of nearly 45 years. When the mother got quite old and had her own household problems, the daughter was moved to a home for moderately mentally retarded people. Living in this home, the patient went for work in an old age...
home. She received a pension from the invalid insurance of Switzerland. At her age of 52 years her mother died whom she was visiting over weekends also during her stay in the home for disabled. The death of mother was a terrible shock for the patient and she went into a severe depression, could not manage her outside work in the old age home. She was put on a tricyclic antidepressive medication with a minimal dosage. An EEG done during the first neurological consultation showed a normal finding. The patient underwent also psychological counseling elsewhere. Under this small dosage of 25 mg trimipramin the patient did not recover sufficiently. The dosage was increased to 50 mg divided in two doses per day which showed considerable improvement in the depression of the patient. She was able to attend her outside work in the old age home at least partly under this medication. The further consultations showed more or less a stable condition even though the patient was not completely free of her depressive mood changes.

Neurological examinations were found not necessary for the patient and she was transferred to the care of a psychiatrist who saw her three to four times a year. In the meantime the patient also had psychological counseling. Certain negative psychosocial events happened in the life of the patient so that she lost one more aunt to whom she was very much attached and who played the role of her mother after mother’s death. Moreover the caretaker in the home changed her job and the patient came under the supervision of a new person. Because of these two events the patient again fell into a severe episode of depression. The psychiatrist increased her medication into a dosage of 200 mg of the same drug, which she was taking for the past
two to three years. Her depressive episodes improved under the increase of dosage of antidepressive drug but she started getting muscle jerks particularly over the shoulders and both arms so that during breakfast she could not take her cup of coffee properly or hold knife and fork without shaking. The clinical examination showed suspected myoclonic seizures accompanied by absences. There was a tendency to secondary generalization because of the clinical phenomena of falling dawn if she had myoclonic jerks in a standing position. The EEG examination showed clear paroxysmal activity in the form of irregular generalized spike wave complexes before and during the hyperventilation, which confirmed the diagnosis of epilepsy.

The antidepressive drug was reduced and later stopped and replaced by sodium valproate 1000 mg/day. Under this medication the patient improved considerably, the myoclonic jerks reduced and after about three weeks stopped, an EEG recorded later showed practically no epileptic activity except in traces of sharp waves in the bifrontal regions. This is a clear case of provoked epilepsy through high dose of antidepressive medication. A provocation through these drugs can happen also in the case of people with controlled seizures. However the use of antidepressive drug during the treatment of epilepsy is not totally contraindicated, but the drug should be selected properly and in a smaller dosage.

Case History 2
This fifty-four years old man came for the drug treatment of occasional grand mal seizures occurring only in sleep. He was the CEO of a large industrial company with nearly
3000 co-workers. There is no history of seizures or any other neurological disease in the family. The patient was a dynamic person, who according to his personal history, started his career with a modest beginning. He completed several professional courses in marketing and business administration and made his way within a period of fifteen to twenty years to be the chief of a large organization. This achievement was possible with very constructive hard work. In his professional life he had to work on an average of 60 hours a week and make several journeys to different countries, sometimes accompanying the political leaders. Consequently, he had to invite different delegations for lunch and dinner, and on the other hand, he was also invited for such occasions from other business companions. Most of the time, he drank alcohol particularly champagne and wine for lunch and dinner.

At the age of 52 during one of his tours in a foreign country he got the first grand mal seizure in sleep in a hotel room. The evening prior to that, he had taken as usual fairly large quantity of alcohol. He got up in the morning with problems of orientation, muscle pain and biting of tongue. The house physician suspected an epileptic seizure and the patient was referred to a neurologist. The EEG in interval did not show any findings but on the assumption of an epileptic seizure, the neurologist advised him to reduce his alcohol consumption. A drug treatment was not initiated by the neurologist after a single provoked epileptic seizure. The patient did not or could not see the necessity of reducing his alcohol consumption. About three months later, the patient had a second grand mal seizure in sleep, this time at home which was observed by his wife. The neurologist started a treatment with phenytoin 300 mg/day, which was later
increased to 400 mg. The patient was otherwise a very healthy person with an athletic constitution having no other health problems. He enjoyed his lifestyle in certain luxury as he was convinced that this was made possible because of his hard work. He drank at least one bottle of wine per day regularly, during business meetings even more. After the introduction of phenytoin he remained free of seizures for nearly six months, had however some difficulties with the drug because of side effects particularly of the central nervous system. The neurologist reduced the dosage of phenytoin to 300 mg/day, when the patient promptly reacted with one more grand mal seizure again in sleep.

The drug was changed slowly to carbamazepine in cross over pattern until a daily dosage of carbamazepine retard 400 mg – 0 – 600 mg was reached. Under this medication the patient remained free of seizures for nearly one year and he had no difficulties of drug tolerance. Later the patient had relapse of seizures in intervals of one to two years, always in sleep. He tried to reduce his alcohol consumption which however was not very successful. The EEG’s in interval did not show any focal paroxysmal findings, the MRI of brain was normal. The epilepsy in this case can be considered as a cryptogenic form with occasional grand mal seizures in sleep provoked by alcohol overuse. In the earlier stages probably the epilepsy could have been controlled even without antiepileptic medication with change of lifestyle particularly reduction of alcohol and regular sleep habits. However after the occurrence of several grand mal seizures an antiepileptic medication is necessary. In such cases a monotherapy with a suitable drug once or twice daily should be given, possibly with the change of lifestyle.


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