According to the Commission on Classification and Terminology of the International League against epilepsy (1989) a syndrome is 'a cluster of signs and symptoms customarily occurring together'. An epileptic syndrome is usually based on all the information available from the patient's and his/her family history, clinical examination, and results of ancillary tests (electrophysiological, imaging and so forth). Epileptic syndromes or epilepsies were divided into localization-related and generalized. Further categories are undetermined epilepsies and special syndromes. Localization-related and generalized epilepsies are, dependent on the underlying condition, either idiopathic (primary or genetically determined epilepsy), symptomatic (secondary epilepsies with known structural epileptogenic lesion), or cryptogenic (secondary epilepsies with causation hidden). Epileptic seizures and epilepsies can occur at any age. Single epileptic seizures like generalized tonic-clonic seizures after alcohol withdrawal should not be considered as epilepsy but they can be a risk factor for the development of epilepsy defined as repeated occurrence of unprovoked seizures. Many epileptic syndromes, especially idiopathic epilepsies, start in childhood and some of them stop at the end of childhood. However, very recently idiopathic localization-related and generalized epilepsies beginning in adulthood have been described. In this overview, the emphasis is more on these newly discovered syndromes that may create diagnostic confusion than on the symptomatic forms of which a vast literature already exists. Epidemiological investigations revealed that approximately half of the epilepsies become manifest under the age of 10 years, and approximately 2 thirds are manifest at the end of the second decade. The incidence of epilepsies is lowest in the middle-aged population but increases again over the age of 60. It was estimated that the incidence of epilepsy at age 70 is at 140 pro 100,000. This high number reflects the increasing number of cerebral insults occurring in this age group. It also explains that in the older age group symptomatic epilepsies caused by vascular or tumorous lesions, and degenerative disorders are common.

**Epileptic syndromes with predominant manifestation in adolescence and adulthood.**

1. Idiopathic localization-related epilepsy syndromes.

   1.1. Familial temporal lobe epilepsy (TLE). Berkovic and coworkers described a syndrome of familial TLE in 1994 first recognized in monozygotic twins. Seizures usually start in early adult life consisting of simple partial seizures suggestive of temporal lobe origin. One of the twins had deja vu auras, the other experiential/cognitive auras. Complex partial and tonic clonic seizures were rare.Intellect and neurological examination were normal. The electroencephalogram (EEG) only showed sparse abnormalities. Seizures could easily be controlled by drugs. This first report was rapidly followed by others describing other families with this type of benign temporal epilepsy. At the AES meeting in Boston, Regesta et al (1997) reported 2 cases with a positive family history and additional 10 cases of a benign TLE suggesting of sporadic idiopathic TLE. At the same meeting Lopes-Cendes et al 1997 reported 11 kindred with familial temporal epilepsy comprising 36 affected individuals. They concluded that the syndrome of familial TLE has heterogeneous clinical manifestations and is not always benign. The heterogeneous presentation of familial TLE with severe clinical course requiring surgery in some patients, and benign course in others suggests that this condition is also genetically heterogeneous. This assumption was corroborated by several reports published in recent years (Picard et al 2000, Kobayashi et al 2003).

   1.2. Familial frontal lobe epilepsy. Scheffer et al (1994) described a distinctive epilepsy syndrome in 6 families, which is the first partial epilepsy syndrome to follow single gene inheritance. The predominant seizure pattern had frontal lobe seizure semiology with clusters of brief motor attacks occurring in sleep. Onset was usually in childhood, but was also found in early adulthood often persisting through adult life. Seizures were often misdiagnosed as benign nocturnal
parasomnias, psychiatric and medical disorders, and the inheritance pattern was often not appreciated. Intercital EEG studies were unhelpful. Ictal video-EEG studies showed that the attacks were partial seizures with frontal lobe seizure semiology. Semiology, however, is not necessarily revealing the real origin of seizures in the brain and some doubts can be expressed whether the origin in all these cases is actually in the frontal lobes (Picard et al 2000, Provini et al 2000). Neuro-imaging was normal. Carbamazepine monotherapy was frequently effective. The electro-clinical picture of this epilepsy has been confirmed in several different kindred (Oldani et al 1996). Intrafamilial variation of the epileptogenic zone in the frontal lobes was found in members of 2 families (Hayman et al 1997). Genetic analysis revealed a missense mutation in the critical M2 domain of the alpha 4 subunit of the neuronal nicotinic acetylcholine receptor (CHRNA4) in one large Australian pedigree. In a Norwegian family a novel mutation in the M2 domain of the CHRNA4 gene was found (Steinlein et al 1997). Comparison of the 2 mutations identified in these 2 families with this autosomal dominant form of nocturnal frontal lobe epilepsy illustrates that different mutations can result in similar phenotypes.

2. Idiopathic generalized epilepsies. The 4 major idiopathic generalized epilepsies (childhood absence epilepsy (CAE); juvenile absence epilepsy (JAE); juvenile myoclonic epilepsy (JME); generalized tonic clonic seizures on awakening (GMA)) may be differentiated by the age at which the first seizure occurs. Following Janz (1994) manifestation age for CAE peaks at 7.5, JAE at 13, JME at 15, and GMA at 18 years of age. Very recently, 2 syndromes of idiopathic generalized epilepsies with onset in the adult age were described. Although these observations need further confirmation, it seems important to be aware of the possibility that idiopathic generalized epileptic syndromes also can become manifest at the middle age.

2.1.1 Adult myoclonic epilepsy. Gilliam et al (2000) presented 11 cases of idiopathic generalized epilepsy that began in adulthood at a mean age of 39 years. All patients had myoclonic jerks, 5 had absence seizures, and 9 had infrequent generalized tonic-clonic seizures. A majority had a family history of seizures. Electroencephalogram in all patients showed generalized epileptiform abnormalities, whereas neuroimaging and neurologic examination results were normal. This series appears to represent a previously undescribed idiopathic generalized epilepsy syndrome of adult myoclonic epilepsy. Seizures were controlled by valproate or lamotrigine. The authors concluded that due to the adult onset this series of patients characterizes an idiopathic generalized epilepsy syndrome with important implications for accurate diagnosis as well as genotypic classification of the idiopathic generalized epilepsies.

2.1.2 Idiopathic generalized epilepsy in adults manifested by phantom absences, generalized tonic-clonic seizures, and frequent absence status. This idiopathic generalized epilepsy syndrome was recently described by Panayiotopoulos et al (1997) which, they found in 13 (3.2%) of 410 consecutive patients older than 16 years with epileptic seizures. Myoclonic jerks were not present in this group of patients (compare MAE in 2.1.1). Mean age at onset of the tonic-clonic seizures was at the age of 31.5 years (SD 15, range 15 - 56 years, median 28 years) and of the absence status at 32.3 years (SD 15.1; range 15 - 56; median 32.5 years). Age at onset of phantom absences defined as mild typical absences being inconspicuous to the patient and imperceptible to the observer and therefore revealed only EEG-video recording could not be determined. Clinical examination and high resolution magnetic resonance imaging (MRI) remained without any abnormalities. In EEGs generalized 3 - 4 Hz spike wave and wave activity was found. The authors conclude that this is an idiopathic generalized epilepsy syndrome in adults which has not been previously recognized and does not fit in any of the recognized or the newly described syndromes of idiopathic generalized epilepsy.
from temporal lobe tissue (namely, designating the ictal onset zone) or show the typical clinical semiology which occurs after ictal activation of temporal lobe tissue (namely, designating the symptomaticogenic zone) but actually may be the result of spread of seizure activity from somewhere else. A clear distinction between these 2 conceptional levels would be helpful in order to avoid the above outlined misunderstandings. A seizure classification based solely on clinical semiology and clearly separated from a syndromatic classification has been proposed (Lüders et al 1993).

### 3.1 Temporal lobe epilepsy

Temporal lobe epilepsy is by far the most frequent symptomatic focal epilepsy. This fact is also reflected by the high number of papers published in this field (a medline literature search at end of December 1997 resulted in 4696 titles when 'temporal lobe epilepsy' was used as search term). It is well known that the mesial parts of the temporal lobe (amygdala, hippocampus, parahippocampal gyrus) belong to the areas of the human brain with the lowest threshold for epileptic activity, a fact that certainly is responsible for the frequent occurrence of this type of focal epilepsy. As was explained above, the phrase temporal in this connection refers to the anatomic site where the focal epileptic activity actually starts from. The methods used in diagnosing focal epilepsies all have restrictions: ictal clinical symptoms almost always are the expression of seizure spread activating a volume of brain sufficient to produce an ictal symptom, for example, an aura; the same is true for the surface EEG which shows ictal activity only if enough brain is synchronously activated to produce electroencephalographically visible graphoelements; although the spatial resolution of invasive EEG (depth or subdural electrodes) is considerably higher than that of scalp EEG the problem is essentially the same with the additional problem of the limited sampling volume, namely, invasive electrodes pick up activity only from the restricted area where the electrode is located; small morphologic lesions revealed by high resolution MRI seem best suitable for localizing the epileptic focus under the assumption that a lesion in the presence of a focal epilepsy is causally related (but this is not always the case meaning that the epileptogenicity of a lesion has to be proven by electrophysiological methods). The only confirmation for the correct localization of the epileptic focus (or epileptogenic zone) is the cessation of seizures after resection of this part of the brain. However, this also can mean that the resected area contains the tissue being able to produce seizures but is not necessarily identical with it. After these more general considerations a description of the symptomatic focal epilepsies subdivided into the 4 main anatomical categories will be given.

#### 3.1.1 Mesial temporal lobe epilepsy (mTLE)

**Etiology:** unknown; febrile convulsions (FC) are frequent in the history of these patients and probably are at least the most frequent so called initial precipitating injury (IPI). There is some evidence that a genetic factor plays a role for the occurrence of FC which on the other hand lead to the morphological changes in the medial temporal lobe called hippocampal sclerosis. Hippocampal sclerosis is the morphological substrate of the mesial TLE. Sixty to 70% of patients with mTLE have FC in their history but only a few percent of patients with FC develop later in life mTLE.

**Course:** The FC occurring during the second and fourth year of life typically are followed by a 'silent period' of several years. The majority of patients experience unprovoked seizures in the second half of the first decade often with relatively mild ictal symptoms in the form of auras or short absences slowly progressing to the typical symptomaticatology of psychomotor seizures of temporal lobe origin. However, longer seizure free periods between FC and onset of seizures may be observed. The longest interval seen by this author was 30 years in a patient who had prolonged FC at the age of one year and experienced her first epigastric auras and psychomotor seizures when she was pregnant with her first child 30 years later. Her seizures did not stop after delivery and finally she developed a refractory mTLE which was confirmed (and cured) after surgery at the age of 45 years. Drug resistance is extremely high in this form of focal epilepsy even when during the first years after beginning of the epilepsy seizures may be mild often only consisting in auras or even longer seizure free intervals. Typically, several psychomotor seizures occur per month with auras preceding seizures but also occurring isolated. Some patients develop clustering of seizures once or twice a month or secondarily generalized tonic clonic seizures. Mesial temporal lobe epilepsy is associated with impairment of cognitive functioning especially episodic memory. This is a common subjective complaint and it can also be verified by using neuropsychological tests. Several studies show that hippocampal sclerosis of the dominant side leads to more severe memory problems than on the non dominant side. In TLE with hippocampal sclerosis remote effects revealed by FDG PET studies (Arnold et al 1996; Jokeit et al 1997) indicating a regional metabolic suppression far from the primary epileptogenic region can be demonstrated. These areas of remote metabolic depressions probably reflect spread of seizure activity (Savic et al 1997) but are also associated with permanent neuropsychological impairments (Arnold et al 1996). It is an open question whether the lesioned mesial temporal structures are solely responsible for the negative cognitive consequences often seen in these patients or whether uncontrolled seizures among many other factors associated with an intractable epilepsy contribute to the deterioration of cognitive abilities, in other words whether mTLE is a progressive disease. Although longitudinal studies investigating the impact of uncontrolled complex focal seizures of mesial temporal lobe origin on the cognitive functioning are missing a cross-sectional study covering duration of TLE over 30 years revealed a deterioration of cognitive abilities dependent on the duration of this form of epilepsy.
Neurosciences  2003; Vol. 8  Supplement 2

is best seen in T1 weighted including inversion recovery (Jackson 1995). Atrophy of the hippocampal formation sclerosis (an excellent review is given in Kuzniecky and morphological substrate of mTLE: the hippocampal and specificity of this method in detecting the MRI. There is vast literature about the high sensitivity usually is in the theta range. That the frequency of ictal activity on the scalp EEG area. This is probably the explanation for the finding by the seizure starting in the amygdalo-hippocampal laterobasal cortex of the temporal lobe has been invaded changes of the surface EEG usually appear only after the metamorphic pattern, namely, rhythmical activity changing with regard to frequency and spatial distribution. As was also observed with depth electrode recordings the typical ictal pattern consists of repetitive rhythmical discharges of 1 to 2Hz progressing to faster frequencies in the upper theta range (Engel 1996?). Ictal changes of the surface EEG usually appear only after the laterobasal cortex of the temporal lobe has been invaded by the seizure starting in the amygdalo-hippocampal area. This is probably the explanation for the finding that the frequency of ictal activity on the scalp EEG usually is in the theta range. Imaging: The method of choice is the high resolution MRI. There is vast literature about the high sensitivity and specificity of this method in detecting the morphological substrate of mTLE: the hippocampal sclerosis (an excellent review is given in Kuzniecky and Jackson 1995). Atrophy of the hippocampal formation is best seen in T1 weighted including inversion recovery sequences whereas the increased signal in T2 weighted images indicates the sclerotic tissue replacing the neuronal loss especially in the CA1, CA3, and CA4 (endofium) region. FLAIR sequences can be helpful in the differentiation of CSF from sclerosis. Regional blood flow, metabolic alterations, and detection of biochemical metabolites is the domain of functional imaging methods, SPECT, PET, and functional MRI. In most cases with mTLE these more sophisticated procedures are not necessary for establishing the syndrome diagnosis but they are extremely important for a better understanding of the pathophysiology of TLE. 3.1.2 Medial temporal lobe epilepsy etiology other than hippocampal sclerosis. Pathologic processes of various etiology such as tumors, cysts, substance defects due to vascular or traumatic origin all can lead to TLE more or less indistinguishable from mTLE except that the course of the disease usually is different with the epilepsy starting dependent on the time when the lesion becomes epileptogenic eventually. This may be the case also in early childhood in many of the mostly benign forms of developmental tumors but can occur at any age. Clinically, medially located tumors relatively often produce olfactory sensation but this is not at all specific. No other discriminating factors are known and this is also true for the EEG. Magnetic resonance imaging is the technique to demonstrate the lesion. 3.1.3 Lateral (neocortical) TLE. From all regions of the temporal neocortex seizures can arise. Here one has to be aware of the fact that wide areas not only of the temporal but also of all other neocortices are silent when electrically stimulated. From this fact one can conclude in analogy that also the intrinsic stimulation by an epileptic seizure produces clinical symptoms only when 'symptomatogenic areas' are directly or secondarily excited by spread of seizure activity from clinically silent regions. Clinical experience and studies have shown that sensations like auditory or visual auras with more complex features are more frequent in neocortical temporal lobe but ictal symptoms occurring later in the course of the seizure are indistinguishable from seizures with medial temporal lobe onset (Ebner 1994). All kinds of structural abnormalities (tumors, vascular, inflammatory, traumatic lesions, and so forth) affecting the temporal neocortex are lesions with possible epileptogenicity. Magnetic resonance imaging is the method of choice to detect the structural alteration, EEG can document the epileptogenicity of the lesion. An interesting phenomenon is the fact of dual pathology, namely, the co-occurrence of an extrametiotemporal lesion with hippocampal sclerosis. It is unclear whether this is a coincidence or whether the hippocampal sclerosis develops secondarily as consequence of the ongoing seizure activity. Dual pathology often poses difficult problems if surgery is considered in medically intractable cases requiring usually invasive EEG recording to figure out whether one or both lesions are epileptogenic. In the EEG, sharp waves with field maxima at the temporal leads are frequent. Ictal EEG more often shows low voltage fast activity at the onset
than rhythmic theta compared to cases with mesial temporal origin.

3.2 Frontal lobe epilepsy. The frontal lobes comprise almost half of the human neocortex. Thus, it is not surprising that a variety of different seizure symptoms may be produced by the various functionally different regions. According to the proposal for revised classification of epilepsies and epileptic seizures (1989) general characteristics of seizures arising in the frontal lobes are: 1. Generally short duration. 2. Complex partial seizures with often only minimal or no postictal confusion. 3. Rapid secondary generalization. 4. Predominant motor manifestations. 5. Complex gestural automatisms at seizure onset. 6. Frequent falling when the discharge is bilateral. However, what was said for the seizures originating in the temporal lobes is even more true for those with onset in the frontal cortex: ictal symptoms are the consequence of epileptic activation of symptomatogenic zones. Under this perspective the clinical semiology not necessarily gives the exact information about the location where the seizure starts from, namely, the ictal onset zone, but rather when the first symptomatogenic zone has been activated. It is well known that seizure activity quite often spreads very rapidly for example from the parietal to the frontal cortex with the corresponding ictal semiology of a focal tonic seizure presenting as 'frontal lobe seizure'. In conclusion, it seems preferable not to classify epileptic seizures according to anatomy but only epileptic syndromes (Lueders 1998). Frontal lobe epilepsy means that seizures originate from frontal lobe cortex. Theoretically, there could be as many frontal lobe epilepsy syndromes as frontal cortical areas capable of producing epileptic activity that leads to manifest ictal symptoms. Nevertheless, in clinical praxis it is probably helpful to subdivide frontal lobe epilepsy into several relatively typical anatomically based electroclinical complexes such as perirolandic, supplementary sensorimotor area, dorsolateral, frontopolar, orbitofrontal, and cingulate. The definition of these frontal lobe syndromes is based on the various diagnostic measures used in the preoperative work up. Probably, the best way to delineate one of the above mentioned frontal lobe syndromes is to detect a small lesion in the MRI, for example a cavernoma in the frontopolar area, and find concordant results in the additional clinical investigations proving the epileptogenicity of this lesion: seizure semiology (for example hypermotor symptomatology), surface EEG and epicortical EEG (ictal activity originating in the immediate neighborhood of the lesion at seizure onset), ictal SPECT (focal hyperperfusion). If this patient becomes seizure free after a lesionectomy it seems justified to call this syndrome a frontopolar epilepsy. Since quite often epileptogenic lesions are more extended, a mixture of findings rather than 'pure' syndromes of the mentioned electroclinical complexes may be observed. Although not as much literature exists about frontal lobe epilepsy (248 articles in the medline search, cf. 3.1) compared to TLE there are some excellent books containing the present knowledge of this field (Chauvel, Lueders, Wolf).

3.2.1 Perirolandic epilepsy. Ictal symptoms produced in the primary motor area typically are rhythmic cloni sometimes showing a ('Jacksonian') march from distal to proximal muscles (or the other way around). Sometimes patients report a tension in the muscles before the real motor activity begins. This sensation can clearly be distinguished from somatosensory sensations felt as tingling that results from parietal (SI) regions. Due to the cortical representation, these simple partial seizures involve the contralateral face or hand area. All kinds of lesions in the rolandic area can be the morphological substrate of an epilepsy of the primary motor area. Focal motor seizures are often not associated with epileptiform activity in the surface EEG probably due to the relatively small area of cortex sufficient to produce this motor symptom. On the other hand, there can be focal clonic seizures as the only seizure type due to large tumors in the frontoparietal area or lesions mostly of vascular origin with widespread lateralized unspecific EEG abnormalities during actual seizure. Perirolandic epilepsy can occur at any age.

3.2.2 Supplementary sensorimotor area epilepsy. Seizures arising and activating the supplementary sensorimotor area typically are brief lasting not longer than 30 or 40 seconds. Usually without any warning, motor manifestations consisting of sudden tonic posturing of one or more extremities can be observed. It is common that both sides of the body are affected simultaneously. Consciousness is usually preserved (although not necessarily responsiveness). Vocalizations such as crying, moaning or repetitive utterances are not rare. At the end of the tonic phase some rhythmic cloni may occur. Seizure frequency is high with several fits per day often clustering during sleep. Neurological examination and intelligence is normal in the majority of patients. Surface EEG is of little localizing value. Sometimes rhythmic slowing in the theta/delta range or epileptiform interictal activity can be seen over the midline in the sleep EEG which has to be distinguished from vertex waves. Ictal EEG often is obscured by the massive EMG artifacts. Response to drugs, especially in the presence of a lesion, is poor.

3.2.3 Dorsolateral Epilepsy. Typical seizure semiology seen in this area are tonic seizures with versive head and eye movements and speech arrest when the dominant hemisphere is affected. Clonic activity indicating involvement of the primary motor area is rather rare.

3.2.4 Frontopolar epilepsy. Ictal semiology described as characteristic for the frontopolar area consists of forced thinking, initial loss of contact progressing to motor activity (aversive head and eye movements, axial clonic jerks and falls). Autonomic signs can be present (piloarrection, facial skin rush/paleness). In the EEG frontal sharp waves maximum at the frontopolar leads may be seen as well as rhythmic activity
indicating an EEG seizure. Lateralization of the epileptiform activity can be difficult.

3.2.5 Orbitofrontal epilepsy. Seizure semiology characteristic for this part of the frontal lobe consists of psychomotor symptoms often of massive rhythmical movements of proximal body parts including thrashing, bicycling and other bizarre movements (hypermotor seizures). Autonomic sensations are frequent. Olfactory sensations may occur but are extremely rare compared to those auras of medial temporal origin. In fact, there are only a few single case reports in the literature describing an olfactory sensation as aura coming from the orbitofrontal area. Intercital as well as ictal EEG usually is not very helpful in localizing the epileptogenic area because of the hidden location of this part of the cortex with respect to the scalp electrodes. Propagated seizure activity over central and frontolateral regions can sometimes be seen and this can be helpful in the differential diagnosis since the sometimes bizarre seizure symptoms may easily be confounded with psychogenic seizures.

3.3 Parietal lobe epilepsies. Seizure symptoms which may be ascribed to parietal cortex are simple focal seizures with somatosensory sensations like tingling (by far the most frequent), vibration, numbness, unpleasant pressure, and rarely pain (Ebner and Baier et al 2000). Parts of the body with the largest representation (hand, face, mouth, tongue) are most frequently affected and there is also a tendency to a Jacksonian march (cf. 3.2.1). Other sensations produced by epileptic activation of the inferior parietal cortex are vertigo or spatial disorientation. Seizures arising from the parietal operculum may be accompanied by sensations of the whole contralateral body and quite often include also the ipsilateral side of the body. The subjective sensations are not different to those coming from the SI region. Other auras ascribed to parietal regions are distortions of the visual perception (metamorphopsias), alterations of the perception of the body (dysmorphopsia/gnosia), and loss of awareness of a part or half of the body (asomatognosia). Spread of epileptic activity to temporal or frontal cortex is frequent. The main seizure type (for example psychomotor, focal tonic and so forth), therefore, is determined by the symptomatogenic zone(s) that is (are) activated by the epileptic discharges. It should be kept in mind that despite the ictal onset zone(s) that is (are) activated by the epileptic discharges, it is not very helpful in localizing the epileptogenic area because of the rapid spread of the seizure discharges to more anterior located brain areas is the rule.

Further Reading