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EPILEPSY
out of the shadows
A Global Campaign Against Epilepsy

EPILEPSY

A manual for Medical and Clinical Officers in Africa

EPILEPSY: A manual for Medical and Clinical Officers in Africa

International League Against Epilepsy

World Health Organization

International Bureau for Epilepsy

Epilepsy

A manual for Medical and Clinical Officers In Africa

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Preface and acknowledgements to the revised edition 2002

The initiative of the International League Against Epilepsy (ILAE), the International Bureau for Epilepsy (IBE) and the World Health Organisation (WHO) to start a Global Campaign Against Epilepsy kindled the search for a textbook, in order to provide medical and clinical officers working in rural areas in Anglophone Africa with sufficient and sound background information.

The choice fell on a manual, written by the late Nelly Dekker, a Dutch expatriate doctor who had worked in Ethiopia and Kenya for many years. She was a co-founder of the Kenyan Association for the Welfare of Epileptics, an initiative of Caroline Pickering, mother of a child with epilepsy. After Dr Dekker's untimely death in 1995 her husband released the copyright of the book to allow for non-profit distribution in the developing world.

In order to update the book and adapt it for use in all of Anglophone Africa the Secretariat of the Global Campaign Against Epilepsy appointed an editorial committee with expertise in Africa, America and Europe. Members of the committee were Bryan Kies (South Africa), Cecilia Bartels (Kenya), Gretchen Birbeck (USA/Zambia), Harry Meinardi (Netherlands), Jens Mielke (Zimbabwe), and Zenebe Gedlie Damtie (Ethiopia). As the original was in English the editorial committee was Anglophone, however, a similar book will be made available in French and in Portuguese.

This committee was charged to refrain from rewriting the book or produce a completely new text, yet to ensure its accordance with present day expert knowledge and opinions. They gratefully acknowledge helpful suggestions and comments from the secretariat of the Global Campaign Against Epilepsy (Pete Engel, Hanneke de Boer and Leonid Prilipko), and the regional advisor for mental health WHO/ AFRO Custodia Mandlhate.

The project would have been much more costly if the editors had not been assisted by the staff of the printer-division of PASWERK, a sheltered workshop also employing people with epilepsy, CRUQUIUS, The Netherlands. In particular the expert help of Ms. Jacky van Ruiten assured that hurdles and pitfalls in the conversion and adaptation of the original text to its present printable form were overcome.

The final responsibility for its contents remains with the editors. They realise that some of their choices are open to criticism but they are confident that an evaluation in five years time whether the book has served its purpose will be positive.

Introduction and acknowledgements to the first edition

The Kenya Association for the Welfare of Epileptics (KAWE) was established in 1982. Through its activities, which include clinics and public education in the form of film and printed materials, people have been made aware that epilepsy is a medical condition and that it can, therefore, be treated medically and be controlled. As a result, the number of patients with epilepsy seeking treatment is increasing rapidly.

Epilepsy is a major public health problem in Kenya.

For this reason a manual has been prepared to help those people (medical officers, clinical officers and nurses) who are responsible for the primary health care of these patients and who may be working in the rural areas.

As early treatment of convulsions and of epilepsy is very important, it is essential to start correct treatment immediately.

But in order to be able to start this treatment, the doctor or clinical officer needs to know the causes of the seizures and epilepsy, what type of seizure and epilepsy the patient has, and which drug should be used.

It is emphasized that not all seizures are a form of epilepsy and therefore it is necessary to know the different causes of seizures in order to be able to distinguish those not due to epilepsy and to treat them adequately. Knowing the cause of epilepsy will also help patients overcome their superstitions about the disease.

The different types of seizures and their general classification of the epilepsies are given in Chapters 7 and 8 [Chapters 5 and 6 in the 2002 edition], while a more detailed discussion of the epilepsies and the epileptic syndromes is in Appendix A.

In this manual the patterns of the EEG findings in different epilepsies are not illustrated or discussed as an EEG can only be done in Nairobi.

As the drugs used in treating patients with epilepsy may be dispensed for years, it is necessary to know a few facts about these medicines. Although the side-effects and interactions with other drugs are not always understood or predictable, these actions must be known by everyone dealing with these drugs. General information about these actions is given, while the individual anticonvulsants are discussed in detail in Appendix B. However, the therapeutic blood levels of the various medicines are not mentioned as they are not routinely determined in Kenya.

Thanks are due to Professor H. Meinardi (Instituut voor Epilepsie bestrijding, Heemstede), for his continuous advice and comments, and my colleagues L.T. Oei and J.C. Doelman (Epilepsiecentrum Kempenhaeghe, Heeze) in the Netherlands, for their help and for providing the necessary references.

I also thank the following colleagues in Kenya who read the manuscript and made valuable comments: Professor R. Ruberti, P. Muiva, P. Muthiga, C. Forbes, G. Rietkerk, D. Franssens, H. Wouters, M. Gajjar (psychologist), W. Nieuwstraten, and M.C.J. Bosman.

Special thanks are due to Dr J. Moore-Webster who was indefatigable in helping to formulate the contents in as concise a manner as possible and to Drs Miyanji and Stanfield who helped make the information readable and arranged in a logical manner.

Mrs A. Melvin and Mrs. C. Pickering are thanked for patient typing and retyping, Mrs C. Agola for editing and Mr G.C. Backhurst for typesetting.

Finally, we are grateful to Christelijke Vereniging voor de Verpleging van Lijders aan Epilepsie, Heemstede, The Netherlands, for assistance in printing this manual.

Nelly Dekker, Nairobi, 1990.

Abbreviations

AED	Antiepileptic drug
AIDS	Acquired immune deficiency syndrome
EEG	Electro-encephalogram
GTCS	Generalized tonic-clonic seizure
HHE	Hemiconvulsions-hemiplegia-epilepsy
HIV	Human immunodeficiency virus
ILAE	International League Against Epilepsy
KAWE	The Kenya Association for the Welfare of Epileptics
REM	Rapid eye movement
SSPE	Subacute sclerosing pan-encephalitis

Glossary

Absence absent; not being there; name given to seizures that only cause a brief lapse of consciousness

Anoxia lack of oxygen reaching the tissues of the body

Anticonvulsant agent preventing or arresting a convulsion

Antiepileptic drug a term often preferred instead of anticonvulsant

Aphasia loss or impairment of the power to use words due to a lesion in the brain

Asphyxia lack of oxygen or excess of carbon dioxide in the body, usually caused by interruption of breathing

Astatic not able to stand

Ataxia loss or impairment of muscular coordination

Atonic without (muscle) tone (used interchangeably with astatic)

Auditory relating to the sense of hearing

Automatism more or less coordinated movements independent of conscious control

Autonomic relating to that part of the vertebrate nervous system that regulates involuntary action (e.g., intestines, heart, glands)

Calcification the process by which tissue becomes hardened by deposits of calcium, or the calcified structure

Choreo-athetosis constantly occurring slow, involuntary abnormal movements

Clonic alternatingly flexing and stretching of limbs

Cryptogenic symptomatic, but whose cause is hidden or occult

Déjà vu an illusion in which a new situation is incorrectly perceived as being a repetition of a previous situation

Dementia organic deterioration of mental or intellectual faculties

Diplegia paralysis of corresponding parts on both sides of the body
Dyskinetic disordered movements
Dystonic disordered muscle tone
Dysphasia words are distorted or used incomprehensibly
Focus an area in the brain that is the starting point of a partial (as opposed to generalized) seizure
Fortification spectra a flashing array of black and white zigzags seen as a warning sign of migraine
Gustatory relating to the sense of taste
Half-life time (i.e., in serum) time it takes the body to eliminate half of an administered dose of drug.
Hemianopsia blindness in one half of the visual field
Hemiplegia paralysis of one side of the body
Ictus refers to seizure or stroke
Idiopathic arising spontaneously (often used interchangeably with genetic)
Idiosyncrasy individual hypersensitivity, for example, to a drug or food
Lesion an abnormal change in the structure of an organ, or part of an organ, due to injury or disease, especially an abnormality that is circumscribed and well defined
Location a particular spot, place, site or position
Olfactory related to the sense of smell
Opisthotonus a form of spasm in which the body curves backwards
Partial part of, or relating to, a part rather than the whole; not general or total
Pyknolepsy composite word formed by pyknos (Greek for numerous) and epilepsy. A term used to describe frequent daily absence seizures like in Childhood Absence Epilepsy
Sensory related to sensation or the senses
Somato-sensory related to sensory activity having its origin elsewhere than in the special sense organs (e.g., eyes or ears) and conveying information about the state of the body proper and its immediate environment
Symptomatic having the characteristics of a particular disease, a disturbance of function due to a disease and not to a genetic cause.
Tetraplegic paralysis of all four limbs
Vertiginous causing, or tendency to cause, dizziness
Visual related to the sense of sight

1 Definitions

EPILEPSY

The word “epilepsy” comes from the Greek and means to be taken, seized or attacked.

Epilepsy is a condition characterized by *repeated seizures* due to a disorder of the brain cells. It is a life-long tendency, though the seizures may start at any time during life and occur sporadically or frequently. Some of the epilepsies are confined to particular age groups. Some suffer from it their whole lives and others only for a few years (average approximately 13 years).

Epilepsy may develop after a particular identifiable event (e.g., asphyxia, head injury, meningitis), in which case it is called *symptomatic epilepsy*, or it may develop without any identifiable cause, and then it is called *idiopathic epilepsy*.

> Sometimes the term “secondary epilepsy” was used for symptomatic epilepsy and “primary epilepsy” for idiopathic epilepsy. But this is confusing and should not be done any more. In this manual the terms primary and secondary are only used in relation to seizures and not in relation to epilepsy. A *secondary generalized seizure* is a seizure which starts in one place and then becomes generalized, while a *primary generalized seizure* is one generalized from its onset.
>
> Further discussion of these terms is in chapters 5 and 6.

SEIZURE

A seizure is a result of excessive nerve-cell discharges in the brain. It is seen as a sudden abnormal function of the body, often with loss of consciousness, an excess of muscular activity, or sometimes a loss of it, or an abnormal sensation.

The excessive nerve-cell discharges or excitation may remain in a small area of the brain (a localized lesion or focus) giving rise to *partial (focal) seizures*, or start immediately in the whole brain or spread from the small area (focus) to the whole brain and spinal cord giving rise to *generalized seizures*.

Not only may these discharges vary in site, but also in severity and extent, therefore a wide variation of clinical forms is seen.

A seizure is also referred to as a **convulsion**, **fit**, or **attack**. However, the words “convulsion” or “fit” are usually used to refer to seizures with tonic-clonic muscle movements.

2 Epidemiology

PREVALENCE

Prevalence is the ratio of those with a certain disease to the entire population.

Epilepsy is a chronic disease with a high prevalence rate. Therefore every medical practitioner will see patients with epilepsy and be asked to treat them. Epilepsy is more common in the developing countries than in the developed ones. Racial differences have not been observed but environmental and social differences seem to be important.

Significant variation in epilepsy prevalence has been noted in relatively local geographic regions despite similar methodologies and case ascertainment suggesting that local circumstances may strongly influence epilepsy epidemiology.

Pierre Marie Preux (2000) reported the prevalence of epilepsy in African countries and found a variation of 5.2/1,000 to 58/1,000. In his review (Literature review 1, page 6) one paper from Tanzania was reported presenting a prevalence of 10.2/1,000. Two years later Rwiza published a second paper the outcome of which is added to the table of Preux reporting a prevalence of 35.8/1,000 from an area near the one reported in his first survey.

INCIDENCE

Incidence is the rate at which new cases of a disease occur within a given period (e.g., a year) in a given population. In the case of epilepsy, the annual incidence is usually calculated per 100,000 population.

In all known surveys the annual incidence rate is highest in the youngest age groups, decreases during childhood, diminishes among adults, and rises again in old age (see fig. 1).

About incidence Hauser (1997) writes: The only data on the incidence of all epileptic syndromes come from Bordeaux, France. The incidence of idiopathic localization-related epilepsy was 1.7/100,000 (7% of all cases). An additional 13.6/100,000 (56%) had symptomatic localization-related epilepsy. Thus, if the same criteria are used as in most other contemporary incidence studies, about 60% of cases can be classified as partial seizures. Each of the following syndromes accounted for about 1% of new cases: juvenile myoclonic epilepsy, awakening grand mal, and West syndrome. About 2% had pyknolepsy (childhood absence epilepsy). These proportions are similar to those provided by the Rochester, Minnesota, studies. Crude incidence for all epilepsy (about 24.5/100,000) was about half that reported in other recent studies in industrialized countries. A few reports of incidence of specific epileptic syndromes in other total-population studies provide data consistent with the above figures.

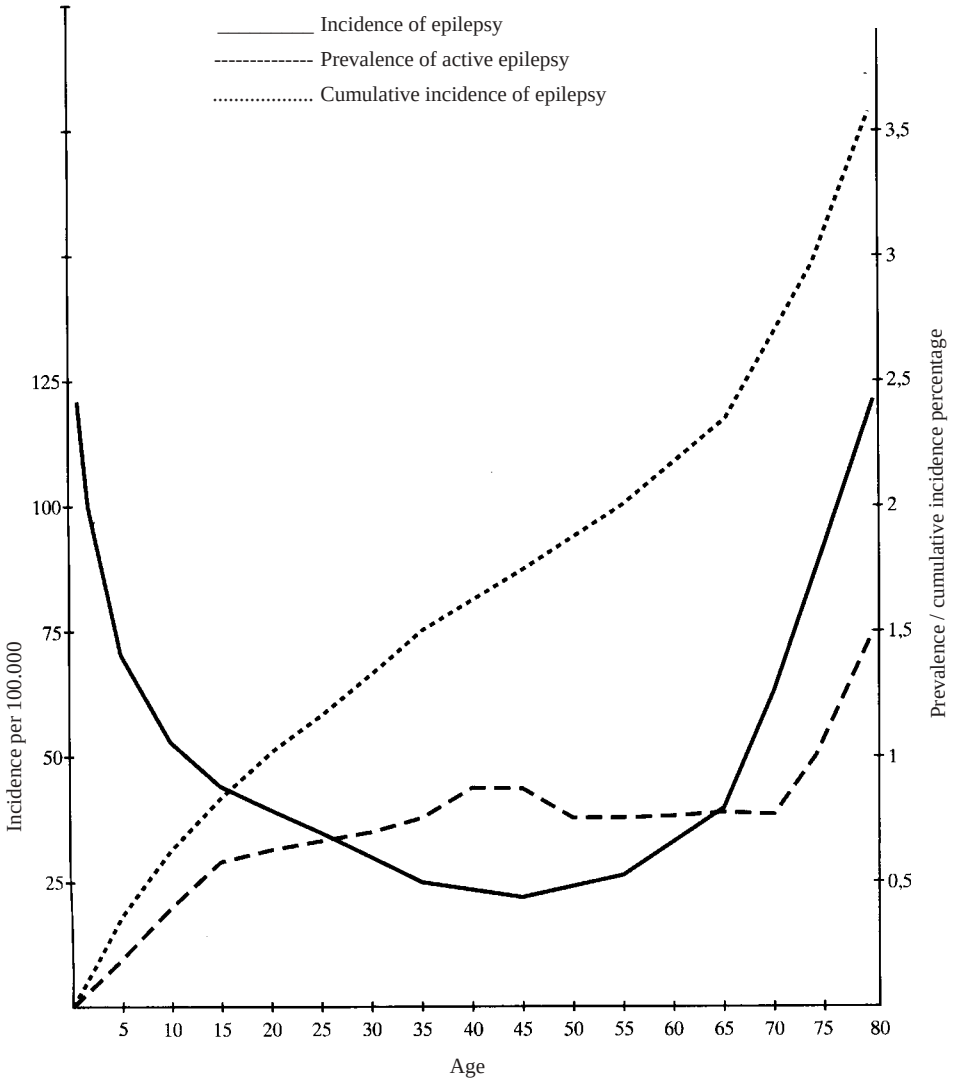


Figure 1. Incidence, prevalence and cumulative incidence rates for epilepsy in Rochester, Minnesota

(adapted from Hauser et al. 1993)

Literature review 1. Prevalence of epilepsy in African countries
Adapted from P.M. Preux, 2000

Country	*Author*	*Cases studied*	*n/1,000*
Cameroon (Bilomo)	Dongmo et al. 1998	1900	58.0
Liberia	Goudsmit et al. 1983	4436	28.0
Senegal	Diop et al. 1996	2803	21.0
Togo	Balogou et al. 2000	9143	18.6
Kenya	Kaamugisha and Feksi 1988	2960	18.2
Togo	Dumas et al. 1989	5264	16.7
Mali	Farnarier et al. 2000	5243	15.6
Benin (Savalou)	Avodé et al. 1996	1443	15.2
Togo (Abekou)	Grunitzky et al. 1996	4182	13.1
Uganda	Kaiser et al. 1996	4743	13.0
Togo (Kloto)	Grunitzky et al. 1991	19241	12.3
Burkina Faso	Debouverie et al. 1993	16627	10.6
Tanzania	Rwiza et al. 1992	18183	10.2
Tanzania	Rwiza 1994	20284	35.8
Senegal	Ndiaye et al. 1986	7682	8.3
Ivory Coast	Kouassi et al. 1988	1176	7.6
Nigeria	Longe and Osuntokun 1989	2925	6.2
Ethiopia	Tekle-Haimanot et al. 1990	60820	5.2

3 Causes

CAUSES OF A SEIZURE

Any person may develop a seizure in certain circumstances. A seizure is a symptom of an abnormal condition. It is imperative to establish which condition is the cause. The various causes of seizures are listed in table 1. Some are common, some are very rare. If no investigations are carried out it is not possible to find out what is wrong. The better our investigation methods are, the more likely we can find a cause. If, for instance, in a newborn baby with a seizure no blood is examined, no one will ever know if the seizure was due to a hypoglycaemia, hypocalcaemia, or something else. X-rays, CT scans, and even more modern investigation methods can show structural lesions, while chemical and serological investigations will show metabolic and parasitic abnormalities. In rural areas where none of these investigations can be done, the cause will often remain obscure. But it is extremely important that every Health Centre, even in the most rural of areas, has at least a small laboratory, so that simple tests can be done. Then common disorders can be recognized as the cause of the seizure and appropriate treatment given—instead of, or before anticonvulsants are used—thus preventing further harm. Many of the metabolic disturbances, bacterial and parasitic infections are easily treated when recognized. The relationship of fever and seizures is discussed on page 69. Table 2 presents causes that may be direct or fever mediated. Three examples, often seen in paediatric practice, are given to illustrate these points:

– A child with vomiting and diarrhoea started to convulse and is brought to the clinic. There is dehydration and therefore an electrolyte imbalance is likely. Treatment consists of fluids and salts.

– A mother cannot wake her child in the morning and brings him/her to the clinic. The child is unconscious and is convulsing. First determine the blood glucose level. If it is low, treat with glucose solution and do *not* give anticonvulsants.

– A child with high fever and convulsions is brought to the clinic. If no other disease is obvious, a blood smear for malaria parasites and a lumbar puncture must be done to diagnose possible meningitis. A bacterial meningitis should be treated as early as possible with adequate intravenous antibiotics to prevent later neurological sequelae. As it takes some days before the antibiotics are effective, anticonvulsants have to be given to control the seizures.

Table 1. Causes of a seizure

Metabolic

- Hypoglycaemia
- Hypocalcaemia
- Electrolyte imbalance
- Hypomagnesaemia
- Hyperbilirubinaemia (kernicterus)
- Pyridoxine deficiency/dependency
- Uraemia
- Phenylketonuria**
- Porphyria

Infections

INTRACRANIAL

- — meningitis*
- — encephalitis*
- — AIDS*
- — Neurosyphylis
- — cerebral malaria*
- — rabies
- — toxoplasmosis
- — cysticercosis
- — encephalopathy (SSPE)

EXTRACRANIAL

- — febrile illnesses (febrile convulsions)*
- — pertussis
- — pertussis immunization
- — tetanus

Trauma

- Birth trauma*
- Head injury in later life*
- Cold injury in newborns
- Hypothermia

Anoxia

- Birth asphyxia*
- Conditions later in life

Toxic

- Alcohol and withdrawal from alcohol*
- Carbon monoxide poisoning
- Drugs (high dose i.v. penicillin, strychnine, etc.)
- Lead poisoning
- Organo-phosphorus insecticide poisoning

Space-occupying lesions

- Haemorrhage
- Abscess
- Tumour
- Tuberculoma*
- Cysticercosis
- Toxoplasmosis

Circulatory disturbances

- Cerebro-vascular accident (stroke)
- Vascular anomalies
- Sickle-cell crisis*

Cerebral oedema

- Hypertensive encephalopathy
- Eclampsia

Congenital

- Malformations of the brain (hydrocephalus, microcephaly, etc.)
- Tuberous sclerosis (Bourneville disease)**
- Neurofibromatosis (von Recklinghausen disease)**
- Encephalo-trigeminal facial angiomatosis (Sturge-Weber's syndrome)**

Degenerative diseases

- Niemann-Pick disease**
- Cerebromacular degeneration**
- Dementias*

Epilepsy

*Most common causes; **Rare topics treated in more detail on page 9

Notes to Table 1

Phenylketonuria
This is a rare disease transmitted by a recessive gene. There is inability to form tyrosine from phenylalanine, resulting in the formation of excessive phenylketone bodies which are excreted in the urine. Infants appear to be normal at birth, but when the plasma phenylalanine levels rise, progressive brain damage begins and reaches a limit at two to three years of age unless a diet low in phenylalanine is started in early life. If no diet is instituted, mental retardation, skin changes (excessive oiliness, scaliness, excematous lesions), musty odour of the urine and of the body occur.

Tuberous sclerosis (T.S., Bourneville disease)
An ectodermal dysplasia inherited as a dominant trait, although almost 50% occur for the first time (i.e., as a result of a sporadic mutation). Mental retardation varying from mild to severe occurs in 60–70% of people with T.S., and in about 90% there is epilepsy. The seizures usually develop during the first year of life in the form of infantile spasms. Later in life they may be myoclonic-astatic seizures.

Behaviour disorders such as hyperactivity and destructiveness are common.

There are lesions in the skin (fibroadenomas of the sebaceous glands over the nose and cheeks, leathery patches, hypopigmented patches, subungual fibromas). Small tumours may occur in the kidneys, liver, spleen, lungs or heart. Nodules and cystic lesions may occur in the eyes, bone or brain. The cortical and subependymal nodules frequently calcify and may then be seen on the skull X-ray or CT scan.

Neurofibromatosis (von Recklinghausen disease)
Inherited as a non-sex-linked dominant. Freckling in the axilla is pathognomonic, and sharply outlined *café au lait* areas occur on the skin. Neurofibromas are found cutaneously and subcutaneously along cranial and spinal nerves, osteitis fibroma cystica in the bones and nodules in the central nervous system.

Encephalo-trigeminal facial angiomatosis (Sturge-Weber's syndrome)
Patients are often mentally retarded, and all develop epilepsy with lateralized seizures. There is a large telangiectasis (port-wine stain) in the trigeminal area involving skin, scalp, skull and meninges. There are typical opacities on the skull X-ray. There may be a haemangioma in the choroid causing glaucoma.

Degenerative diseases
The features of these diseases are progressive loss of previously acquired intellectual, motor and sensory functions. Early manifestations of degeneration of cerebral grey matter show as dementia and seizures, whereas degeneration of cerebral white matter shows as spasticity, hypotonia or ataxia. But eventually in both forms the entire nervous system tends to be affected and the person becomes totally helpless with loss of intellectual and voluntary motor functions.

Cerebromacular degeneration
Transmission is on an autosomal recessive basis. These degenerations are ganglioside-storage diseases.

- Infantile form (*Tay-Sachs' disease*)
  Onset is at 2–6 months of age. The infant becomes apathetic and loses interest in his surroundings. There is progressive blindness (macular degeneration with macular cherry-red or black spots in the fundi), spasticity, seizures, wasting, dementia, and death usually occurs before the third birthday.
- Late infantile form (*Bielschowsky syndrome*)
  Onset is between the ages of 1 and 3 with seizures, ataxia, dementia, spasticity and blindness. Death occurs within three to five years.
- Juvenile form (*Spielmeyer-Vogt or Batten disease*)
  Onset between 3 and 7 years with the same symptoms but a much slower course than above.

Niemann-Pick disease
This is a heredo-familial disease with a disturbance of the lipid metabolism. Soon after birth physical and mental retardation starts. There is general emaciation, but the abdomen is distended due to the enlarged liver and spleen. In the fundus a cherry-red spot may be seen, as in Tay-Sachs' disease. There is progressive deterioration, and death usually occurs before the third year of life.

Dementias
Of the dementias in later life Alzheimer's disease is probably the most frequent cause.

Table 2. Fever and convulsions

Intracranial infections
– meningitis/encephalitis
– cerebral malaria
Extracranial infections
Febrile Convulsions (FC) are often associated with
– otitis media
– upper respiratory infections
– lower respiratory infections
– shigellosis
– urinary tract infections
– measles, roseola infantum
– malaria

When the disorder that caused seizures is cured the brain may have been permanently altered so as to give rise to spontaneous seizures. This person then has epilepsy.

CAUSES OF EPILEPSY

Epilepsy is a condition *with recurrent seizures.* These may be idiopathic or symptomatic. Epilepsies can start at any age. A rough outline of the relationship between cause and age of onset is presented in fig. 2.

If an acute disturbance, a metabolic like hypocalcaemia, or an infection such as meningitis, or a poisoning or any of the other causes mentioned in table 1 are recognized and treated adequately, epilepsy will not follow.

If the acute disorder was too severe, or not treated correctly, convulsions might have become prolonged and continuous, resulting in anoxia of the brain with subsequent brain damage followed by epilepsy.

In some infections, e.g., tuberculosis, toxoplasmosis, cysticercosis, the disease may leave calcified areas in the brain.

Some diseases—tuberous sclerosis, Sturge-Weber's syndrome—present with calcifications in the brain.

A haemorrhage, abscess or tumour may present with repeated seizures but when the blood, pus or tumour has been successfully removed surgically, no epilepsy needs to follow.

Any head injury, including birth trauma, may result in permanent changes of brain tissue, i.e., scar tissue.

Any area with abnormal brain tissue (calcifications, scars, or vascular abnormalities) may act as a focus from where abnormal activity of the neurons takes place causing "symptomatic epilepsy".

The causes mentioned in table 1 might lead to epilepsy. Some of them are very common in Africa (cerebral malaria, birth trauma, infectious diseases and accidents later in life), while others are very rare.

Neurocysticercosis, a parasitic infection associated with pig-rearing and poor hygiene is very common in Latin America and India. Only people coming or returning from a country with prevalent neurocysticercosis might suffer from it.

Oncocerciasis has recently been suspected of causing epilepsy as well. It has to be kept in mind if a patient has come from an endemic area.

Some diseases are so rare that the average doctor will not know about them and will not, therefore, recognize them if they are present. Such diseases can only be diagnosed by specialists. A number of these diseases are mentioned on page 9 so that if any *are* suspected, the patient should be referred to a specialist.

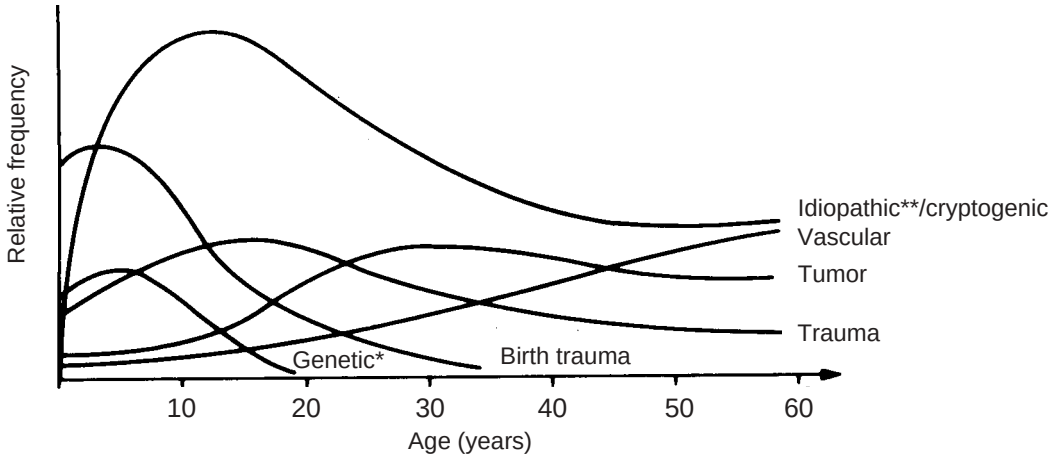


Figure 2. Approximate frequency of different causes of epilepsy, developing at different years

** Genetic brain disorders with epilepsy*

***Idiopathic = genetic epilepsy without other disorders = epilepsy sui generis*

EPILEPSY AFTER HEAD INJURY

The onset of these seizures depends on the age at the time of the accident, e.g., birth trauma will give seizures in the first year of life.

Not everyone who has had a head injury will develop seizures. Seizures are more common when the injury has been penetrating, when there was a depressed skull fracture, an intracranial haematoma, or if in the acute state there was post-traumatic amnesia of more than 24 hours' duration. Fifty percent of post-traumatic seizures develop in the first year following the accident, and another 20% will develop by the end of the second year. The use of prophylactic anticonvulsants after a serious head injury should be considered.

EPILEPSY CAUSED BY A BRAIN TUMOUR

A tumour, benign, malignant or a metastasis, may occur in any age group, but is more common in the older age group.

Epilepsy starting after the age of 20 years should always raise suspicion for a tumour, and full investigations, preferably with CT scan should be done.

EPILEPSY FOLLOWING CEREBRO-VASCULAR DISEASE

In people over 50 years old, cerebro-vascular disease is a common cause of epilepsy. Seizures may follow a cerebro-vascular accident (stroke), or may develop during the course of subclinical cerebro-vascular disease.

In all these groups (injury, tumour, cerebro-vascular accident) the type of seizure depends on the localization of the injury.

Preferred treatment is with phenytoin or carbamazepine.

When there are secondary generalized seizures, phenobarbitone may be used as an alternative.

It is worth bearing in mind that a cause for the underlying seizures can be found in only 30–40% of epilepsy patients. In the rural areas, where people live far from health care facilities, the percentage of symptomatic epilepsy is probably higher than in the urban areas. And the prevalence rate of epilepsy in developing countries is likely higher than in developed countries due to higher rates of perinatal injuries, more perinatal and childhood infections, and less timely treatment than is available in industrialized countries.

Prevalence of epilepsy among mentally handicapped is high, between 20–35%. Conversely, concomitant mental handicap is present in about 10–15% of people with epilepsy.
In Tanzania, Matuja (1990) found that 48% of persons with epilepsy treated in Muhimbili Medical Centre had organic brain disease and psychological disturbances.

In 60–70% of patients (at least in developed countries) where no cause for the epilepsy can be found, part of these persons suffer from “idiopathic epilepsy” (idiopathic = spontaneous, self-generated, genetic).
In those cases where secondary damage is the probable cause, although such damage cannot be proven, the epilepsy is classified as “cryptogenic”.

4 Contributory factors

GENETIC FACTORS

In many, if not all, epilepsies there is a genetic factor which influences the threshold for seizures (fig. 3). Even in symptomatic epilepsy this factor plays a role, e.g., many people have had a head injury but only some develop epileptic seizures afterwards (see page 93).

If one parent has idiopathic epilepsy the risk of a child developing epilepsy is 4–6%, compared to a risk of 0.3-0.5% in the general population (Europe). If both parents have idiopathic epilepsy, the risk rises to 12–20%.

In parents with symptomatic epilepsy, there is still a slight increase in the risk—up to 2% in European studies.

EFFECTS OF BRAIN MATURATION

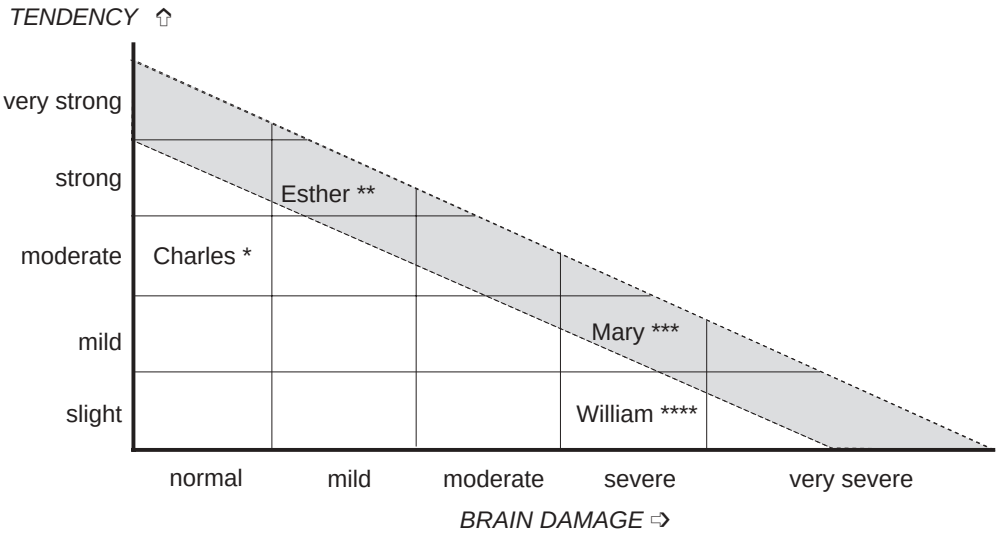
The resistance to seizures also depends on the maturation of the brain. The resistance in the first year of life (except during the newborn period) is very high, and therefore only a severe injury such as severe brain damage since birth, meningitis or tuberous sclerosis, will produce seizures.

Between the ages of one and four the resistance to seizures is very low. A simple febrile disease may precipitate seizures. After the age of four the resistance is again high, and seizures are mainly seen in already-brain-damaged children. This resistance diminishes again from about the seventh year when the idiopathic epilepsies tend to appear. The resistance is at its lowest around the time of the prepubertal growth spurt (Brown, 1982).

OTHER PRECIPITATING FACTORS

Apart from the condition and maturation of the brain and the genetic threshold, other factors may trigger a seizure. These factors may be different for each individual patient. Some patients learn which factors are important for them, and so they can modify their behaviour or activities to try to avoid seizures (see also page 75).

The most common factors are mentioned in table 3.



grey: seizures, white: no seizures

* Charles: moderate tendency, no brain damage, no seizures
** Esther: strong tendency, mild brain damage, has seizures
*** Mary: mild tendency, severe brain damage, has seizures
**** William: very slight tendency, severe brain damage, no seizures

Figure 3. Relation between brain damage and tendency to develop seizures

Table 3. Common precipitating factors

– Flashing lights (resulting in reflex epilepsy)
– Hyperventilation
– Lower alertness, sleep itself and lack of enough sleep
– Emotion
– Physical stress
– Special smells, sounds or sensations of touch
– Alcohol
– Hormonal changes, e.g., during menses
– High fever
– Overhydration

Some of these triggers are used to provoke epileptic activity for an EEG recording (see page 44).

5 Seizures

Four components of a seizure can be distinguished (table 4). Not all seizure types will have all these stages. The presence or absence and the nature of them are important for diagnosing the seizure type.

Table 4. Components of a seizure

– Prodromal phase
– Aura
– Seizure (ictus)
– Post-ictal phase

Prodromal phase
This phase begins a few hours or even days before the actual seizure and should not be confused with the aura. Prodromal symptoms are: headache, irritability, insomnia, bad temper, depression or increased activity.

Aura
An aura precedes the seizure by seconds or a few minutes. It is the beginning of the seizure and signals the focal onset of the seizure. The symptoms depend on the location of this focus. The feelings of the aura are often vague and indescribable, leading to extreme fear. Strange epigastric sensations, dreamlike experiences, unpleasant smells, etc. may occur. The patient remembers the aura very well, and although he/she will not always be able to recount it, he/she can affirm the presence of it, as it happens before consciousness is lost.

Seizure (ictus)
The characteristics important to know for their classification are mentioned in table 5. In most seizures there is a loss of consciousness, and the patient is therefore not able to give any information about the actual ictus. For this we are dependent on witnesses who have seen the actual seizure. The patient has no memory of the seizure.

Post-ictal phase

This phase may be absent, brief or may last several hours, and sometimes even days. There is usually a deep sleep and waking up with headache, tiredness, irritability, vomiting, confusion, muscular aches or ataxia. Transient paralysis of a part of the body, known as Todd's paresis may occur for a few hours or days. Altered speech or aphasia may occur when the dominant hemisphere of the brain has been involved. Altered behaviour and emotional outbursts may occur, and if these are interfered with, violent behaviour is likely.

Table 5. Characteristics of a seizure

– The type of seizure (see classification of seizures table 6)
– The duration of the seizure
– The frequency of the seizures
– The time of day or night that the seizure occurs, and its relation to sleep
– The presence of an aura
– The presence of a post-ictal phase
– The age of onset

Table 6. International classification of epileptic seizures

I. PARTIAL SEIZURES (seizures beginning locally)

A. Simple partial seizures (consciousness not impaired)

1. With motor symptoms
2. With somatosensory or special sensory symptoms
3. With autonomic symptoms
4. With psychic symptoms

B. Complex partial seizures (with impairment of consciousness)

1. Beginning as simple partial seizures and progressing to impairment of consciousness
   (a) With no other features
   (b) With features as in A 1–4
   (c) With automatisms
2. With impairment of consciousness at onset
   (a) With no other features
   (b) With features as in A 1–4
   (c) With automatisms

C. Partial seizures secondary generalized

II. GENERALIZED SEIZURES (bilaterally symmetrical and without local onset)

A. 1. Absence seizures
   2. Atypical absence seizures

B. Myoclonic seizures

C. Clonic seizures

D. Tonic seizures

E. Tonic-clonic seizures

F. Atonic seizures

III. UNCLASSIFIED EPILEPTIC SEIZURES (inadequate or incomplete data)

Source: Commission on Classification and Terminology of the International League Against Epilepsy, 1981

CLASSIFICATION OF EPILEPTIC SEIZURES

Table 6 is the International classification of epileptic seizures proposed by the Commission on Classification and Terminology of the International League against Epilepsy (ILAE) and approved in September 1981. This classification is based on the clinical expression of the seizure and the electroencephalographic picture during and between the seizures. The main division in this classification is into *partial seizures* and *generalized seizures*.

In the *partial seizures* the abnormal electrical discharges start in a localized area of the brain. The symptoms/signs are dependent on which part of the brain is affected. These discharges may remain localized, or they may spread to other parts of the brain and then the seizures become generalized (secondary generalized seizures).

In *generalized seizures*, on the other hand, the seizure is generalized from the onset (i.e., primary generalized seizures), starting in both hemispheres of the brain simultaneously.

As we often do not have an EEG to help in making this division, we are completely dependent on the clinical expression: the medical history, and the ability of the observer to describe the seizure. The patient himself has no memory of the seizure, except in simple partial seizures and only of the aura of other seizures. If he is not too young, he can inform us about the presence and the nature of an aura.

A definite aura is an indication that the seizure is of focal (partial) onset.

During his lifetime, a patient does not necessarily have only one type of seizure. The type may change over the years, depending on the age and maturation of the brain. Moreover, one patient may have a combination of different seizure types.

PARTIAL SEIZURES (fig.4)

The partial seizures are first divided into two groups, those where the consciousness is maintained, and where there is an impairment of the consciousness. Both these groups may develop into generalized seizures, then forming a third group.

Simple partial seizures

The patient does not lose consciousness, and therefore is able to tell what happened, but the experience may be so strange that he may not be able to express himself properly. What happens is dependent on the location of the affected area.

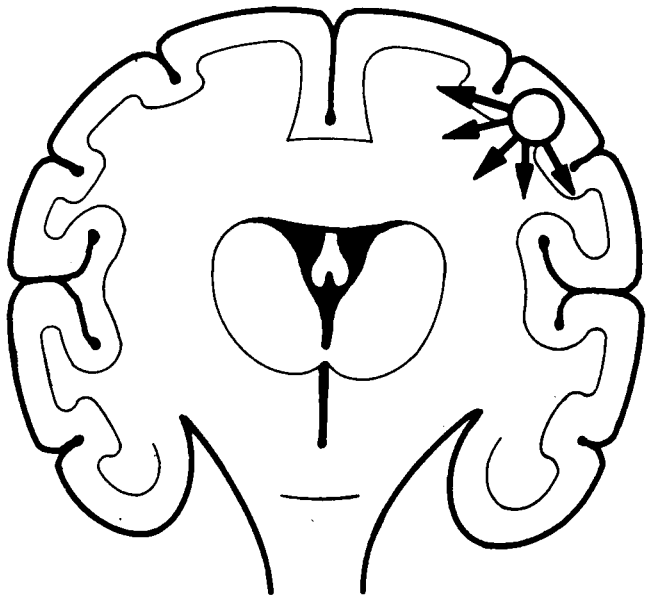


Figure 4. Partial seizure: discharge remains localized

In *motor* seizures, the focus is in the primary motor cortex. There are twitchings, starting in a distal part of the extremity, or in the face. The twitching may remain there, or spread up the whole extremity and even become completely generalized. The spreading is called a Jacksonian march (named after Huglings Jackson 1835 - 1911).

The *sensory* seizures have their focus in the post central gyrus (primary sensory cortex). There might be feelings of tingling, pins and needles, cold or heat, or numbness of a limb. Sometimes there may be strange feelings with visual signs, or hearing or smelling sensations.

The *autonomic* seizures are associated with foci in the temporal lobe. There maybe: a sensation rising from the epigastrium to the throat, palpitations, sweating or flushing.

The *psychic* symptoms may consist of changes in mood, memory, or thought (thinking). There may be distorted perceptions (time, space, or person) or problems with language. Structured hallucinations could occur (music, scenes).

These simple partial seizures are usually only recognized as epileptic seizures when they develop into generalized seizures.

Complex partial seizures

Here the patient has impaired consciousness, there is no complete loss of consciousness, he is slightly aware of what is going on, but he cannot respond to anything, neither can he change his behaviour during an attack. There is an aura, a strange feeling in the stomach rising up to the throat and head, or a sensation of light, smell, sound or taste. The seizure may occur with changes in perception, e.g., of time (time seems to pass too slowly or too fast), of light or sound or space. The surroundings may suddenly seem completely strange and different in scale (things seem larger or smaller than usual), or there is *déjà vu* (a sensation of things having happened before). These feelings can cause the patient a great deal of anxiety.

Sometimes the seizure occurs with hallucinations or with psychomotor symptoms such as automatisms, automatic movements, e.g., pulling at the clothes, chewing, lip smacking, or repeated aimless movements. These automatisms may become very complex, the patient is able to perform difficult tasks, or travel somewhere, but later not remember having done such a thing. He suddenly comes to again and finds himself in a completely different place. During such an automatism the patient may become aggressive and violent when restrained. There is a slow recovery after a complex partial seizure, with a period of confusion. After the attack there is complete amnesia of it. These seizures were previously called ‘psychomotor seizures’, and as the localization of the abnormal discharge is often in the temporal lobe, the epilepsy is often called ‘temporal lobe epilepsy’ (the focus might occur in the frontal lobe too).

Partial seizures secondary generalized (fig. 5)
Both the simple partial seizures and the complex partial seizures may become generalized tonic-clonic seizures. The beginning is as described above, but they end alike the primary generalized tonic-clonic seizures as described below.

GENERALIZED SEIZURES (fig. 6)

The primary generalized seizures are characterized by a complete loss of consciousness and the absence of an aura. They come on suddenly and unexpectedly, and if the patients fall, they may injure themselves.

The generalized seizures consist of six different seizure types, of which the primary generalized tonic-clonic seizure (GTCS) is the most common. Although less common, all seizure types can be seen in special epilepsy clinics.

Absence seizures

These are short periods of loss of consciousness lasting only a few seconds (not more than half a minute). They are of sudden onset, there are usually no, or only minimal motor manifestations. There is a blank stare, brief upward rotation of the eyes, an interruption of ongoing activity. The child is unresponsive when spoken to. It is suddenly over, and the child continues what he was doing before the seizure came. The child has no memory of these seizures. They should not be confused with brief complex partial seizures (table 7).
Typical absences occur in school-aged children, during childhood because of Childhood Absence Epilepsy, and in adolescence because of Juvenile Absence Epilepsy (see classification of epilepsies). They occur many times a day. During such an absence seizure the child does not hear what the teacher is saying, and as they occur so often the child cannot follow the lessons any more. Unless the teacher is aware of this condition, he will scold the child for daydreaming and inattentiveness.

Most parents are unaware of these small seizures, and even when they observe them, do not think them important and will not mention them to the doctor. Unless these children also suffer from generalized tonic-clonic seizures they are not brought to a clinic, and especially not to an epilepsy clinic, as people are unaware that these absences are epileptic seizures.

Absences are easily provoked by overbreathing (hyperventilation). They have a typical EEG pattern and therefore are easily recognized on an EEG.

A child with absence seizures may, in addition, have other types of seizures, such as primary GTCS, or myoclonic seizures (see Appendix A page 85 and following where the special syndromes are discussed). Previously, these seizures were called petit mal seizures, or pyknolepsy (because they occurred so frequently). The term “petit mal” (little illness) should no longer be used as it is very unspecific.

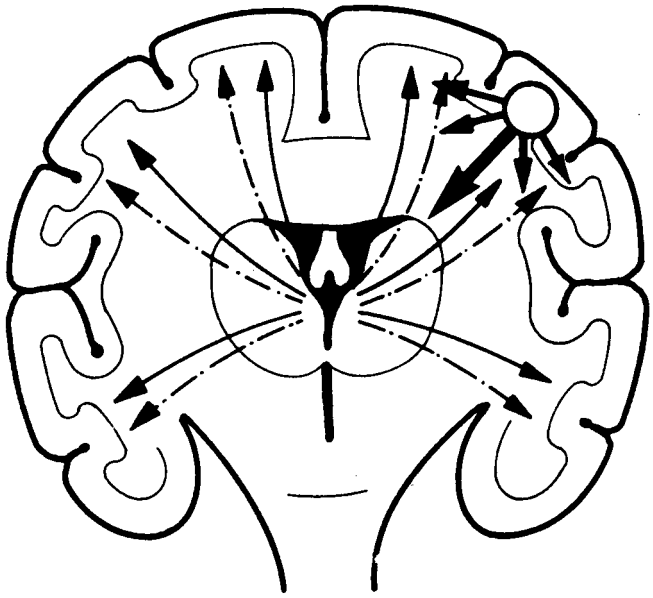


Figure 5. Secondary generalized seizure: epileptic discharge initially localized and then spreads to trigger a generalized seizure

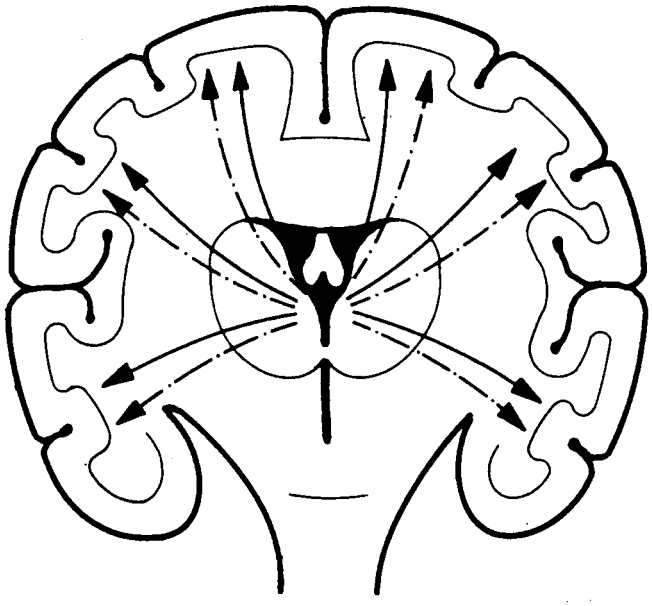


Figure 6. Generalized seizure: epileptic discharge affects both hemispheres

Myoclonic seizures
These seizures consist of sudden, brief, shock-like muscle contractions, either occurring in one limb, or more widespread and bilateral. They may be single jerks, or jerks repeated over longer periods. They are often seen in combination with other seizure types occurring in special epileptic syndromes as discussed in Appendix A.

Clonic seizures
These seizures are generalized seizures, where the tonic component is not present, only repetitive clonic jerks (clonic jerks are repetitive rhythmic flexing and streching of limbs). When the frequency diminishes the amplitude of the jerks do not.

Tonic seizures
Tonic seizures are sudden sustained muscle contractions, fixing the limbs in some strained position. There is immediate loss of consciousness. Often there is a deviation of the eyes and head towards one side, sometimes rotation of the whole body. They are seen mainly in paediatric practice.

Tonic-clonic seizures (GTCS)
The patient loses consciousness, falls down, sometimes with a scream, and develops a generalized stiffness (the tonic phase). Breathing stops, as all the muscles of the trunk are in spasm, and the patient becomes cyanotic, the head is retracted, the arms flexed and the legs extended. After a while, this tonic phase is followed by the clonic phase, when the muscles alternately contract and relax, resulting in clonic movements. With this jerking the patient might bite his tongue, pass urine, or sometimes stool. The clonic phase may last several minutes. When all the jerking stops and the patient regains consciousness, he may feel very tired with a headache and confusion. He has no memory of what happened, and may find himself on the floor in a strange position. Often he falls into a deep sleep.

These seizures are not as frequent as absence seizures. Their frequency may vary from one a day to one a month or once a year, or even once every few years.

Generalized tonic-clonic seizures can occur in generalized epilepsies and in partial epilepsies. To distinguish the two they are called primary or secondary generalized (table 8). Primary GTCS occur without any warning, i.e., they are not preceded by an aura or other partial seizure. Secondary GTCS occur in partial epilepsies and are always preceded by an aura or other partial seizure, however, the generalization may be so rapid that the preceding seizures are not noticed.

This type of seizure is not seen in the newborn period or infancy.

Table 7. Differences between complex partial seizures and generalized absence seizures

	complex partial seizures	generalized absence seizures
Age	any age	childhood or early adult
Aetiology	symptomatic or idiopathic	idiopathic
Duration of attacks	several minutes	short, usually <30 s
Other clinical manifestations	there may be marked tone changes or motor phenomena, including automatism	slight tone changes or motor phenomena
Post-ictal	gradual recovery often with confusion	quick recovery
Frequency	not as frequent	numerous, often clustered
EEG	focal temporal disturbance	3-Hz spike and wave

Table 8. Points in favour of secondary and of primary GTCS

	secondary GTCS	primary GTCS
Aura	present	absent
Time of occurrence	often during sleep	often daytime, or just after falling asleep, or just when waking up
Aetiology	symptomatic	idiopathic
Age of onset	early in life < 5 yr or late in life > 20 or 25 yr or after known trauma	between 5 and 20–25 yr
Other handicaps	might be present	usually absent
In family	less often	more often

Atonic seizures (astatic seizures)

There is a sudden loss of muscle tone causing the head or a limb to drop, and often the patient falls suddenly to the floor. They are therefore also called "drop attacks". There is loss of consciousness, a sudden onset and no post-ictal phase. The patient stands up and continues what he was doing. The seizure is very short, only seconds, but may occur several times a day. The patients often present with scars or fresh wounds on chin, cheek or forehead, or the back of the head. A protective helmet is recommended for these patients. Sometimes these patients may have, in addition to atonic seizures, absence or myoclonic seizures (pages 87-88).

Infantile spasms

Before 1981, *infantile spasms* were seen as one of the seizure types. In the present classification they are classified under the generalized syndromes (table 10, page 34) and discussed in Appendix A (page 87). They are flexor spasms of the head, bending of the knees and flexion with abduction of the arms. They occur in the first year of life, and are very difficult to treat. ACTH or prednisolone is the drug of choice.

UNCLASSIFIED EPILEPTIC SEIZURES

This category includes all seizures which cannot be classified because of inadequate or incomplete data, or seizures that defy classification in the categories as presently defined.

WHICH SEIZURES DO WE SEE IN DAILY PRACTICE?

The majority of our patients (70–80%) present with *generalized tonic-clonic seizures, GTCS* for short. This is a new name for what were previously called "grand mal" (French for the big illness) seizures.

But GTCS is a combination of two seizure types, the secondary GTCS (group I, C) and the primary GTCS (group II, E)— see table 6. Both these seizure types are seen equally commonly: 35–40% will have secondary GTCS, and the same percentage will have primary GTCS. The differentiation is important, as the drug of choice is different in each group. As most of our patients have to be treated without the help of an EEG recording, we rely on the medical history for this differentiation. In table 8 some points are mentioned in favour of one or the other.

The four main antiepileptic drugs (AEDs) can be used for all GTCS. But the drug of choice for the secondary GTCS is phenytoin or carbamazepine, and for the primary GTCS phenobarbitone or valproate.

The minority of our patients present with the other seizure types as they are often not recognized by the patient, their family or even the primary health workers to be caused by epilepsy. Or they are considered to cause too little problems to take the trouble of a visit to a clinic.

Most of the patients who do not present with GTCS present with *complex partial seizures* (I, B); approximately 15%. They are a strange mixture of feelings and signs, and were previously called psychomotor seizures or temporal lobe epilepsy because the origin is often in the temporal lobe. These complex partial seizures should not be called complex absences, but should be differentiated from the generalized absences. In table 7 the points in favour of one or the other are mentioned. The drug of choice for complex partial seizures is carbamazepine or phenytoin.

From 1–4% of our patients will present with *generalized absences* (II, A). valproate is the drug of choice. When they have only generalized absences, they can be treated with ethosuximide, but when they have other types as well, then valproate is the drug of choice. Phenobarbital alone can take care of primary GTCS but is not effective against absences.

Simple partial seizures might occur in a small percentage of our patients, and the drug of choice is then phenytoin or carbamazepine, while the rest of our patients might have *myoclonic* or *astatic* seizures, for which the drug of choice is valproate.

Definite figures of the occurrence of these seizures in Africa cannot be given, as the diagnosis is made on a clinical impression, and not verified by an EEG recording.

STATUS EPILEPTICUS

A status epilepticus occurs whenever a seizure persists for at least 30 minutes, or is repeated so frequently that recovery between attacks does not occur.

A status is a medical emergency and the patient should be transferred to a clinic where, with i.v. injections the status could be stopped as quickly as possible (table 22, page 66). It is a dangerous condition which may result in brain damage (cerebral necrosis) with severe morbidity or death. A status may be the patient's first epileptic event, or may be precipitated by suddenly discontinuing anticonvulsant therapy.

An initial status epilepticus in an adult may be due to a brain tumour and requires full investigation.

A status is again classified according to the different seizure types, but in two groups as presented in table 9.

Table 9. Classification of status epilepticus

I Convulsive status

Focal or partial

– Partial motor status (epilepsia partialis continua, Kojewnikow's syndrome)

Continuous motor seizures with retained consciousness. Occurs mainly in adults with structural brain damage due to trauma or vascular disease, or in children with severe brain disease

Generalized

– Tonic-clonic (previously grand mal) status
– Myoclonic status
– Febrile status epilepticus
Prolonged febrile convulsions (see page 69)

II Non-convulsive or stupor status

– Complex partial status, or psychomotor status
Prolonged period of automatic behaviour
– Absence status
Repeated absence seizures may cause prolonged periods of confused behaviour in children. Is occasionally seen in adults. This may be detected on an EEG, and controlled by diazepam

6 Classification of epilepsies

In addition to the international classification of epileptic seizures, there is an International Classification of Epilepsies and Epileptic Syndromes, of which the latest revised classification is given in table 10 (page 34), according to the Commission on Classification and Terminology of the International League Against Epilepsy (1989).

An epileptic syndrome is an epileptic disorder characterized by a cluster of signs and symptoms customarily occurring together. These include such items as seizure type, aetiology, precipitating factors, age of onset, severity, chronicity, diurnal and circadian cycling, and sometimes prognosis.

Two main groups are again distinguished, depending on the character of the presenting seizure type:

PARTIAL or **LOCALIZATION-RELATED**, and

GENERALIZED.

In this new classification, each is then divided into three groups as the term cryptogenic has now been introduced. The three groups are:

- **Idiopathic epilepsies**
  There is no underlying cause other than a possible hereditary predisposition. Idiopathic epilepsies are defined by age-related onset, clinical and electroencephalographic characteristics, and a presumed genetic aetiology of the epilepsy. This does not include other genetic brain disorders associated with epilepsy such as those grouped under congenital and degenerative diseases in table 1.
- **Symptomatic epilepsies**
  They are considered to be the consequence of a known or suspected disorder of the central nervous system.
- **Cryptogenic epilepsies**
  The term refers to a disorder whose cause is hidden or occult. These are presumed to be symptomatic, but there is no clear evidence of an aetiological factor. The cryptogenic epilepsies are also age-related, but often do not have well defined electro-clinical characteristics.

SYNDROMES where it is impossible to determine whether the seizures are focal (localized) or generalized, is the third main group.

SPECIAL SYNDROMES in which epileptic seizures are the main component, and of these *febrile convulsions* (page 69) are the most common and important are collected in a fourth main group.

This classification is important as it often tells us about the *prognosis*, and indicates the appropriate *treatment* (table 12, page 37) it also facilitates discussion with the patient or other medical experts, e.g., by mail or telephone.

1. LOCALIZATION-RELATED EPILEPSIES

Most of the localization-related (partial) epilepsies are *symptomatic*. With intensive investigation methods, a lesion or focus can be found. The pattern of the seizures and other characteristics are dependent on the site of the lesion. The focus might be in the frontal, temporal, parietal or occipital lobes of the brain or in the motor cortex (table 10).

These focal symptomatic seizures respond better to treatment than the generalized symptomatic group, but not as well as the idiopathic epilepsies.

The appropriate drugs in this group are phenytoin or carbamazepine. With these anticonvulsants, the seizures are less severe and less frequent, but will sometimes still occur. If there is insufficient improvement, phenobarbitone or valproate may be tried. Fatigue, sleep deprivation, alcohol and emotional stress may trigger these seizures. Lifestyle instructions are important.

The *idiopathic* localization-related epilepsies are not common, but have a good prognosis, and respond well to treatment (phenytoin or carbamazepine). They are discussed in more detail in Appendix A.

2. GENERALIZED EPILEPSIES

Most of the generalized epilepsies are *idiopathic*. There are no neurological deficits, psychological abnormalities or mental handicaps. Epilepsy in the family is more common than in the other groups. The prognosis is good. The response to treatment is usually good. The seizure types found are absences (treatment: valproate or ethosuximide), myoclonus (treatment: valproate and benzodiazepines, but difficult to treat if it occurs in infancy or early childhood), and generalized tonic-clonic (treatment: phenobarbitone, valproate or carbamazepine).

Some of the generalized epilepsies are *symptomatic* (in Europe approximately 10% of all epilepsies). They result from diffuse brain damage following birth asphyxia or occur in diseases with inborn errors

of metabolism. These children often have multiple handicaps and have spasticity and/or mental retardation in addition to their epilepsy. Treatment is very difficult and phenobarbitone, phenytoin, carbamazepine, valproate and benzodiazepines may be tried. The seizure types seen are tonic-clonic, tonic, atonic, atypical absences and infantile spasms. In the latter case ACTH or prednisolone are often used.

Age of onset

In addition to the *seizure type* and the *aetiology*, the *age of onset*, i.e., the age at which the first seizure occurs, is a helpful tool in classifying the different epilepsies and syndromes.

All the *symptomatic* epilepsies occur after (sometimes years after) the event resulting in the epilepsy and therefore depend upon the age (birth or later) at which the event took place.

The *idiopathic* epilepsies, however, might commence at any time, but age-related groups are now well recognized. As the age of onset is a definite fact, table 10 is discussed not as it is presented, but according to the age of onset of the different epilepsies in Appendix A.

Time of occurrence of seizure

Another important factor is the *time* of day or night that the seizure occurs and its relation to the sleep-waking cycle.

I. – Partial seizures of the idiopathic type (benign focal epilepsy) occur mainly during sleep.

– Complex partial seizures are uncommon during sleep.

– Partial seizures secondary generalized are much more common at night than primary generalized seizures.

II. – Absences occur mainly during the day-time.

– Seizures seen just after awakening are often associated with myoclonic seizures.

– Primary generalized tonic-clonic seizures are more commonly seen during the daytime, but if they do occur at night it is soon after falling asleep, or in the period of early morning sleep.

The treatment for these seizures is indicated in table 12. However, phenobarbitone increases the amount of deep sleep, and is therefore best avoided in epilepsy with predominantly nocturnal seizures. Phenytoin and carbamazepine, which have less hypnotic effect, are indicated for sleep provoked epilepsy.

Table 10. International classification of epilepsies and epileptic syndromes and related seizure disorders

1. *Localization-related (local, focal, partial) epilepsies and syndromes*
   - 1.1 Idiopathic (with age-related onset)
     - Benign childhood epilepsy with centro-temporal spikes
     - Childhood epilepsy with occipital paroxysms
     - Primary reading epilepsy
   - 1.2 Symptomatic
     - Chronic progressive epilepsia partialis continua
     - Syndromes characterized by seizures with specific modes of precipitation
     - Temporal lobe epilepsies *
     - Frontal lobe epilepsies *
     - Parietal lobe epilepsies *
     - Occipital lobe epilepsies *

* see table 11 page 36

   - 1.3 Cryptogenic

2. *Generalized epilepsies and syndromes*
   - 2.1 Idiopathic (with age-related onset)
     - Benign neonatal familial convulsions
     - Benign neonatal convulsions
     - Benign myoclonic epilepsy in infancy
     - Childhood absence epilepsy
     - Juvenile absence epilepsy
     - Juvenile myoclonic epilepsy (impulsive petit mal, Janz syndrome)
     - Epilepsy with grand mal seizures (GTCS) on awakening
     - Other generalized idiopathic epilepsies
     - Epilepsies with seizures precipitated by specific modes of activation
   - 2.2 Cryptogenic or symptomatic
     - West syndrome (infantile spasms)
     - Lennox-Gastaut syndrome
     - Epilepsy with myoclonic-astatic seizures
     - Epilepsy with myoclonic absences
   - 2.3 Symptomatic
     - 2.3.1 Non-specific aetiology
       - Early myoclonic encephalopathy
       - Early infantile epileptic encephalopathy with suppression bursts
       - Other symptomatic generalized epilepsies
     - 2.3.2 Specific syndromes
       - Epileptic seizures complicating other disease states

continued on p. 35

Table 10, *continued*

3. *Epilepsies and syndromes undetermined whether local or generalized*
   - 3.1 With both generalized and focal seizures
     - Neonatal seizures
     - Severe myoclonic epilepsy in infancy
     - Epilepsy with continuous spike waves during slow wave sleep
     - Acquired epileptic aphasia (Landau-Kleffner syndrome)
     - Other undetermined epilepsies
   - 3.2 Without unequivocal generalized or focal features

4. *Special syndromes*
   - 4.1 Situation-related seizures
     - Febrile convulsions
     - Isolated seizures or isolated status epilepticus
     - Seizures occurring only with acute metabolic or toxic events

From the Commission on Classification and Terminology of the International League Against Epilepsy, 1989

Table 11. Syndromes related to anatomic localization

Frontal lobe epilepsy	
Seizure type	simple partial and complex partial often rapid secondary generalization status epilepticus is frequent
Symptoms	versive movements of the head prominent motor manifestations, which are tonic or postural, especially in the legs complex gestural automatisms at onset
Special features	short seizures, several times a day and often during sleep despite impairment of consciousness, often minimal or no postictal confusion sometimes mistaken for psychogenic seizures
Temporal lobe epilepsy	
Seizure type	complex partial, simple partial and sometimes secondary generalization
Symptoms	epigastric rising sensation and hallucinations motor arrest followed by oroalimentary automatisms, followed by other automatisms
Special features	there is frequently a history of febrile convulsions a family history of convulsions is common memory deficits occur onset is frequently in childhood or young adulthood seizures occur in clusters at intervals or randomly postictal confusion and gradual recovery
Parietal lobe epilepsy	
Seizure type	simple partial ± secondary GTCS
Symptoms	sensory, like tingling or a feeling of electricity numbness, sometimes painful sensations, usually in hand, arm or face, may spread in a Jacksonian manner
Occipital lobe epilepsy	
Seizure type	simple partial ± secondary GTCS
Symptoms	fleeting visual manifestations like sparks, flashes and phoshenes perceptive illusions

Table 12. The relationship between epilepsy, prognosis and treatment

Epilepsy	*Prognosis*	*Treatment*
1. Localization-related		
1.1 Idiopathic	good	phenytoin, carbamazepine
1.2 Symptomatic	depends on the lesion	phenytoin, carbamazepine (phenobarbitone)
2. Generalized		
2.1 Idiopathic	good	
Absence		ethosuximide, valproate
Myoclonus		valproate, benzodiazepines
Generalized tonic-clonic		phenobarbitone, valproate, carbamazepine
2.2 Cryptogenic/symptomatic	poor	
Infantile spasms		ACTH, oral steroids, valproate, benzodiazepines
Lennox-Gastaut		prednisolone, valproate, benzodiazepines
2.3 Symptomatic	poor	phenobarbitone, phenytoin, carbamazepine
3. Epilepsies and syndromes undetermined as to whether they are focal or generalized	see Appendix A	
4. Special syndromes		
4.1 Situation-related seizures	good	valproate
4.2 Febrile convulsions	good	benzodiazepines

CONCLUSION

To classify an epilepsy (and therefore to know which anticonvulsant is the most appropriate and to attempt to make a possible prognosis) the following factors are important:

– Type of seizure

– Aetiology

– Age of onset of seizures

– Time of occurrence of seizure.

If the medical history and the physical examination do not enable determination of seizure type and aetiology, treat with phenobarbitone for daytime seizures and phenytoin for nocturnal seizures. If the seizures occur both in the daytime and at night treat with phenobarbitone. If no improvement occurs, change over to phenytoin.

In patients with true absences, however, neither of these drugs is effective and phenytoin and carbamazepine may even aggravate the condition.

7 History, examination and investigations

MEDICAL HISTORY

A carefully taken medical history is the most important need of all in a patient with repeated seizures. As the patient cannot recollect the seizures an accompanying person has to help in answering questions about the seizures.

First we let the patient and his companion tell their story, then we have to ask pertinent questions about the present seizures and previous medical history.

Seizures

Onset

- At what age was the first seizure? (Explain what is covered by the term "seizure", mimic absences, complex partial seizures, etc.)
- Was it in association with a particular *event*, accident or illness?
- Was there *fever* with the first seizure?
- Is there always fever with the seizures?

Pre-ictal phase

- Does the patient know of any *precipitating* factors such as hunger (pointing to hypoglycaemia), lack of sleep, emotion, alcohol, flashing lights, etc?
- Are there any *prodromal* symptoms?
- Is there an *aura*? What does it consist of?

Ictal phase (description of seizure itself)

- Does the patient get flushed or become pale? Does he see grey scintillations (pointing to a faint)? Does he scream?
- Where and how does it start, turning face to one side, or in one hand?
- Does he jerk? If so, with both arms and both legs, or only one side?
- Is the patient unconscious? Does he fall down?
- Does he fumble with his clothes, smack his lips, mumble or make any other noises?

Duration

- How long does the seizure last?

Post-ictal phase

– What is the patient's behaviour like after the seizure—sleepy, aggressive, continues what he was doing?
– Is there any focal sign (e.g., Todd's paralysis)?

Time

– Is it always in the day time, always when he is asleep, or on awakening?

Frequency

– How often does it happen?

Family history

– Is there any similar disease in any of the siblings, the parents, or the parents' families?

Perinatal history

How was the *pregnancy*:

– Any diseases or complaints?
  – Were medicines or alcohol used, was the mother a chain smoker?
– Was it of normal duration?

How was the *delivery*:

– Normal, vacuum, forceps, or Caesarean section?
– Was it of normal duration, prolonged, or precipitate?
– Did the baby cry immediately after birth, or had he to be resuscitated?
– Did the baby have a low birth weight?
– Did he look yellow?
– Did the baby suck well?
– Was there any disease after birth?
– Did he get the usual vaccinations?

Development

– Were the *milestones* normal?
– Does or did he go to school and how is/was he performing there?
– If of school-age and not attending school, why not?
– If over school age does he have a job?
– What is his behaviour like?
– Does he sleep well?

What has been done up till now about the seizures?

– Has he been admitted to a hospital for his seizures or for any other disease or accident? (Or would he have been admitted if a hospital had been accessible?)
– What kind of treatment has he had in the past?
– Is he on treatment now?
– Which medicines, what dosage?
– If his drugs were changed what was the reason—allergy or ineffectiveness?
– Is he treated by a traditional healer? If so what treatment has been prescribed?

SOCIAL HISTORY

– Where does the patient live? With parents? With sibs? With wife/husband or child?
– Is it far from the clinic? How long does it take to reach the clinic? How does he travel—by foot, etc.
– What are the parents' occupations? If he is married, who earns a living?
– What is the educational level of the parents/the household member?
– Are the parents together?
– Who is looking after the patient,in case of need?
– How many siblings are there?/How many children are there?
– Are they all well/normal? If not, what is wrong?
– How is the patient doing at school/in his job? Is he coping?
– Are there any others in the class, the school, the workplace, or the neighbourhood with the same problem?
– Are there any problems with his teachers, superiors or colleagues, neighbourhood, (extended) family because of the epilepsy?

ANY PROBLEMS NOT YET MENTIONED

– Ask the patient or the parent to tell what problem they would like to talk about that has not yet been dealt with.

EXAMINATION

Physical examination

This starts with:

Observation

- From the moment the patient enters the consulting room notice whether he walks normally, or is there weakness or spasticity on one or both sides?
- Does he act appropriately to the new surroundings or is he too quiet, or too active?
- Is he able to communicate?
- Is the speech normal for his age?

Measurements

- Weight
- Height
- Head circumference (a graph of normal values is given in Appendix C).

General physical examination

Routine examination of all the systems. Note especially:

- Scars, bruises, change in pigmentation, adenoma sebaceum, haemangioma
- Asymmetry, congenital anomalies
- In acutely ill children note:

  fever, bulging fontanels, neck stiffness, rash, level of consciousness

Neurological examination

- Eyes—size and reaction of pupils, visual fields, nystagmus, fundoscopy if possible
- Other cranial nerves
- Muscle power and tone—hyper- or hypotonic?
- Reflexes
- Is there any difference between right and left?
- Are there any signs of drug toxicity, e.g., ataxia, drowsiness, sleepiness, nystagmus
- Finger-nose test
- Dysdiadochokinesis (slowing or overshooting when alternating pronation and supination of the hands)

INVESTIGATIONS

Laboratory investigations

If available, it is good to have baseline information on the general condition of the patient:

- Haemoglobin, WBC count and differentiation, blood platelets, ESR, blood film, urinalysis, and stool examination
- Specific tests are sometimes indicated to find the basic cause of the convulsions (blood glucose, electrolytes, parasites, etc.)
- HIV/syphylis serology in suspected cases
- Liver-function tests are indicated in the first months after starting an antiepileptic drug
- Lumbar puncture is indicated when there is an acute illness with fever, convulsions and signs of meningitis (neck stiffness, in infants bulging fontanels) or, in the absence of these signs, in a very ill patient with no other obvious disease
- Exceptionally it may be necessary to measure the level of AED in serum (see page 65)

Skull X-ray

- Signs of intracranial calcifications may be detected. Calcifications may follow tuberculosis (tuberculoma), tuberous sclerosis, intrauterine cytomegalovirus (CMV) disease, Sturge-Weber syndrome, toxoplasmosis or cysticercosis.
- Signs of raised intracranial pressure might be seen (tumour).

Electroencephalography (EEG)

This is a painless non-invasive and safe procedure whereby the electrical activity of the brain is registered, amplified and recorded by a number of electrodes placed in a specific manner on the head. (The head does not have to be shaved.)

- There are nearly always abnormal discharges to see on the EEG during a seizure, and often in between seizures (inter-ictal).
- An EEG is often helpful in differentiating between partial and generalized seizures.
- The EEG has a characteristic pattern in a number of the epileptic syndromes (e.g., absences).

– Epileptic abnormalities can sometimes be provoked by hyperventilation, photic stimulation, sleep and deprivation of one night's sleep. During an EEG recording, hyperventilation and photic stimulation are always used. When sleep is required, it can be induced, for instance with chloral hydrate. On indication, the EEG is recorded after a night's sleep deprivation.

However, this examination can be carried out only in a few top-referral hospitals on selected cases only, and treatment is usually given without the help of the additional information given by an EEG.

Computer-assisted tomography (CT) scan

Computer-assisted tomography (computerized axial tomography) is a safe and non-invasive procedure. Serial X-ray pictures of horizontal sections of the skull and brain are taken resulting in an accurate anatomical picture. A low radiation dose is used. This technique is able to demonstrate tumours, haemorrhages, subdural haematomas, vascular anomalies and other structural abnormalities. Sometimes a contrasting medium is given intravenously, and the two pictures, with and without medium, can be compared to further facilitate a diagnosis. CT scanning is a very helpful but very costly examination and can only be carried out in top-referral hospitals.

Magnetic resonance imaging (MRI)

Magnetic resonance imaging is based on the absorption and emission of energy in the radio frequency range of the electromagnetic spectrum. The human body is primary fat and water. Fat and water have many hydrogen atoms. The human body is comprised of approximately 63% hydrogen atoms. Hydrogen nuclei have a Nuclear Magnetic Resonance (NMR) signal. For these reasons MRI primary images the NMR signal from the hydrogen nuclei. MRI started out as a tomographic imaging technique, i.e., it produced an image of the NMR signal in a thin slice through the human body. MRI has advanced beyond a tomographic imaging technique to a volume imaging technique.

(From Joseph P. Hornak, Ph.D. at http://www.cis.rit.edu/htbooks/mri/inside.htm)

MRI has enormously advanced knowledge of the central nervous system. However, it is still a very expensive technique that is only sparsely available in economically evolving countries.

PSYCHOLOGICAL EVALUATION

Psychological evaluation by a psychologist is desirable, but opportunities for this are limited in Africa.

Assessment of the intelligence, potential, or particular problems of the patient is of value, for instance in placement at an appropriate school and to provide counselling for the patient, family and teachers to enable him/her to live as normal a life as possible.

Information may be obtained by carefully watching the child and by questioning the mother who can compare this child to her other children (milestones, speech, daily activities such as eating, dressing, toilet training and behaviour).

A simple grading of the intelligence can be done as described on pages 53-54.

Institutional care may be necessary, not only because of the degree of mental retardation, but also because of the need to control the epileptic seizures and the degree of other related physical handicaps (e.g., spasticity).

For a review of this chapter see table 13.

Table 13. What has to be asked and done

Medical history
Seizures
Family history
Perinatal history
Development
Previous seizure management
Social history
Examination
Observation
Measurements
General physical examination
Neurological examination
Investigation
Laboratory
Skull X-ray
Electroencephalography (EEG)
Computer-assisted tomography (CT) scan
(Magnetic Resonance Imagining)
Psychological evaluation

8 Disorders to be distinguished from epilepsy

Before treatment with anticonvulsants is started, the diagnosis of epilepsy must be as certain as possible. When treatment with anticonvulsants has started, and no improvement occurs at all, then the diagnosis of epilepsy should be reconsidered.

The main conditions, which are often mistaken for epileptic seizures, are *fainting attacks* and *psychogenic pseudoepileptic seizures* (pseudo = look alike). Also physiological jerks when falling asleep (hypnagogic or hypnic, jerks) are sometimes mistaken for a brief seizure.

A detailed medical history, and a clear witnessed account of the attacks are a must for differentiating these conditions (table 14).

Table 14. Conditions often confused with epilepsy

– Reflex syncope
– Cardiac syncope
– Postural syncope
– Psychogenic seizures
– Breath-holding spells
– Nightmares, night terrors, sleepwalking
– Narcolepsy
– Sleep apnoea
– Transient ischaemic attacks
– Senile falls
– Dizziness
– Migraine
– Trigeminal neuralgia
– Tetanus
– Hypoglycaemia
– Jitteriness in the newborn
– Temper tantrum
– Hypnagogic (hypnic) jerks

SYNCOPE (FAINTING)

Syncope is much more common than epilepsy, and the main differences from epileptic seizures are shown in table 15. There is loss of consciousness due to a sudden decrease in the cerebral blood flow. Syncope may be divided further into three groups:

Reflex syncope (vasovagal syncope)

This is the most common type and includes simple fainting. Precipitating factors are anxiety, hunger or any unpleasant experience causing vagal nerve stimulation and reduced venous return. Standing at parades in warm weather (when venous pooling occurs in the legs) is a common cause of fainting. The onset is often gradual, with a feeling of faintness, nausea or dizziness. Blurring or blacking out of vision is often present before the patient slumps to the floor. Loss of consciousness is short, and often there are some uncoordinated clonic jerks (causing the confusion with epileptic seizures). There is pallor and sweating and the pulse is slow. Recovery is quick without confusion. Treatment is to increase the blood flow to the head by putting the head between the knees, or to lie down.

Cardiac syncope

This is caused by heart disease, disturbance of the heart's rhythm or reduced cardiac output. The attacks can occur in any situation; in children it is often seen after exertion. A prolonged ECG may be necessary to make the right diagnosis.

Postural syncope

This occurs within seconds or minutes of assuming an upright position in patients whose postural reflexes are impaired (elderly people, diabetic patients, or due to medication or alcohol).

PSYCHOGENIC NON-EPILEPTIC SEIZURES

(PSYCHOGENIC PSEUDO-EPILEPTIC SEIZURES, FUNCTIONAL SEIZURES, HYSTERIA)

These seizures simulate generalized tonic-clonic seizures and may occur in patients with epilepsy or in patients who do not have epilepsy themselves. These pseudo-seizures may occur in several pupils in the same class or school after having witnessed someone with a real epileptic seizure. It is an attention-seeking device in patients with emotional disturbances who cannot cope with the expectations of their surroundings. The seizures are variable, do not follow a typical pattern, and usually occur when there is an audience and are often prolonged. In the classical hysterical seizure, the hips are lifted from the floor. (However, pelvic thrusting may also occur in frontal lobe seizures.) There is rarely incontinence. There is no improvement with anticonvulsants. In table 16 the main differences are shown.

Table 15. Differentiation between epileptic seizures and fainting attacks (reflex syncope)

	Epileptic seizure	Syncope
Precipitant	unusual	usual (emotion, pain)
Circumstances	any	usually upright position; crowded, hot surroundings emotional stressful situations
Onset	sudden or aura	gradual
Motor phenomena	tonic or tonic-clonic clonic movements with characteristic amplitude and frequency	flaccid uncoordinated clonic jerks of low amplitude
Skin colour	pale or flushed	pale
Respiration	stertorious, foaming	shallow, slow
Incontinence	common	rare
Tongue-biting	common	rare
Vomiting	unusual	often
Injury	common	rare
Post-ictal	drowsy, confusion sleep	usally rapid recovery without confusion
Duration	minutes	seconds

Table 16. Differentiation between epileptic seizures and psychogenic seizures

	Epileptic seizure	Psychogenic seizure
Precipitant	unusual	usual (emotion)
Circumstances		
in sleep	common	rare
when alone	common	less common
Prodroma	rare	common
Onset	sudden or aura	gradual
Cry at onset	common	unusual
Vocalization	during automatism only	groans and moans or cries usually throughout fit
Motor phenomena	stereotyped, usually both tonic *and* clonic; clonic movements slow as seizure continues and increase in amplitude	variable, usually tonic *or* clonic; clonic movements vary in amplitude and frequency; pelvic thrusting (also in frontal lobe epilepsy!)
Injury	common	rare
Incontinence	common	rare
Tongue-biting	common	rare
Consciousness	lost in GTCS, reduced in CPS	usually not lost; may not respond
Resistance to passive limb movement or eye opening	unusual	common
Duration	seconds or minutes	many minutes
Termination of attack	usually rapid; confusion, drowsiness or sleep common	gradual, often with emotional display; confusion, drowsiness or sleep unusual
Recall of seizure events	very rare	possible or elicitable by hypnotic recall

OTHER DISORDERS

Besides these pseudo-seizures, there are also other attacks, such as swoons and tantrums, which might be confused with simple partial or complex partial seizures. Jerks (hypnagogic startles; hypnic jerks) when falling asleep are not rare, but usually are not mistaken for epilepsy.

In a *swoon*, there is a sinking to the floor, with closed eyes, followed by lying inert on the floor with peculiar eyelid flickering. Swoons are a way of avoiding difficult situations, unpleasant thoughts or memories.

In a *tantrum*, the subject throws himself to the floor screaming, thrashing about and kicking. Often the subject bites himself or even bites onlookers. Tantrums frequently occur in children and immature, brain-damaged or underprivileged people as an expression of anger and frustration.

Two other forms of pseudo seizures are *panic attacks* and *episodic confusion*. A *panic* attack is characterized by shortness of breath, smothering sensations, choking and chest pains while *episodic confusion* can occur after the use of such drugs as barbiturates, organic solvents (glue sniffing), and adulterated alcohol.

Less common disorders to be differentiated are covered below.

Breath-holding spells

These occur in infants and children between one and five years old. They are caused by anger or pain in children who cannot restrain their emotions. There is a sudden arrest of the respiration followed by cyanosis, unconsciousness, and sometimes twitching lasting a few seconds. The attack stops spontaneously and never results in brain damage.

Nightmares, night terrors and sleepwalking

These are often familial and occur in childhood, mostly between the ages of 4 and 14. Nightmares occur during REM sleep. Night terror (pavor nocturnus) and sleep walking occur during deep sleep.

Narcolepsy

These are attacks of sleeping many times a day under the strangest circumstances. It is often familial and occurs mostly between the ages of 15 and 30. The condition usually becomes chronic, but spontaneous improvement sometimes occurs. Stimulants like ephedrine or methylphenidate or antidepressants like clomipramine may be tried.

Sleep apnoea
Sleep apnoea is a disturbance of the respiration during sleep, with discontinuation of the respiration for about half a minute or longer up to a hundred times a night. The patient is not aware of these spells.

Transient ischaemic attack (TIA)
These attacks occur in an older age group and are caused by a transient reduction in blood supply to parts of the brain, usually secondary to arteriosclerosis of the cerebral vessels and vessels in the neck. Disturbances of consciousness may be associated with focal paralysis, disturbance of speech or loss of vision which occurs for minutes or hours. More prolonged symptoms may indicate a more serious cerebrovascular accident (stroke).

Senile falls
In elderly people sudden falls may be triggered by turning of the head or looking upwards. In this case reduced cerebral blood flow is caused by kinking of a calcified blood vessel.

Dizziness
Real vertigo is an attack associated with a spinning sensation, loss of posture, nausea and vomiting caused by diseases of the inner ear.

In Menière's disease, i.e., deafness and tinnitus in one ear, attacks of vertigo may last from half an hour to several hours.
In acute labyrinthitis severe vertigo may last for several days.

Vague sensations of dizziness with loss of balance is a common complaint in many people.

Migraine
Migraine is a paroxysmal headache, often unilateral, but sometimes generalized. The headache may be preceded by an "aura" which is commonly a visual disturbance, e.g., flashing lights, fortification spectra or hemianopsia, but there may be numbness and tingling in the face or limbs or even a hemiparesis. These symptoms last for 15–30 minutes and are invariably followed by severe headache. The aura in an epileptic attack lasts only a few seconds. Very rarely, an acute migraine attack may result in a permanent neurological disturbance, for example epilepsy or a defect of vision. Migraine attacks may precipitate seizures.

Trigeminal neuralgia
Periodic attacks of severe pain on one side of the face, of unknown cause, but most effectively treated by carbamazepine.

Tetanus
A wound infection with *Clostridium tetani*. After a variable incubation period (5–30 days) the first clinical manifestations are intermittent clonic convulsions. Episodic muscle spasms, especially of jaw and neck, with difficulty in opening the mouth (lockjaw) occur. There is a typical facial expression, "risus sardonicus", board-like rigidity of the body, and pronounced opisthotonus with legs and feet extended, stiff arms and clenched fists. These spasms are precipitated by the slightest stimulus (touching the patient, noise and light). As the disease progresses the intervals between the spasms are less obvious. Fever is common. Without treatment the disease is usually fatal within a week.

In addition to the conditions mentioned in this chapter, all the conditions given in table 1 have to be considered in the differential diagnosis of epilepsy. The most common of these conditions are hypoglycaemia, meningitis, cerebral malaria, electrolyte imbalance and poisoning. If these conditions are appropriately treated and the patient recovers, prolonged protection with antiepileptic drugs (anticonvulsants) like in epilepsy will not be necessary until there is proof that the disorder, e.g., meningitis or cerebral malaria has brought epilepsy in its wake.

9 Conditions co-existing with epilepsy

Sometimes the insult to the brain is so severe (e.g., in birth trauma, birth asphyxia, etc.) that in addition to the epilepsy there may be other impairments, e.g., cerebral palsy and/or mental retardation. Of the patients attending KAWE clinics, 32% have, besides their epilepsy, another handicap, while 12% of all patients have multiple handicaps.

CEREBRAL PALSY

In Europe the incidence of cerebral palsy is 2 per 1,000 live births. The condition is classified into the following syndromes:

- Spastic (hemiplegic, tetraplegic and diplegic)
- Ataxic
- Dyskinetic (choreo-athetotic and dystonic)

Epilepsy is most common in the spastic and rare in the ataxic and dyskinetic syndromes.

MENTAL RETARDATION

In Europe about 3% of all children have a certain degree of mental retardation, while 0.3% of all children have it in a severe degree. The condition is graded from borderline, mild, moderate, severe to profound, depending on the results obtained by testing the IQ (intelligence quotient). As the tests for measuring IQ are not yet standardized in every country, a simple grading can be done according to the following definitions:

- **Mild mental retardation, the educable group**
  These children can master basic academic skills up to Standard IV to VI with extra help, and are able to master simple vocational skills and adjust fairly well to social demands (social accomplishment level of a 7–9 year-old child).
- **Moderate mental retardation, the trainable group**
  May acquire very basic academic skills (5–7 year-old level). May be taught self-help-care skills and could work in a sheltered workshop under supervision.

– **Severe mental retardation**
  Require custodial and sometimes nursing care. Can be taught most basic self-help-care skills such as eating, drinking and toilet training (3–5 year-old level).

– **Profound mental retardation**
  These children cannot be tested (neither can they be trained) and require complete care (3 year-old level or less).

Epilepsy is common in mentally handicapped children, the proportion rising as the degree of retardation increases (from 6 to 30%; Corbett, 1985 and from 13.7% to 44.4% in Kibwezi, Kenya, see Baldwin 1990).

The occurrence of epilepsy varies in the different syndromes associated with mental retardation. It is very common in children with tuberous sclerosis, common in those with spastic tetra- and hemiplegia, and not so common in children with Down's syndrome.

Although epilepsy is common in mentally handicapped children, mental retardation is not as common in patients with epilepsy. In Europe it is said that one out of three retarded children cared for institutions has epilepsy, while one out of ten epilepsy patients is mentally handicapped.

In Africa there is, however, a great difference between the findings in a rural clinic and an urban clinic. For example in Kenya in the rural clinic 32.5% were retarded, in an urban clinic this was 21.4% (table 17). Also, the physically handicapped were more common in the rural clinic than in the urban one—20.3% and 11.4% respectively.

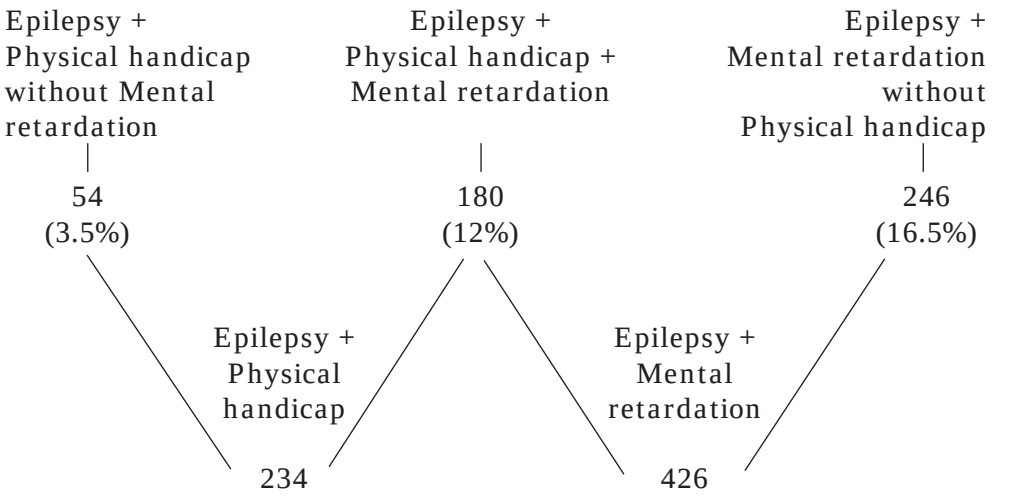
The overall distribution of people with epilepsy, with or without mental retardation and or physical handicap for the KAWE clinics is presented in table 18.

Most probably, in the rural areas, where people live far from health facilities, especially hospitals, more children develop severe brain damage following birth trauma, birth asphyxia, or childhood infections resulting in more multiple handicapped children with severe forms of epilepsy. However, another explanation may be that assistance of health authorities is more likely to be looked for when there are multiple handicaps or severe epilepsy.

Table 17. Difference between data from one rural clinic, *n* = 442, and one urban clinic, *n* = 597, as percentages

	Epilepsy + Physical handicap (± Mental retardation)	Epilepsy + Mental retardation (± Physical handicap)
Rural	20.3%	32.5%
Urban	11.4%	21.4%

Table 18. Data of 1493 patients with epilepsy attending three KAWE clinics (90% of the patients were below the age of 20 yr)



PSYCHIATRIC PROBLEMS

Epilepsy is not a mental disease, although a small number of patients will develop psychiatric problems.

This is more likely when there is organic brain damage, an early age of onset, a chronic form of epilepsy, special location (e.g., temporal lobe epilepsy), or a difficult adjustment to social surroundings.

Psychotic breakdown does not usually occur before puberty. Referral to a psychiatrist is indicated in all cases where the patient or his relatives cannot cope with the emotional and/or psychiatric morbidity. When the psychiatric problems need medical treatment, it must be remembered that chlorpromazine (Largactil) and haloperidol (Serenace) lower the threshold for seizures. If possible, benzodiazepines or other less seizure-inducing antipsychotics should be used.

BEHAVIOUR DISORDERS

Brain lesions (from minimal brain damage to more severe damage) can also result in behaviour problems such as hyperactivity, irritability, lack of concentration and aggression, especially in left-sided temporal lobe (if dominant) dysfunction. Right temporal lobe dysfunction tends to make the patient introverted. Occasionally, especially in children, the behaviour problem is a side-effect of the medication (phenobarbitone or clonazepam).

LEARNING DISORDERS

Sometimes there are specific learning problems. Although these children may have normal intelligence, they are often unable to attend normal classes in a normal school because of their restlessness and lack of concentration.
Some causes of these learning disabilities are given in table 19.

Table 19. Causes for learning disabilities

- Presence of actual seizures
- Presence of subclinical epileptic activity
- Structural brain abnormality

  Lesions in the left temporal lobe (if dominant) carry a greater risk of speech and language disorders.

  Lesions in the right temporal lobe (if non-dominant) carry a greater risk of problems with mathematics.
- Use of anticonvulsant drugs
- Unfavourable environmental factors at school and at home causing emotional problems, which might be the most important factors causing academic and social under-achievement.

DEMENTIA

When there are many long-lasting seizures, or repeated status epilepticus, loss of nerve cells results, with the development of early dementia. Early and quick medical control of seizures is therefore very important.

10 Treatment

The first action when a person has a seizure is seizure management (table 20). The second is to find a reason for the seizures (see diagnositic procedures chapter 7). The third is starting treatment.

Table 20. Management during a seizure (fig. 7)

1. Move patient away from fire, traffic or water
2. Take away any objects that could harm the patient
3. Loosen tight clothes, remove glasses
4. Put something soft under the head
5. Turn patient on his or her side, so that saliva and mucus can run out of the mouth
6. Remain with the patient until he or she regains consciousness
7. Let the patient rest and then resume whatever activity he was doing, if he feels like it

Some Don'ts

1. Do NOT try to put anything into the mouth
2. Do NOT give anything to drink
3. Do NOT try to stop the jerking, or restrain the movements.

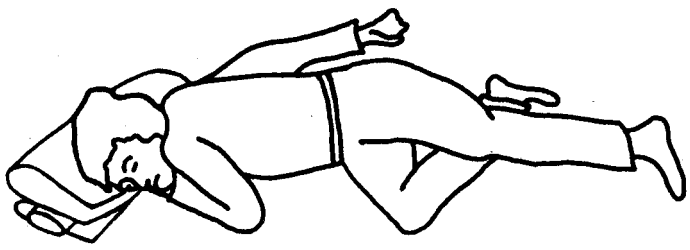


Figure 7. The coma position. Unconscious patients should be placed in this semi-prone position to minimize the risk of obstruction or inhalation of vomit

DRUG THERAPY

More than one seizure should have occurred, and other causes for the convulsions (e.g., hypoglycaemia) excluded (treated) before regular treatment with antiepileptic drugs (AEDs) is begun.

The aim is to try and prevent further seizures, either completely or to reduce their frequency and severity as much as possible with the least possible side-effects (see also table 26, page 75).

The medication should be given daily for many years, sometimes life-long, sometimes less. After a seizure-free period with medication for at least two years in idiopathic, and at least three years in symptomatic epilepsy, the dosage might be reduced very gradually over many months, and, if no relapse has occurred, discontinued. In cases where the epilepsy was very severe before treatment was started, or where there is a known brain lesion, it is better to continue the treatment for much longer, as the chance of a relapse is then much greater. Dose frequency is determined by the elimination half-life time and the need to avoid toxic peaklevels. Guiding principles how to start medication in newly diagnosed patients are summarized in table 21.

A sudden discontinuation may lead to a dangerous status epilepticus. (For treatment see table 22, page 66)

The treatment should be started with *one drug* only. Ideally, the choice of the drug depends on the type of epilepsy and the seizure type. In practice, however, it also depends on the availability and affordability of the drug.

As it is very difficult to know in the beginning which type of epilepsy there is, treatment is usually started according to the presenting seizure type. The most common seizures are the generalized tonic-clonic seizures (GTCS). The main four AEDs—phenobarbitone, phenytoin, carbamazepine and valproate—are almost equally effective for these seizures. If we are able to differentiate between primary and secondary generalized tonic-clonic seizures, then phenobarbitone or valproate are the drug of choice for the primary GTCS and phenytoin or carbamazepine for the secondary GTCS, but all four are effective and can be tried separately if necessary.

Phenobarbitone, if it is the only available drug in a dispensary or health centre, then all patients with epilepsy might be started with phenobarbitone treatment. This medicine is no longer advocated in the developed world, but it is still a useful, effective and cheap anticonvulsant. But if there is no improvement, or even a worsening of the condition, the dosage should not be increased beyond 120 mg daily, and the patient referred to a clinic or hospital where other anticonvulsants are available.

Table 21. Guiding principles to start anticonvulsant drug treatment in previously untreated patients

1. Carefully establish diagnosis.
2. Start drug treatment with one drug.
3. Start drug treatment with a small dose.
4. Gradually increase dosage until complete seizure control. This is the minimum maintenance dose.
5. The aim of treatment is to achieve the lowest maintenance dose which provides complete seizure control.
6. A gradual introduction of an anticonvulsant can produce therapeutic effects just as fast as rapid initiation with large doses, but with fewer side-effects.
7. Severe “intoxication” side-effects appearing at the beginning of the treatment can indicate too rapid or too large dose increases. Side-effects to anticipate include fatigue, excess sleep need, dizziness, or difficulty walking (ataxia).
8. If the initial drug of choice is not well tolerated, e.g., if side-effects occur or if the maximum tolerated dose does not produce seizure control, substitute the initial drug with another first line anticonvulsant.
9. A second anticonvulsant should be added gradually and the first then slowly withdrawn.
10. In case of acute withdrawal symptoms, e.g., recurrence of seizures, use diazepam as a control drug.
11. Regular compliance is the key to successful seizure control, and counselling the patient is the most critical factor in compliance.

The main side-effects of phenobarbitone are drowsiness, especially during the first week of treatment, slowly disappearing, and only recurring when the dosage becomes too high. In some children there might be a reduction in scholastic performance or changes in the behaviour, such as hyperactivity and sometimes aggressiveness. Phenobarbitone has a long half-life time and therefore it will take a few weeks before reaching a therapeutic and effective level. It also means that it can be given only once a day, preferably after the evening meal before retiring to bed. The main indications are the idiopathic generalized epilepsies. But it is also reasonably effective in other generalized seizures and in partial seizures. It is not effective in generalized absences, and it might worsen nocturnal seizures, as it increases the deep sleep. It is the drug of choice, when prophylactic treatment for febrile convulsions is indicated, however, if rectal diazepam can be easily obtained at a reasonable price then instead of prophylactic treatment, intervention when a febrile seizure re-occurs is the preferred strategy.

Phenytoin is also a very effective anticonvulsant for partial and GTCS and seizures during sleep. The main problem is the small margin between the therapeutic level and the level where the metabolizing enzyme gets saturated and the serum level rises steeply to reach toxic values. Increments should be not larger than 50 mg to prevent toxic side-effects. The side-effects are drowsiness, gum hypertrophy and hirsutism, and when the dosage is too high ataxia and nystagmus. Besides these reversible cerebellar signs at high dosage, it has been suggested that a permanent cerebellar syndrome may also result from chronic therapy. A mild sub-clinical neuropathy is common after prolonged phenytoin therapy, but may occur with other drugs too. If toxicity has appeared, the dosage should be omitted for one day and then restarted on a lower level. If at all possible, a change-over to another anticonvulsant could be made to prevent further mishaps.

When medicines are made by different factories, there will be a slight change in the bioavailability and the rate of absorption of the different tablets. Usually this has no therapeutic consequences, except in anticonvulsant therapy, and especially in treatment with phenytoin. A slight increase in absorption of the tablets could result in toxicity, while a slight decrease in absorption might result in recurrence of seizures. As these changes have proved to be unavoidable, the dosage of the anticonvulsant has to be adjusted after the change, preferably assisted by measurement of the serum level.

Phenytoin has also a long half-life time, which is furthermore dose-dependent, being longer at higher doses, and it may take up to two weeks before it becomes effective. It can be given in a once daily dose. As it is slightly irritating to the stomach, it should always be given after a meal, and when the dosage is high, it might be better to divide it into two doses.

Carbamazepine is a drug marketed after 1960. The main indication is for complex partial seizures. But it is also effective for other partial seizures and for all GTCS. It is not effective for generalized absences and myoclonic seizures. In the beginning of the treatment drowsiness and dizziness occur, and occur again when the dosage becomes too high. Then there might be also double vision and ataxia. It does not have a long half-life time and therefore it *cannot* be given once daily. It should be given twice daily and when combined with other drugs it *must* be given three times daily.

Valproate has been marketed since 1966. The main indications are the generalized absences, myoclonic seizures, and the drop attacks. It is also used for the GTCS occurring after awakening. And if necessary it might be used for all other seizure types. When phenobarbitone cannot be used as prophylaxis for febrile convulsions, valproate can be used instead. It has a short half-life time. Although its pharmacodynamic action in the central nervous system exceeds its presence in serum, it should be given three times daily in order to avoid high peak concentrations. The specific side-effects are increase in body weight, loss of hair, and gastric irritation. The effect on the foetus is more serious, as spina bifida might occur. The risk of spina bifida is reduced by supplementing folate in all women at risk of being pregnant.

Ethosuximide is only used when there are absence seizures. If other seizure types are present in the same patient, other medicines have to be added to control these other seizure types. In epileptic syndromes, where absences, myoclonic seizures, drop attacks, or GTCS occur in combination, it is easier to use valproate, as this will take care of all the different seizures.

Clonazepam is rarely used on its own. It is usually added when there is not sufficient control of the seizures, often in children with drop attacks and myoclonic seizures.

Diazepam is used for status epilepticus or febrile convulsion status. It is also used to abort a febrile convulsion to prevent a prolonged febrile convulsion. It should be given intravenously, but if the vein cannot be found, the same solution can be given rectally.

Newer drugs, such as **vigabatrin**, **oxcarbazepine**, **lamotrigine**, **felbamate, gabapentin, topiramate, and levetiracetam** are not discussed as they are not widely available on the African market.

Monotherapy

When treatment is started it is with one drug only. A small starting dose (as detailed in Appendix B for each individual drug) is given for 3–4 weeks (phenobarbitone or phenytoin) or for one week (carbamazepine or valproate) then increased with increments at regular intervals until the seizures are controlled, or until side-effects appear, or until the maximum dosage for the drug has been reached.

If side-effects appear and the seizures are not yet controlled a second drug is introduced and the first drug continued at the level before the side-effects appeared. When the second drug has become effective, the first drug is gradually withdrawn. If seizures recur, the second drug is increased. Only when both drugs have been tried alone up to a level where side-effects occur may a combination of the two drugs be tried.

In a small number of cases (often brain damaged small children) a third drug has to be added, or it has to be accepted that in some cases adequate seizure control cannot be achieved.

In many cases, the first drug will soon be effective, but in some cases it will take many months before the most effective treatment is found. During this difficult period the support and advice of the Epilepsy Aide (page 79) will be extremely important for the patient and his relatives.

The costs of the various medicines makes some unaffordable in Africa. Relative prices are given in table 29 page 83.

Elimination half-life time

Both phenobarbitone and phenytoin have a long half-life time (the time it takes to reduce the concentration of the drug to 50% as it is eliminated, metabolized and excreted). It takes about five times the half-life time before the drug reaches its therapeutic level and the steady state in the blood (see details of individual drugs in Appendix B). It has to be explained carefully to the patient and his caretakers that the seizures will not stop immediately after the medication has begun, but that a change will be noticed only after some weeks.

For the same reason, dosage increments above the expected effective dose should only be made after an interval of 3–4 weeks.

Because of this long half-life time of phenobarbitone and phenytoin it is *not* necessary to give these drugs three times daily. A once-daily dose is sufficient and much more convenient for the patient. Only in small children, who metabolize quicker, is a twice-daily dose indicated.

In newborns the half-life time is even longer and drugs have to be administered with great caution.

Carbamazepine and valproate have a much shorter half-life time; their increments should be given weekly, the therapeutic level is reached much quicker. But the medicines have to be administered three times daily.

At the very onset of therapy the metabolic rate adapts to the presence of certain drugs. This class of drugs is called enzyme-inducers to which belong carbamazepine, phenytoin and phenobarbitone. Therefore, during the first weeks (± 3) the half-life gradually gets shorter. This is a reason to start with small doses.

Interaction

A problem with all medicines, but which is especially noticeable in drugs taken over a long period, is interaction with other drugs. Phenobarbitone, phenytoin and carbamazepine have a *liver-enzyme inducing action*. These increased enzymes metabolize and excrete simultaneously given medicines faster and therefore these medicines do not reach as high a level as would be expected from their dosage.

Valproate *inhibits the action of the liver enzymes* and therefore medicines given simultaneously may reach a higher or even toxic level in the serum than expected from the dosage given.

Phenytoin is bound to plasma proteins to a large extent, but may be displaced by other protein-bound medicines, such as valproate. The results of all these interactions are not always predictable and as routine laboratory facilities for determination of serum drug levels are not yet everywhere available in Africa, patients on anticonvulsant treatment have to be watched closely.

It is very important to remember that anticonvulsants interact with each other; for example, phenobarbitone or phenytoin decreases the carbamazepine level, whereas valproate increases the phenobarbitone level (see individual drugs in Appendix B).

Anticonvulsant drugs also react with other medicines of which the most important are the contraceptive pill, warfarin, antituberculosis medicines, antimycotics, some antibiotics, vitamin D and folates.

The level of contraceptive medication in the serum is decreased by the anticonvulsants phenobarbitone, phenytoin and carbamazepine. Therefore, the action of the contraceptive is no longer reliable and higher doses or other methods of family planning have to be used when the woman is on this therapy.

Antituberculous drugs might increase the level of anticonvulsants and therefore the latter might reach toxic levels.

Side-effects

All drugs have side-effects. These effects can be divided into four main groups, as shown below and specified in more detail in the descriptions of the various drugs in Appendix B.

1. Local effects

Irritation of the gastro-intestinal tract when the drug is taken orally. These can be overcome by taking the medication after meals or when a large dose has to be taken, by *dividing* it into two.

2. Dose-determined effects

A too-high dosage of most of the anticonvulsants might cause drowsiness, nystagmus, diplopia and ataxia. More specific changes are dependent on the particular drug. The dosage should be *decreased*.

3. Idiosyncratic effects

These are allergic reactions such as skin rash, fever or eosinophilia, but also bone-marrow depression or hepatitis.

When these reactions occur the treatment should be *discontinued* immediately and another anticonvulsant used instead.

4. Effects on the foetus and newborn

Congenital malformations might occur when taking the drugs during early pregnancy, but the risk is much less if only one drug is being used. However, the mother's seizures are also dangerous for the young foetus, and treatment has to be continued, but if possible only one drug should be used. During pregnancy the combination of phenobarbitone and caffeine should be avoided.

Anticonvulsants might lead to an increased bleeding tendency in the newborn. Vitamin K has to be given prophylactically to the newborn.

Pregnancy

During the last months of pregnancy an increase in medication is often necessary. This can be reduced again after the baby has been born.

Breast milk

Most of the anticonvulsants are present in breast milk. Very occasionally phenobarbitone causes drowsiness in the baby; with phenytoin the effects are not noticeable. There is no contraindication for breast feeding.

When there is no improvement at all after starting the treatment, the following reasons have to be considered:

– The diagnosis is wrong, it is not epilepsy (the seizures might be fainting attacks or pseudo-seizures).
– The medicine is wrong, wrong drug of choice (e.g., phenytoin for generalized absences), wrong dosage too low or too high, or wrong frequency of administration, e.g., daily dose of carbamazepine given only once a day, instead of divided over two or three times.
– The relation between dosage and serum level is not as it should be as patient does not comply (this can also lead to status epilepticus). Guidelines to promote compliance are given in table 23, page 68.

MONITORING SERUM LEVELS OF AEDS

Several reasons have been mentioned why the dosage may not correspond with the level of the drug in serum. Some persons metabolize these drugs faster than others; or in the case of phenytoin, the enzyme system that metabolizes the drug may get saturated, and the level suddenly rises to a toxic amount. A drug with a long half-life like phenobarbitone may gradually accumulate and unexplained fatigue ensues due to an unexpected toxic level.

A drug may not be absorbed, because of diarrhoea. Or the patient may not take the drug because he forgets or is afraid of taking it. To make sure that the level of the drug in serum is as expected, this level can be measured. However, such investigation is expensive and not available everywhere.

Like there is no absolute effective dose, only a usually effective one, so there is no absolute therapeutic/toxic level.

Pregnancy alters both metabolism and distribution of antiepileptic drugs that may call for adjustment of drug dosage.

DIET

Besides therapy with anticonvulsants, a ketogenic diet has been used in children with intractable seizures. Although it might be effective, it is costly and difficult to follow.

SURGERY

In some cases surgery could be indicated. Required conditions are:

– Long-term appropriate anticonvulsant therapy has not controlled the seizures.
– A clearly defined focal lesion has been demonstrated. Lesions in the frontal part of a temporal lobe are especially suitable for surgery.
– Surgery of this focal lesion should not introduce other neurological problems such as aphasia, or paralysis.

Table 22. Management of status epilepticus

While making arrangements to set up an i.v. line, a few questions must be asked of the accompanying persons (a detailed history can be taken later). Instead of writing "he/she" throughout, "he" is used.

1. Questions

- Is the patient known to suffer from epilepsy? Did he take anticonvulsants? Did he discontinue the intake? If so, when?
- Is the patient known to use alcohol or other drugs? Did he discontinue to use this recently?
- Have any symptoms been noticed that might indicate a disorder apt to cause convulsions?
- When was the last meal taken?
- Were any traditional medicines, especially herbs, taken recently?

The answers to the last three questions above could indicate a hypoglycaemic state.

2. Diagnostic procedures

- If there is no laboratory, a blood glucose determination can be done with dextrostix.
- If there is a laboratory, blood to be taken for more investigations (blood glucose, calcium, electrolytes and urea).
- Lumbar puncture to be done when fever is present or patient's immune system function is poor.
- Other investigations to be done after the seizures are under control.

3. Start i.v. line with 5% glucose solution.

4. Start monitoring pulse, respiration and blood pressure. Prevent aspiration, maintain clear airway.

5. Medicines (Inject into the i.v. line)

a. **Glucose** solution
50 ml of 50% glucose with 100 mg thiamine.

b. **Diazepam**
0.3 mg/kg i.v. very slowly, 1 mg/min, until seizures stop *or* up to 5 mg in children under 5 years; 10 mg in children 5–10 years; 15 mg in older children and 20 mg in adults.

May be repeated after 20–30 min, and once again 30 min later.
If not successful in finding a vein:

- the same solution in the same dosages can be given rectally via a catheter or syringe. (In other countries special "rectioles" with diazepam are available for this purpose.)

N.B. Do not give diazepam i.m.

Continued on page 67

Table 22, *continued*

or give:

c. **Paraldehyde** 0.15–0.20 ml/kg intramuscularly.

N.B. **Paraldehyde reacts with plastic, therefore use a glass syringe.**

Painful injection—avoid if possible.

6. Loading dose

Give loading dose, to prevent recurrence of seizures, 20 minutes after last diazepam injection.

a. **Phenytoin**

15–18 mg/kg very slowly i.v. into the line not more than 50 mg/min, not exceeding 1,000 mg, *or* give

5–6 mg/kg i.v. three times with 30 min in between.

N.B. **Dextrose solutions may precipitate phenytoin.**

N.B. **Do not give these high dosages when patient is already on anticonvulsants.**

N.B. **Do not give phenytoin i.m.**

or

b. **Phenobarbitone**

3–5 mg/kg two or three times during the first 24 hours i.m.

Continue checking pulse, respiration and blood pressure.

7. Maintenance dose

After the loading dose is given, continue with the maintenance dose. When a patient is able to swallow, continue maintenance therapy orally. Give either:

1. phenytoin 5 mg/kg/day orally

   or

2. phenobarbitone 2-3 mg/kg/day orally.

8. Other therapy

Depends on the results of investigations (for instance, if meningitis, start i.v. antibiotics).

9. Further diagnostic procedures

A status epilepticus might be the first sign of a brain tumour.
Skull X-ray, EEG to be done, or patient referred for these investigations. (CT scan.)

NB: The medical emergency is to stop status epilepticus; the appropriate special investigations can be done later once the seizures have been stopped.

Table 23. Promoting compliance

The patient's adherence to any prescribed treatment will increase if the following points are considered. In the particular case of treatment with AEDs (before starting the treatment and during all its duration) the patient has to be warned especially in a clear and understandable way to bear in mind the points e-h. Make sure if:

a. the patient perceives his clinical condition (in this case, seizures) as a problem;

b. the patient is convinced: that the proposed treatment has a reasonable probability of improving his clinical condition (i.e.,, decreasing the magnitude of the problem); that disappearence of seizures does not mean that treatment is no longer necessary;

c. the side-effects (and all other inconveniences involved) are bearable and justified in terms of the perceived benefits;

d. the treatment procedures are easy to follow;

e. the goal of the treatment is the reduction of seizures to a minimum possible. For some patients this could represent no more seizures, but for others only less seizures;

f. the treatment has no immediate effect; it takes a few weeks (two to six) before the drug reaches a protective blood level;

g. prescribed dose should not be altered by the patient and his/her family, regardless of the degree of seizure control. Only the health worker can modify the prescribed dose;

h. abrupt interruption of drug intake should be avoided at all costs as this may precipitate continuous seizures. Provisions should be made for timely procurement of the drug.

The language, the terms and the contextual meaning must be those of the patient. It is also important to enquire about the reasons for non-compliance and to deal appropriately with those reasons.

The following procedures have successfully proven to help in promoting compliance with treatment:

1. Use of family reminders;
2. Linking drug intake to specific daily activities; and
3. Increased home visits with repeated explanation of:
   - the necessity for continuous long-term treatment, and
   - possible side-effects.

Source: Initiative of support to people with epilepsy. Division of Mental Health, World Health Organization, Geneva 1990

11 Febrile convulsions

This syndrome is discussed separately in this chapter as it is one of the most commonly seen syndromes.

A febrile convulsion has been defined as an event in infancy or childhood that occurs between three months and five years of age, associated with a fever but without evidence of intracranial infection or defined cause (Consensus Development Panel, 1980).

The highest incidence is in children between nine and 20 months.

About 3% of all children develop febrile convulsions. A genetic trait is most probably present, disposing a particular child to get it easily. It often occurs in siblings as well.

It is usually a benign disorder occurring in children of normal development and occurring early in a recognizable illness, when the temperature is rising. They are single, brief, bilateral tonic-clonic seizures. The prognosis is good. A recurrence may occur in one third of the cases, but then the children grow out of it.

A minority of the seizures, however, are of longer duration (more than 15–20 minutes) or occur repeatedly within 24 hours or show partial or unilateral features. These are the so called complex or complicated febrile convulsions.

These prolonged seizures are not so benign and may lead to cerebral atrophy and mesial temporal sclerosis, which could result in temporal lobe epilepsy with or without permanent neurological deficit. Prolonged seizures might become unilateral and a special syndrome, HHE syndrome (a condition of Hemiconvulsions, Hemiplegia and later Epilepsy) has been recognized in association with these febrile status epilepticus.

While the prognosis of febrile convulsions in most cases is excellent, there are three risk factors causing febrile convulsions to become epilepsy. They are:

– A history of epilepsy in a first degree relative
– A neurological abnormality present after the first febrile convulsion
– A complex first febrile convulsion (multiple, focal or prolonged).

Several studies have been done but only the figures from the American

National Collaborative Perinatal Project are presented here and they show that:

– 1.6% of all children with febrile convulsions develop epilepsy
– 10% of children with two or three risk factors develop epilepsy
– 0.5% of children who do not have febrile convulsions develop epilepsy.

Other studies quote different data, e.g., double or triple risks to develop epilepsy.

MANAGEMENT OF FEBRILE CONVULSIONS (table 24)

When a child is brought to the clinic after a febrile convulsion, the cause should be actively sought. When no obvious disease is found, a lumbar puncture must be done to rule out a possible meningitis. The original disease should be treated, and the mother reassured. Although most children have only one febrile convulsion in their life, it may recur with a following febrile disease. Therefore, the mother should be told that if the child develops a fever again, she should give paracetamol **n.b. not salicylates** and do tepid sponging to control the temperature. If a recurrence still takes place, then it might be necessary to give prophylactic treatment after the second period.

Indications for prophylactic treatment are:

– two or more febrile convulsions
– one complex febrile convulsion (multiple, focal or prolonged)
– one febrile convulsion with a family history of epilepsy or febrile convulsions
– one febrile convulsion and a neurological abnormality.

Prophylactic treatment can be done in two ways:

– abortion of each febrile convulsion with rectal diazepam, or
– continuous administration of phenobarbitone or valproate.

Although the second method is no longer advocated in the developed countries, as long as diazepam for rectal use is not available, it should be done, especially in areas where malaria and childhood infections are common. Phenobarbitone is very effective and can be given in one daily dose before bedtime. If phenobarbitone causes side-effects in the form of behaviour disturbances, then valproate might be given wherever available and affordable.

The prophylaxis should continue till the child reaches five years of age with a one-year seizure-free period. If, however, seizures still occur, the prophylaxis should be continued beyond the age of five years until a one-year free period has been reached.

If seizures have occurred without fever, then the condition has become epilepsy and the administration of phenobarbitone (or valproate) should be continued until a two-year seizure-free period has been reached.

Table 24. Management of febrile convulsions

1. When a seizure lasts longer than 15 min, then it should be stopped with either
   a. diazepam, 0.3–0.5 mg/kg bodyweight slowly intravenously, or the same solution in the same dosage given rectally in a syringe via a short catheter. (Do not give it intramuscularly.) If necessary once again,

   or

   b. paraldehyde, 0.15–0.20 ml/kg bodyweight intramuscularly up to 5 ml. This injection is painful. Use a glass syringe or the newest plastic syringe; ordinary plastic syringes will be spoilt.

2. Ensure a clear airway.

3. Reduce temperature with
   – tepid sponging and
   – antipyretics, e.g., paracetamol 120–240 mg 6-hourly. (Aspirin, i.e., salicylate should not be used as it might cause Rye's syndrome.)

4. Treat original disease.

5. Start prophylactic treatment, if required, with
   – phenobarbitone, 5 mg/kg once daily as an evening dose, or
   – valproate 20–30 mg/kg divided into two doses.

   Note: phenytoin and carbamazepine are not indicated.

6. Prevent malaria attacks by use of mosquito nets, and childhood infections such as measles with vaccination.

12 Prognosis

Prognosis was mentioned briefly in table 12, page 37. It is very difficult to predict the course of the epilepsy in any individual patient. However, it has been agreed by several authors that some factors give a poorer prognosis and some forms are more difficult to treat than others. The factors associated with a poor prognosis are given in table 25.

Rodin (1968) noted that a general opinion was that the seizures of 60–80% of all patients could be satisfactorily controlled by current medication, but complete cessation for at least a two-year period was only found in a third of all patients. Recent data with more, although expensive antiepileptic drugs available claim that now complete cessation can be reached in over 70% (JWAS Sander and Matti Sillanpää, 1998).

In a follow-up of 200 children, treated with the means now generally available in Africa, after 25 years, two-thirds suffered minimal ill-effects, but one-third were difficult to treat and a number of them had to be cared for in an institution or were invalids at home.

In a similar study where 20,000 patients were followed, complete control was found in 60%, seizures were reduced in frequency and/or severity in another 25%, and these patients could also lead essentially normal lives, but seizures were refractory to all therapeutic measures in the remaining 15% (Livingston, 1972).

From these studies it has been found that the generalized idiopathic epilepsies and the partial idiopathic epilepsies had the best prognosis. The condition could be improved upon in the partial symptomatic epilepsies, but the generalized symptomatic epilepsies were resistant to treatment.

Shorvon and Reynolds (1982) found that a prognosis could be made early in the course of the epilepsy. If treatment was started early after the onset of the seizures and good control was achieved soon, the prognosis was excellent. If, however, the seizures are still present after some years of treatment, the chances of complete remission are much less.

For the patient it is of vital importance that not only are his seizures controlled, but that the quality of his life is as good as possible.

In all patients, therefore, continuous medical guidance and supervision are necessary, and the assistance of an Epilepsy Aide is indispensable in overcoming the social difficulties that the epilepsy patient experiences.

Table 25. Factors associated with a poor prognosis

– A combination of different seizure types in one patient (as in symptomatic or cryptogenic generalized epilepsies)
– Complex partial seizures
– Late start with treatment
– Somatic neurological deficits
– Psychiatric abnormalities
– Neonatal seizures
– Infantile spasms
– Occurrence of status epilepticus

13 Prevention

In a number of patients symptomatic epilepsy could have been prevented.

From our knowledge of the main causes of epilepsy in Africa we know that the following preventive measures should be considered:

- Provision of waiting areas for pregnant women near hospitals for timely intervention (Caesarean section, vacuum delivery, etc.) at the time of delivery to save the mother and prevent life-long disabilities from birth asphyxia or trauma in the newborn child;
- Early diagnosis and early adequate treatment of bacterial meningitis (transfer to clinic for i.v. treatment);
- Adequate malaria treatment in areas where chloroquine resistance has developed. Primary health workers should be informed about the changing resistance pattern;
- Prevention of malaria attacks (mosquito nets, etc.);
- Prevention of cysticercosis (hygiene; no human manure for agriculture);
- Measles vaccination;
- Prevention of road traffic accidents and other trauma;
- Improvement in treatment and management of other conditions mentioned in table 1 (page 8), such as metabolic disturbances, e.g., hypoglycaemia, electrolyte imbalance following diarrhoea and/or vomiting, hyperbilirubinaemia, etc.;
- Improvement in treatment and management of prolonged febrile convulsions;
- Effective and early treatment of seizures and status epilepticus so that further brain damage is prevented (table 26);
- Genetic counselling where a hereditary disease is diagnosed.

Table 26. Seizure prevention: some precipitating factors and possible preventive measures

Flashing lights	wear sunglasses when travelling by car or bus, sit as far as possible from a TV screen;
Alcohol	avoid becoming drunk (an occasional drink is not harmful);
Hypoglycaemia	do not skip meals, eat at regular times;
Physical stress	find out how far you can go, what is your limit;
Mental stress	stress cannot always be avoided; for very limited time periods such as sitting for an examination, a mild tranquillizer may be added;
Sleep deprivation	keep regular hours. If working shifts, a sleeping tablet may be necessary when changing shift duties;
Physical systemic illness	to be treated promptly.

14 Social aspects

Any seizure is a frightening experience, especially for the parents of a child, and for the close relatives of anyone with epilepsy. And the impact of epilepsy logically is a source of stress.

Throughout the world and through the ages epilepsy has been regarded as a supernatural happening as it is inexplicable and unpredictable. It is often believed to be a consequence of possession, curse(s), witchcraft or punishment for some ancestral error.

Epilepsy is often believed to be a contagious disease, and that anyone who touches the patient, or his excreta, will acquire the disease themselves. These beliefs make the patient and his family very unpopular and isolated. The frightening experience of the seizures can make people try any available means to lessen their severity, e.g., witchcraft, herbalism, offerings, prayers, and also modern drugs. As complete cure is the real aim, various treatments are tried and/or discarded and others tried, sometimes simultaneously.

Before we start our treatment some points have to be made very clear. The more time the doctor and the Epilepsy Aide take over this the better will be the compliance of the patient and the longer the follow-up. The points given in table 27 page 78, have to be made clear.

It is impossible for a doctor to get all these points across to the patient and his parents in five minutes during a visit to the clinic. For this reason the Kenya Association for the Welfare of Epileptics has employed people called “Epilepsy Aides” who are specially trained to deal with the problems arising from epilepsy. Each clinic has such an Epilepsy Aide (page 79).

When the child with epilepsy is of normal intelligence he can attend a normal school. But often teachers and heads have to be reassured that the condition is not dangerous to the staff and other pupils. Teachers and parents should be given appropriate counselling so that they learn to accept that epilepsy is not a disabling condition but one that can usually be controlled and lived with. Families of people with epilepsy benefit from proper counselling and they can then help the patient feel more accepted by the family and the community.

Some children, although of normal intelligence, have specific learning disabilities, which require special attention from the teacher.

When the child with epilepsy is of subnormal intelligence (and we may expect 20–30% of our patients to be so), assessment has to be made to see what kind of special education is needed, e.g., normal school with special supervision, special class in normal school, or special school. For example, the Kenya Institute of Special Education (KISE) has established 40 assessment centres throughout the country. The Epilepsy Aide, with the help of such a centre, can determine the best available educational facility for the child.

If the child has a severe or profound mental retardation (one-third of the mentally retarded group), institutional care may be necessary, especially if there is also a physical handicap. There are not yet sufficient institutions to accommodate all the children requiring such facilities in Africa, therefore, the Epilepsy Aide, with the help of a social worker and an occupational therapist, should assist the mother as much as possible with the care of the child.

For adults with epilepsy counselling is as necessary as for children, and they may need special advice and help with choice of work. For example, they should not become professional drivers or do a job requiring standing on ladders, climbing trees or using heavy machinery until seizures have been controlled (no seizures at all) for at least two years. Otherwise nearly any type of work is open to people with epilepsy. However, it is important that the person's colleagues know that seizures may occur sometimes and are instructed how to handle such a situation.

There are situations which the patient learns may precipitate a seizure. Then it is better to avoid these situations, or if they are unavoidable, to ask for an increased dosage of the anticonvulsant drug so as to enjoy as normal a life as possible. Some of the well-known precipitating factors and the possible preventive measures are given in table 26, page 75.

When the seizures are not completely controlled, precautions have to be taken when swimming or bathing. Someone else should always be near at hand, and when going to the toilet the door should not be locked.

FIRE HAZARD

Many mothers cook on *jikos* (charcoal stoves). These are usually placed on the ground. Any young child may fall on such a *jiko*, but children with seizure disorders are even more prone to be burned. To prevent accidents with fires, a protective shield should be made around the stove or it should be raised off the ground. Similar precautions should be taken to protect children and adults with epilepsy from burning themselves on open fires or electrical appliances.

Table 27. Facts to be stressed to an epilepsy patient and relatives

– Drugs have to be taken for many years, possibly a life-time;
– Discontinuation of the drugs will result in recurrence of the seizures;
– Sudden discontinuation may result in life-threatening status epilepticus;
– It may take several days to a few weeks before the drugs have any effect;
– A combination with herbal treatment might be dangerous as interaction between the drugs and the herbs cannot be predicted;
– The disease is not contagious and anyone can touch the person while he is having a seizure (e.g., to remove him from the danger of fire or water), or in between the seizures;
– If the child is of normal intelligence he should be placed in a normal school;
– Over-protection is not helpful in a child's upbringing, but reasonable precautions should be taken if there are still occasional seizures (e.g., protection from fire, swimming under supervision, not climbing trees);
– Epilepsy has to be talked about in the family, at school or in the work surroundings;
– Epilepsy is not a reason for being unable to marry and have a family.

15 Special epilepsy clinics

As the number of patients with epilepsy who are seeking medical treatment is rapidly increasing, they should be seen and treated in the existing health services. But every patient with epilepsy needs attention in a different way from a patient with, for example, tonsillitis who will be cured in a few days. Therefore a clinic especially for epilepsy patients is advocated where special attention can be given more easily than in a busy general out-patients department.

The patient with epilepsy has to be informed about his/her chronic disease. Explanations have to be given about the medicines and their use, as compliance with drug taking is essential in seizure control. To suddenly stop taking medicines may result in a dangerous status epilepticus.

Depending on the number of patients attending, a clinic once a week or once a month is sufficient. An interval longer than a month is not advisable as a patient has to be seen more often after initiating the treatment. In the beginning, a monthly visit is necessary to observe seizure control and reactions to the medication. If allergic side-effects occur even this interval is too long.

Patients must be informed that if reactions such as skin rash or fever occur they must visit the medical centre before the appointed date.

When good seizure control has been achieved a three-monthly visit schedule is sufficient.

FIRST VISIT

The process of history-taking and counselling of the patient and his family is very time consuming. Not only are there the medical problems, but the social problems also have to be discussed as these are sometimes more worrying than the actual seizures. Registration cards have to be made out.

THE "EPILEPSY AIDE"

Within a clinic it is very valuable to employ an Epilepsy Aide or social worker. In KAWE clinics these are persons with secondary-school education who come from the area where a clinic is situated and speak the same language as the patients in that clinic. They are specially trained to deal with problems arising from epilepsy such as schooling, unemployment, social ostracism, non-compliance and so on.

If the community already has a Community Health Worker, he/she will identify the patients with epilepsy in that community and refer them to the Epilepsy Aide, who will take a full medical and social history before referring the patient to the Epilepsy Clinic.

If, however, the community does not have a Community Health Worker, the Epilepsy Aide himself has to identify patients with epilepsy in the community.

The Epilepsy Aide sees the patient before, during and after clinic hours so as to be able to answer the many questions arising from this special condition and its treatment. The Aide also gives advice on the necessity for drug compliance. Moreover, the Aide keeps in contact with the patient and his/her relatives between visits to the clinic to help with any problems, e.g., school, job, recreation.

To help parents, teachers and health workers, National Epilepsy Support Foundations have published booklets. If such an organization does not yet exist in the country the International Bureau for Epilepsy can be contacted (see useful addresses page 122).

REGISTRATION CARDS AND RECORD KEEPING

Patients with epilepsy are treated for many years and information has to be kept for a very long time. Records should be clear and easily accessible so that anyone can continue the treatment in the absence of the usual medical worker. Patients and the medical worker must know the present medication and what has been given before. If the therapy has been changed, what was the reason, e.g., allergy, no response, etc?

At every visit the patient must get a date for the next appointment, so he realizes that treatment has to be continued. In KAWE clinics instructions are given to return left-over tablets. Compliance can be measured by counting them and warnings given if necessary.

It may be useful to make out the registration and record-keeping cards as detailed in table 28.

Table 28. Useful registration and record cards

1. Epilepsy treatment record card (kept in the clinic)
The history taken by the Aide should be kept, but a summary with the positive findings should be entered on this card. Initial treatment and number of tablets dispensed is recorded. Progress notes are made here, and the number of seizures noted. Samples of these cards are given in Appendix D. When the epilepsy clinic is held in an established health facility, the usual clinic cards can be adapted for use in the epilepsy clinic.

2. Seizure record card
This card is kept by the patient or by a member of the family. Seizures are recorded by the day and any unusual symptoms are noted.

3. Epilepsy appointment card
This card is kept by the patient. Besides the clinic's and patient's name and registration number, the date of the next appointment is given. Present medication is recorded on this card.

For card numbers 2 and 3, an ordinary exercise book cut in half is very useful.

4. Appointment book
This book is kept at the clinic.

After every clinic the book is checked to see which patients did not attend, and the Aide can take action accordingly.

5. Epilepsy register
This register is kept at every epilepsy clinic by the medical worker running the clinic. The information entered on this register is used for annual reporting. If every clinic uses the same register uniform reporting is guaranteed and information for epidemiology studies can be collected (see sample in Appendix D).

6. Annual report form
Information from the epilepsy register is entered on this form and sent yearly to the District Medical Officer of Health (see Appendix D).

7. Recording of drugs used
This can either be done on the Epilepsy Register or on a separate sheet of paper.

MEDICINES AND COSTS

Supply

When an epilepsy clinic is opened it is **absolutely essential that a regular drug supply be maintained.** This is even more important in epilepsy than for any other medical condition. Irregular treatment is as bad as no treatment at all (indeed it may be worse as *status epilepticus* may be precipitated).

Costs

A disorder that requires therapy for many years or for life is, in addition to being a medical and social problem, a great financial burden to the patient, parents and other relatives.

This burden can be alleviated by not charging for consultation. Because costs have to be covered, some cost-sharing has to be introduced. For example, KAWE has introduced cost-sharing in 1996 and sells drugs at cost price. Still many poor patients can not afford the drugs and those are now being sponsored. KAWE encourages each clinic to form a Community Based Organization, consisting of patients, relatives and well-wishers. They have tasks such as awareness creation, counselling, home-visits, helping out in the clinic and they will put in place modalities to carry together the financial burden for the poor patients.

The costs are dependent on the type of drug used. If phenobarbitone is used alone and bought wholesale from local manufacturers the cost per patient per year is (prices of the year 2000) between US$ 0.9 - US$1.35 (Burkina Faso) and US$ 11.- - US$ 16.- (Togo). But when carbamazepine is used the costs per year per patient may reach at least US$ 18.- (Cameroon) to US$ 146.- (Gabon) and for valproate annual costs for adults would lie between US$ 237.- (South Africa) and US$ 420.- (Gabon).

Prices do change continuously. In table 29 the relative costs of the defined daily dose (the usually effective dose/day) of various AEDs is compared with the cost of phenobarbitone.

Syrups are more expensive than tablets. As most children can take tablets quite easily, syrups are not really necessary. If there are problems with swallowing, all uncoated tablets (phenobarbitone, carbamazepine, clonazepam, and sometimes phenytoin) can be crushed and administered in milk, tea or porridge. Only if tablets are coated (valproate and sometimes phenytoin) might syrups be indicated.

If, however, no funds are available for the medicines, cost sharing can be worked out according to the policy of the health institution where the epilepsy clinic is held.

Table 29. Relative cost of the daily requirement of anticonvulsants

Antiepileptic drug	Usually effective daily dose (mg)	Price relative to Phenobarbitone
Phenobarbitone	100	1,00
Phenytoin	300	1,13
Carbamazepine	800	4,89
Clonazepam	8	5,03
Ethosuximide	1250	6,41
Valproate	1500	7,52
Oxcarbazepine	1500	15,53
Vigabatrin	2000	32,59
Lamotrigine	300	41,54
Gabapentin	1800	44,87
Topiramate	300	52,17
Levetiracetam	2000	59,34
Felbamate	2400	82,43

The relation of the costs are based on a specific set of data from one country, therefore the multiplication factor may vary in other places; however, in general this will not influence the ranking very much.

Other costs

The setting up of a special epilepsy clinic need not involve many other costs. The Medical or Clinical Officer has only to re-allocate his time: he works in his normal surroundings. A member of staff could be trained as an Epilepsy Aide, or someone has to be employed for this function.
A national epilepsy support organization may be able to provide assistance on request. The Epilepsy Aide should make home visits. The best method of transport is probably by bicycle/motorcycle.

photo: J. Loeber

"Please give me my daily medicines"

Appendices

APPENDIX A

Review of the epilepsies and their treatment according to age-linked groups

Seizures starting in the first three years of life are often symptomatic. With modern investigation methods and laboratory techniques it is often possible to find the cause.

Seizures starting in the 5–15 years age group are often idiopathic, while seizures beginning in adults are again often symptomatic.

Treatment of seizures in the newborn

All newborns with seizures should be transferred to hospital to determine the cause (hypocalcaemia, hypoglycaemia, meningitis, jaundice, etc.) and treatment given accordingly.

To stop the seizures one injection of diazepam 0.5 mg/kg i.v. may be given followed by phenobarbitone, loading dose 15–20 mg/kg i.v., then maintenance dose 3.5 mg/kg daily.

N.B. If pyridoxine-dependent epilepsy, then treatment is 100 mg pyridoxine daily until dietary pyridoxine can take over.

If pyridoxine deficiency, supply 5 mg pyridoxine daily.

EPILEPSIES IN THE NEWBORN

(In the first 28 days about 0.5% of neonates have seizures)

Idiopathic

– *Benign neonatal familial convulsions (prevalence unknown)*

Occurrence:	on the second and third day of life
Seizure type:	clonic or apnoeic spells
Aetiology:	it is a rare, dominantly inherited disorder, without a known aetiological factor
Prognosis:	about 14% develop epilepsy.

– *Benign neonatal convulsions (2%-7% of all neonatal convulsions)*

Occurrence:	around the fifth day
Seizure type:	frequently repeated clonic or apnoeic seizures
Aetiology:	no known aetiological factor
Prognosis:	good, no recurrence of seizures, psychomotor development not affected.

Symptomatic

Seizure type:	focal-clonic, tonic, clonic, or apnoeic spells
Aetiology:	birth asphyxia, intracranial haemorrhage, infections, metabolic disorders, developmental abnormalities, pyridoxine dependency
Prognosis:	depends on the degree of brain damage from complete recovery, recovery with lasting neurological sequelae (spastic quadri- and hemiplegia, mental retardation) or death

– *Pyridoxine-dependent epilepsy (prevalence rare)*

Onset:	within the first 24 hours of life
Seizure type:	focal and generalized child is very irritable, has brisk reflexes and hypotonia
Aetiology:	an autosomal recessive disorder
Prognosis:	poor, may die *or* survive with mental handicap

– *Pyridoxine deficiency (prevalence rare)*

Onset:	maybe later than Pyridoxine dependency
Seizure type:	generalized
Aetiology:	lack of vitamin B6 in the diet malnutrition, malabsorption interference by other drugs such as isoniazid

– *Early myoclonic encephalopathy (prevalence rare)*

Onset:	before 3 months of age
Seizure type:	initially fragmentary myoclonus, then erratic partial seizures, massive myoclonus, or tonic spasms
Aetiology:	familial cases are frequent and suggest the influence of one or several congenital metabolic errors.
Prognosis:	poor, psychomotor development is arrested, death may occur during the first year

– *Early infantile epileptic encephalopathy with suppression burst (Ohtahara's syndrome; prevalence rare)*

Onset:	within the first few months of life
Seizure type:	frequent tonic spasms, partial seizures may occur, myclonic seizures rare
Aetiology:	obscure
Prognosis:	poor with severe psychomotor retardation, seizure intractability, often there is evolution to West's syndrome at age 4–6 months

EPILEPSIES STARTING IN CHILDREN AGED 3 MONTHS TO 3–4 YEARS

Many forms of epilepsy begin in this age group, e.g.,

- The localization-related symptomatic epilepsies (after injury or infection);
- The generalized symptomatic epilepsies (often the epilepsies occurring as a result of inborn errors of metabolism);
- The special syndromes (West, Lennox-Gastaut);
- The myoclonic epilepsies.

There is a frequent association with neurological signs and/or mental retardation. The outcome is often unfavourable.

The seizures in this age group are characterized by the rarity of generalized tonic-clonic seizures, most probably due to incomplete maturation of the inter-hemispherical pathways. Generalized tonic seizures and myoclonic seizures are the main seizure types.

- *Infantile spasms (West's syndrome;hypsarrhythmia;* 2.65% of all epilepsies: Loiseau 1991)

  Onset: between 4 and 7 months, always before 1 year

  Seizure type: most often a flexor spasm, a sudden flexion of the head, bending of the knees, and flexion with abduction of the arms (Salaam attack); sometimes an extensor spasm, like a Moro reflex, with abduction and extension of the arms, neck, trunk and legs; *or*

  a mixed picture with arms and head flexed and legs extended;

  they last only a few seconds, or even less than a second, but may be repeated many times some seconds apart

  Aetiology: most often organic brain damage caused by
  - infections (pre- or postnatal) such as cytomegalovirus, toxoplasmosis, viral encephalitis, rubella or syphilis;
  - birth asphyxia, low birthweight;
  - congenital malformations and metabolic diseases;
  - idiopathic, no known cause

  Prognosis: depends on the degree of brain damage, about 80% are mentally retarded, a smaller group also having cerebral palsy;

  in the idiopathic group, the prognosis is favourable when treated early

  Treatment: to be carried out in hospital
  - ACTH, 20–60 int. units daily i.m. for one or more months followed by prednisolone; *or*
  - prednisolone from the start, 2 mg/kg daily;
  - nitrazepam, clonazepam, or valproate, although less effective, can also be used.

– *Lennox-Gastaut syndrome* (0.78% of all epilepsies: Loiseau 1991)

Onset:	usually between 3–5 years (2–7)
Seizure type:	a combination of absences, myoclonic jerks and atonic falls, many times daily, often with injuries to chin, teeth, nose, forehead and occiput (a protective helmet is recommended);
	status epilepticus is frequent
Aetiology:	– following infantile spasms
	– measles encephalitis
	– subacute sclerosing pan-encephalitis (*see page 92)
	– anoxia, e.g., after a prolonged febrile convulsion
	– lead poisoning
	– degenerative brain diseases
	– cryptogenic
	– idiopathic
Prognosis:	very poor, may persist into adult life;
	90% are mentally retarded;
	progressive dementia, ataxia may occur;
	very difficult to treat
Treatment:	seizures very resistant to the usual anticonvulsants;
	many drugs are tried, and often these children are overtreated with a combination of more than three drugs, without success.

– *Epilepsy with myoclonic-astatic seizures (Doose's syndrome,* 0.16% of all epilepsies: Loiseau 1991)

Onset:	mostly between 2 and 5 years (7 months–6 years)
Seizure type:	myoclonic, astatic, myoclonic-astatic, absences with clonic and tonic components;
	status frequently occurs;
	difficult to differentiate from the Lennox-Gastaut syndrome
Aetiology:	often idiopathic;
	usually a normal developmental background
Prognosis:	course and outcome variable
Treatment:	valproate, clonazepam.

– *Benign myoclonic epilepsy in infancy* (1.25% of all epilepsies: Loiseau 1991)

Onset:	during first or second year of life
Seizure type:	generalized myoclonus in brief bursts
Aetiology:	often a family history
Prognosis:	easily controlled by treatment;
	may be accompanied by a relative delay of intellectual development and minor personality disorders
Treatment:	valproate.

– *Severe myoclonic epilepsy in infancy*

(7% of the epilepsies with onset before 3 years: Dalla Bernadina et al. 1982)

Onset:	during the first year of life
Seizure type:	generalized or unilateral febrile clonic seizures, then myoclonic jerks and often partial seizures
Aetiology:	a family history of epilepsy or febrile convulsions; normal development before onset
Prognosis:	psychomotor development is retarded from the second year of life onwards; ataxia, pyramidal signs and interictal myoclonus appear
Treatment:	very resistant to all forms of treatment.

SEIZURES OCCURRING BETWEEN 6 MONTHS AND 5 YEARS

Seizures occurring in children in this age group are often febrile convulsions. This is usually a benign condition and is discussed in Chapter 11.

EPILEPSY STARTING IN CHILDREN AGED BETWEEN 3 AND 10 YEARS

In this age group the symptomatic epilepsies still start, depending on the age at which the disease or injury occurred.

But this age group is more characterized by the emergence of the idiopathic epilepsies. These occur in both groups, the epilepsies with partial onset of seizures, and the group with generalized onset of seizures. The prognosis is often favourable.

Localization-related epilepsies, idiopathic

– *Benign childhood epilepsy with centro-temporal spikes (Rolandic epilepsy;* 7.47% of all epilepsies: Loiseau 1991)

Onset:	between 3 and 13 years (peak 9–10 years)
Seizure type:	partial motor, often affecting the face; related to sleep, no loss of consciousness; may develop into generalized tonic-clonic seizures
Aetiology:	idiopathic
Prognosis:	good, usually disappears with or without treatment before the age of 16
Treatment:	if necessary, carbamazepine to be continued until a two-year seizure free period has been reached; if seizures occur only at night and if side-effects of carbamazepine are evident, or in case of adverse social aspects, e.g., stigmatization, not starting or withdrawal of treatment can be considered.

– *Childhood epilepsies with occipital paroxysms*
(0.78% of all epilepsies: Loiseau 1991)

Onset:	childhood
Seizure type:	seizures start with visual symptoms or hallucinations together with anxiety, often followed by a hemiclonic seizure or automatisms, followed by migrainous headaches
Aetiology:	idiopathic
Prognosis:	not certain
Treatment:	as in benign childhood epilepsy, above.

Localization-related epilepsies, symptomatic

(40% of all epilepsies in children younger than 15 years: Vianni et al. 1988)

Onset:	throughout childhood viral, bacterial and parasitic diseases may occur, neurological sequelae with seizures may develop months or years after the event;
	accidents are also a common cause
Seizure type:	partial with or without secondary generalization
Aetiology:	often cryptogenic;
	usually a normal developmental background
Prognosis:	depends on the brain lesion
Treatment:	phenytoin, carbamazepine;
	if the seizures become secondary generalized, phenobarbitone may be used.

Generalized epilepsies

– *Childhood absence epilepsy (pyknolepsy;* 9.35% of all epilepsies: Loiseau 1991)

Onset:	children of school age, with peak manifestation 6–7 years
Seizure type:	see page 23
Aetiology:	idiopathic
Prognosis:	remits in adolescence, but may be replaced by generalized tonic-clonic seizures (GTCS)
Treatment:	ethosuximide, valproate.

– *Epilepsy with myoclonic absences* (0.16% of all epilepsies: Loiseau 1991)

Onset:	between 1 and 12 years
Seizure type:	absence accompanied by severe bilateral rhythmical clonic jerks, often associated with tonic contractions;
	they may occur many times a day;
	the patient may be aware of the jerking movement
Aetiology:	not defined

Prognosis: less favourable than in childhood absence epilepsy; mental deterioration occurs; possible evolution to other types of epilepsy such as Lennox-Gastaut syndrome.
Treatment: resistant to treatment

– *Acquired epileptic aphasia (Landau-Kleffner syndrome;* 0.2% of a children's hospital cohort of epilepsies: Kramer et al. 1998)

Onset: childhood
Seizure type: generalized convulsive or partial
Other symptoms: rapid reduction of spontaneous speech; behavioural and psychomotor disturbances
Prognosis: remission before the age of 15.
Treatment: valproate, ethosuximide, benzodiazepines or corticosteroids (phenytoin and phenobarbitone may aggravate the condition)

SEIZURES STARTING IN A CHILD OF OVER 9

In this age group there is still onset of a number of idiopathic epilepsy syndromes.

– *Juvenile absence epilepsy (*2.65% of all epilepsies: Loiseau 1991)

Onset: around puberty
Seizure type: as in childhood absence, but less frequent and more sporadic; often there are GTCS in addition
Aetiology: idiopathic
Prognosis: good, however, treatment has to be maintained throughout life
Treatment: valproate.

– *Juvenile myoclonic epilepsy (impulsive petit mal; Janz syndrome;* 4.83% of all epilepsies: Loiseau 1991)

Onset: around puberty
Seizure type: bilateral, single or repetitive, arrhythmic, irregular myoclonic jerks on awakening, predominantly in the arms; a fall from a jerk might occur, no disturbance of consciousness; often there are GTCS, and less often infrequent absences in addition; sleep deprivation may precipitate seizures; seizures are often photostimulated
Aetiology: idiopathic
Prognosis: good, however, treatment has to be maintained throughout life

Treatment: valproate is the treatment of choice but phenobarbitone could be tried;
night-time sleep should be sufficient.

– *Epilepsy with GTCS on awakening* (1.87% of all epilepsies: Loiseau 1991)

Onset: second decade of life
Seizure type: generalized tonic-clonic seizures shortly after awakening;
sometimes they occur in the evening in the period of relaxation;
may be precipitated by sleep deprivation;
significant correlation with photosensitivity;
other seizure types like myoclonic jerks and absence may occur
Aetiology: idiopathic
Prognosis: good, however, treatment has to be maintained throughout life
Treatment: valproate is the treatment of choice but phenobarbitone could be tried;
night-time sleep should be sufficient.

– *Primary reading epilepsy* (prevalence rare)

Onset: late puberty
Seizure type: simple partial motor involving masticatory muscles or visual, and if the stimulus is not interrupted, GTCS may occur
Aetiology: this syndrome may be inherited
Precipitating factor: reading, especially aloud, independent of the content of the text
Prognosis: benign, little tendency to spontaneous seizures; there are no abnormal neurological findings, but an abnormal EEG pattern.
Treatment: valproate (not always necessary).

* *Subacute sclerosing pan-encephalitis (SSPE) is a rare, encephalitis of decreasing incidence as its aetiology the measles virus is eradicated. It is a slow virus infection, the encephalitis occurring several years after the primary measles infection. Prognosis is poor, over a period of several months there is deterioration of intellectual function, motor function, and there is generalized myoclonic jerking. The patient becomes bedridden, this phase may last for some years and leads to death. Treatment is supportive; corticosteroids may be tried.*

EPILEPSY AFTER HEAD INJURY

The onset of these seizures depends on the age at the time of the accident, e.g., birth trauma will give seizures in the first year of life.

Not everyone who has had a head injury will develop seizures. Seizures are more common when the injury has been penetrating, when there was a depressed skull fracture, an intracranial haematoma, or if in the acute state there was post-traumatic amnesia of more than 24 hours' duration. Post-traumatic seizures develop in 50% in the first year following the accident, and another 20% will have developed by the end of the second year. The use of prophylactic anticonvulsants after a serious head injury may be considered. Thus far studies on prophylaxis have not been able to demonstrate an effective approach.

EPILEPSY CAUSED BY A BRAIN TUMOUR

A tumour, benign, malignant or a metastasis, may occur in any age group, but is more common in the older age group.

Epilepsy starting after the age of 20 years is always suspicious and full investigations, preferably with CT scan should be done.

EPILEPSY FOLLOWING CEREBRO-VASCULAR DISEASE

In people over 50 years old, cerebro-vascular disease is a common cause of epilepsy. The seizures may follow a cerebro-vascular accident (stroke), or may develop during the course of a subclinical cerebro-vascular disease.

In all these groups (injury, tumour, cerebro-vascular accident) the type of seizure depends on the localization of the injury.

Treatment is with phenytoin or carbamazepine.

When there are secondary generalized seizures, phenobarbitone may be used as an alternative.

APPENDIX B

Antiepileptic Drugs (AEDs)

PHENOBARBITONE

Starting dose

Newborns:	15–20 mg/kg once only (loading dose)
Children:	30 mg daily (N.B. children with febrile convulsions 5 mg/kg immediately, usually 45–60 mg daily)
Adults:	60 mg daily.

Increments

30 mg every 4 weeks.

Maintenance dose

Newborns:	3.5 mg/kg/day
Children:	2–6 mg/kg/day
Adults:	0.5–4 mg/kg/day, maximum 180 mg/day.

Elimination half-life time

Newborns:	± 100 hours
Children:	30–70 hours
Adults:	60–150 hours

Infants and children metabolize phenobarbitone quicker than adults. Therefore a higher dose per kilogram body weight has to be given. But in newborns, half-life time is longer—up to 100 hours and in pre-term newborns it is up to 200 hours.

Steady state (reached after five times the half-life)

Reached in children in 1½ weeks after starting therapy

Reached in adults in 3–4 weeks after starting therapy.

Dose frequency

In children and adults:	once daily
In infants:	twice daily.

Indications

First drug in:

- primary and secondary generalized tonic-clonic seizures
- febrile convulsions.

Not indicated in

- absence-seizures
- seizures which occur mainly during sleep
- children with hyperactive behaviour.

Interactions

Phenobarbitone **decreases** the serum levels of:

- bilirubin, folate, cortisol, vitamin D and K
- carbamazepine, phenytoin, valproate
- chloramphenicol in neonates, doxycycline
- digitoxin, griseofulvin, warfarin,
- contraceptive hormones

Phenobarbitone levels are **increased** by:

- phenytoin, valproate
- frusemide.

Pregnancy

During pregnancy the phenobarbitone level tends to fall and it rises again in the puerperium.

Toxicity

Local effects

- very rare.

Dose-determined effects

- during the first few days of treatment drowsiness may occur, but this disappears by itself without reducing the dosage
- when increasing the dosage drowsiness may recur, now a sign of toxicity, and dosage should be reduced
- hyperactivity and irritability occur in children but the condition of the children should be noted before treatment is started: the irritability and hyperactivity might be due to the organic brain damage rather than the phenobarbitone
- decline in scholastic performance
- lethargy, hypoactivity, ataxia
- confusion in the aged.

Idiosyncratic effects

- skin rash, exfoliative dermatitis, porphyrinuria;
- agranulocytosis, aplastic anaemia, jaundice and hepatitis, but very rarely;
- Dupuytren's contracture and frozen shoulder are more common.

Effects on the foetus and newborn

- congenital malformations are sometimes associated with phenobarbitone therapy especially when caffeine or other anticonvulsants are used in addition
- increased bleeding tendency due to decreased vitamin K levels in the newborn
- phenobarbitone-withdrawal syndrome (hypotonia and irritability) in newborns born to mothers on phenobarbitone treatment—may be prevented by breastfeeding.

Breast milk

Phenobarbitone is present in breast milk, and sometimes produces drowsiness in infants when the mother is on a high dosage.

PHENYTOIN (DIPHENYL HYDANTOIN)

Starting dose

3 mg/kg/daily

For instance:	1–6 years:	50 mg daily
	7–14 years:	100 mg daily
	adults:	200 mg daily

Increments

25 mg in children every 3–4 weeks

50 mg in adults every 3–4 weeks.

Maintenance dose

3–8 mg/kg/daily (maximum 400 mg if serum levels are not available. If they are available, serum level generally to be kept below 20 µg/ml, but may exceed this level if need be and if toxicity is not a problem).

Elimination half-life time

From 9–140 hours.

The half-life depends on the dosage and the duration of intake. The elimination time becomes longer the higher the dosage. On the other hand, when treatment is started, people metabolize phenytoin slower until more liver enzymes are induced. The enzyme system is satiable, therefore at higher doses a small increase in the dosage could suddenly result in a toxic phenytoin serum level. Patients who, on genetic basis, metabolize phenytoin slowly will get intoxication more easily.

Children metabolize quicker and therefore need more mg/kg a day than an adult.

Increments should never be 100 mg, but always 50 or 25 mg in adults and, as available, 25–30 mg in children.

Steady state

Steady state is reached in 7–30 days after starting therapy.

Dose frequency

In children:	twice daily
In adults:	once daily (unless gastrointestinal discomfort, then divide into two dosages)

Absorption

Absorption is different in tablets and capsules from different manufacturers. If possible, do not change suddenly from one make to another. If such a change is unavoidable check sooner than usual.

Indications

As first drug in:

– partial seizures with or without secondary generalization

Also active in:

– primary generalized tonic-clonic seizures (beware of provocation of absence seizures)

– status epilepticus (see page 66)

NB Not indicated in: absence- and myoclonic seizures or febrile convulsions.

Interaction

Phenytoin **decreases** the serum levels of:

– folate, vitamin D, griseofulvin
– carbamazepine, clonazepam
– contraceptive hormones
– vitamin K in newborns

Phenytoin sometimes **increases** the levels of:

– phenobarbitone

The phenytoin level may be **increased** by:

– INH, rifampicin and ketoconazole.

Toxicity

Local effects

– slight upper abdominal discomfort, nausea, vomiting.

Dose-determined effects

– nystagmus, ataxia, diplopia, drowsiness, slurred speech
– vomiting, choreiform movements
– gingival hypertrophy, can be reduced by good dental hygiene (regular teeth brushing)
– hirsutism, acne, coarse facies
– re-occurrence of seizures
– cerebellar syndrome.

Idiosyncratic effects

– morbilliform rash rarely going into exfoliative dermatitis
– lymphadenopathy, fever, eosinophilia
– bone-marrow depression
– hepatitis.

Effects on the foetus and newborn

– there is an increased occurrence of cleft lip and palate, and increased congenital heart malformations.
– in the newborn vitamin K deficiency with bleeding may occur.

Breast milk

– phenytoin is present in breast milk but in amounts too small to be harmful. So continue breastfeeding.

CARBAMAZEPINE

Starting dose (First week administer half the starting dose)

Under 1 year:	100 mg daily
1–5 years :	150 mg daily
6–10 years:	200 mg daily
11–15 years:	200–300 mg daily
Adult:	200–400 mg daily.

Increments

Children:	50 mg weekly
Adults:	100 mg every 1–2 weeks.

Maintenance dose

Children:	10–30 mg/kg/day
Adults:	10–20 mg/kg/day (400–1400 mg).

Elimination half-life time

Up to 36 hours after the first dose

Decreasing to up to 12 hours when taken regularly, and even shorter when combined with phenobarbitone and/or phenytoin.

Steady state

Reached in up to 8 days.

Dose frequency

2 times daily when it is the only drug

3 times daily when the dosage is high or in combination with other drugs.

Indications

- benign childhood epilepsy with centrotemporal spikes
- childhood epilepsies with occipital paroxysms
- all other partial seizures, with simple and complex symptomatology
- primary generalized tonic-clonic seizures (beware of provocation of absence seizure)
- secondary generalized tonic-clonic seizures.

NB Not indicated in: absence- and myoclonic seizures or febrile convulsions.

Interactions

Carbamazepine **decreases** the serum levels of:

- folates, warfarin, doxycycline and oral contraceptives

Carbamazepine serum levels are **decreased** by:

- phenytoin and phenobarbitone

Carbamazepine levels are **increased** by:

- erythromycin and INH.

Toxicity

Local effects

– occasionally anorexia, nausea or vomiting.

Dose-determined effects

– headache, dizziness, somnolence, ataxia
– disturbed vision, diplopia
– overdosage might give tremor, excitation and convulsions.

Idiosyncratic effects

– hepatitis, jaundice, fever
– skin rashes (especially sunshine induced), generalized erythema, erythema multiforme exudativum (Stevens-Johnson syndrome), exfoliative dermatitis, lymph-node swelling
– aplastic anaemia, leucopenia, neutropenia.

Effects on the foetus and newborn

– Congenital malformations have been reported (spina bifida). Treatment with carbamazepine can be continued during pregnancy when given as monotherapy.

Breast milk

– Carbamazepine passes into the breast milk, but not in sufficient amounts to stop breastfeeding.

VALPROIC ACID (valproate; dipropylacetic acid)

Valproate is manufactured either as the acid, the sodium salt (sodium valproate) or the magnesium salt (magnesium valproate).

Starting dose

Children:	15–20 mg/kg/day
Adults:	10–15 mg/kg/day
For instance:	
1–2 years:	150–200 mg daily
3–5 years:	200–300 mg daily
6–10 years:	300–400 mg daily
11–15 years:	450 mg daily
adults:	600 mg daily.

Increments

In children:	10 mg/kg daily every 4–7 days
In adults:	200 mg daily every 4–7 days.

Maintenance dose

10–30 mg/kg/day (in adults 600–2400 mg daily).

Elimination half-life time

Approximately 16 hours.

Steady state

Reached in 3–4 days.

Dose frequency

Three times daily.

Indications

- absence-seizures
- myoclonic forms of generalized epilepsy
- febrile convulsions
- all generalized tonic, clonic or tonic-clonic seizures
- all varieties of partial seizures
- photosensitive epilepsy.

NB Not indicated in: Hepatic impairment; infants with severe epilepsy combined with phenobarbitone and/or phenytoin

Interactions

Valproate i**ncreases** the serum level of:

- phenobarbitone, lamotrigine, phenothiazines and antidepressants

Valproate levels are **decreased** by:

- phenytoin and phenobarbitone but not by carbamazepine.

Toxicity

Local effects

- mild, like nausea, vomiting, diarrhoea occur, mainly at the beginning of treatment
- decreased but also increased appetite with weight gain may occur
- if the tablets are not enteric-coated gastric distress is frequent.

Dose-determined effects

- tremor, weakness, ataxia
- excitement, mental stimulation.

Idiosyncratic effects

- thrombocytopenia and prolonged bleeding time
- Acquired factor VIII deficiency (Von Willebrand disease)
- hair loss (temporary and reversible)
- impaired hepatic function, especially in children under two on polytherapy (but an isolated increase in gamma GT in some cases is not a reason to lower the valproate dose)
- polycystic ovaries
- pancreatitis.

Effects on the foetus and newborn

- as other antiepileptic drugs, in particular spina bifida.

Breast milk

- valproate passes into the breast milk. No reason to stop breastfeeding.

ETHOSUXIMIDE

Starting dose

3–6 years:	250 mg daily
Over 6 years:	500 mg daily
Adults:	500 mg daily.

Increments

250 mg per day at weekly intervals.

Maintenance dose

Children:	10–25 mg/kg/day
Adults:	10–20 mg/kg/day (750–1500 mg).

Elimination half-life time

Children:	10–40 hours
Adults:	40–70 hours.

Steady state

Reached:

- in children in about 7 days
- in adults in 10–14 days.

Dose frequency

Children under 6 years:	3 times daily
Children above 6 years:	2 times daily
Adults:	once daily is sufficient, but because of gastric irritation twice daily is better.

Indications

Absence seizures (next choice after valproate).

Interactions

Ethosuximide levels are **increased** by:

- valproate and isoniazid

Ethosuximide levels are **decreased** by:

- phenytoin and carbamazepine.

Toxicity

Local effects

- nausea, vomiting or anorexia.

Dose-determined effects

- headache, tiredness, drowsiness, ataxia
- psychotic states with hallucinations.

Idiosyncratic effects

- skin rashes, a lupus erythematosis syndrome
- leucopenia, agranulocytosis.

CLONAZEPAM

Starting dose

0.01–0.03 mg/kg/day

For instance:

up to 1 year:	0.125 mg daily
1–5 years:	0.250 mg daily
6–12 years:	0.500 mg daily
Adults:	1 mg daily.

Increments

Children under 6 years:	0.250 mg daily at weekly intervals
Children over 6 years:	0.500 mg daily at weekly intervals
Adults:	1 mg daily at weekly intervals.

Maintenance dose

Up to 1 year:	0.5–1 mg daily
1–5 years:	1–3 mg daily
6–12 years:	3–6 mg daily
Over 12 years:	4–8 mg daily.

Elimination half-life time

20–60 hours.

Steady state

Reached in 8–14 days.

Dose frequency

A once-daily dose is possible in adults

In children it should be divided into 2–3 doses.

Indications

- symptomatic generalized epilepsy
- idiopathic epilepsy
- status epilepticus
- myoclonic seizures.

Interactions

Clonazepam serum levels are **decreased** by:

- phenobarbitone, phenytoin and carbamazepine

Clonazepam **increases** the effects of alcohol.

Toxicity

Local effects

- almost no local effects.

Dose-determined effects

- drowsiness, fatigue, dizziness
- muscle weakness, ataxia
- increased bronchial excretion and salivation
- paradoxical aggression, irritability, hyperactivity.

Idiosyncratic effects

– skin rash (very rarely).

Teratogenic effects

– an increased risk of oral clefts has been reported.

Breast milk

– lethargy and weight loss may occur in infants.

Note:

A good measure of tolerance is usually developed so that the dosage has to be increased over time to give the same antiepileptic effect. If this tolerance has caused the clonazepam to reach too high a dosage, it is better to withdraw the clonazepam *very* gradually and to introduce another anticonvulsant.

Caution:

Never cease clonazepam therapy suddenly, severe withdrawal symptoms may occur, and a status epilepticus be introduced.

DIAZEPAM

This drug is mainly used to curb status epilepticus, or prolonged febrile convulsions.

It is then given intravenously or rectally (do not give intramuscularly as then action is unpredictable and absorption slow).

Dosage in status epilepticus or prolonged febrile convulsions:

1 mg/minute i.v. until seizures stop, but not more than:

5 mg in children under 5 years

10 mg in children 5–10 years

15–20 mg in older children and adults

The same solution may be given after 20–30 minutes and once again after 30 minutes.

Side-effects

Respiratory depression is possible, especially if patient is on maintenance dose of phenobarbitone.

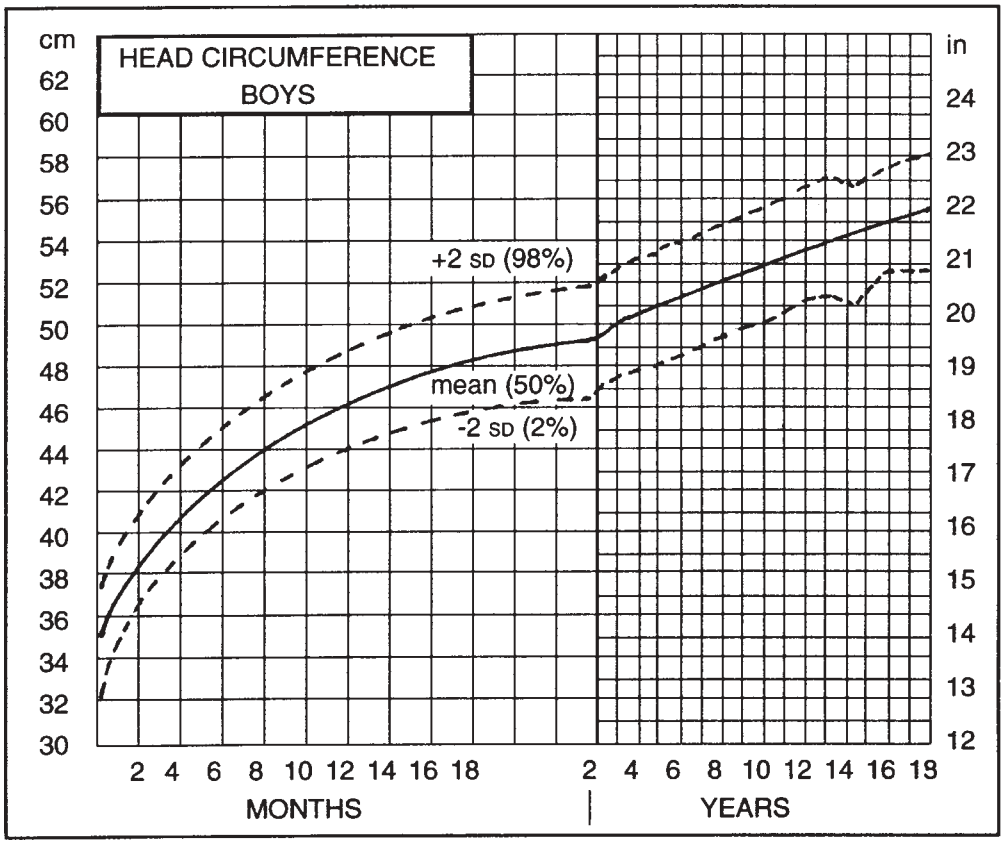
Table A. **Summary of the main information given in Appendix B**

	Phenobarbitone	Phenytoin	Carbamazepine	Valproate	Ethosuximide	Clonazepam
Starting dose						
newborn	15–20 mg/kg once					
infant	30 mg/day		100 mg/day			0.125 mg/day
1–5 yr	30–60 mg/day	50 mg/day	150 mg/day	150 mg/day	250 mg/day	0.250 mg/day
6–10 yr	60 mg/day	100 mg/day	200 mg/day	300 mg/day	500 mg/day	0.500 mg/day
11–15 yr	60 mg/day	100 mg/day	200 mg/day	450 mg/day	500 mg/day	0.500 mg/day
adult	60 mg/day	200 mg/day	200 mg/day	600 mg/day	500 mg/day	1 mg/day
Increment of daily dose						
child	30 mg 4 weekly	25 mg 3–4 wkly	50 mg/wkly	10 mg/kg	250 mg/wkly	0.250 mg/wkly
adult	30 mg 4 weekly	50 mg 3–4 wkly	100 mg/wkly	200 mg/4–7 days	250 mg/wkly	1 mg/wkly
Maintenance dose						
newborn/infant	3.5 mg/kg/day					0.5–1 mg/day
child	2–6 mg/kg/day	3–8 mg/kg/day	10–30 mg/kg/day	10–30 mg/kg/day	10–25 mg/kg/day	1–6 mg/day
adult	0.5–4 mg/kg/day	3–8 mg/kg/day	10–20 mg/kg/day	10–35 mg/kg/day	10–20 mg/kg/day	4–8 mg/day
in adult	60–250 mg	max 400 mg	400–1400 mg	600–2400 mg	750–1500 mg	
Half-life time						
newborn	± 100 hours					
child	30–70 hours		first—36 hours		10–40 hours	
adult	60–150 hours	9–140 hours	later—12 hours	± 16 hours	40–70 hours	20–60 hours
Frequency of dosage			2 times when			
child	once daily	2 times	only drug	3 times	3 times daily	2–3 times
adult	once daily	once daily	3 times when more drugs	3 times	2 times daily	once daily

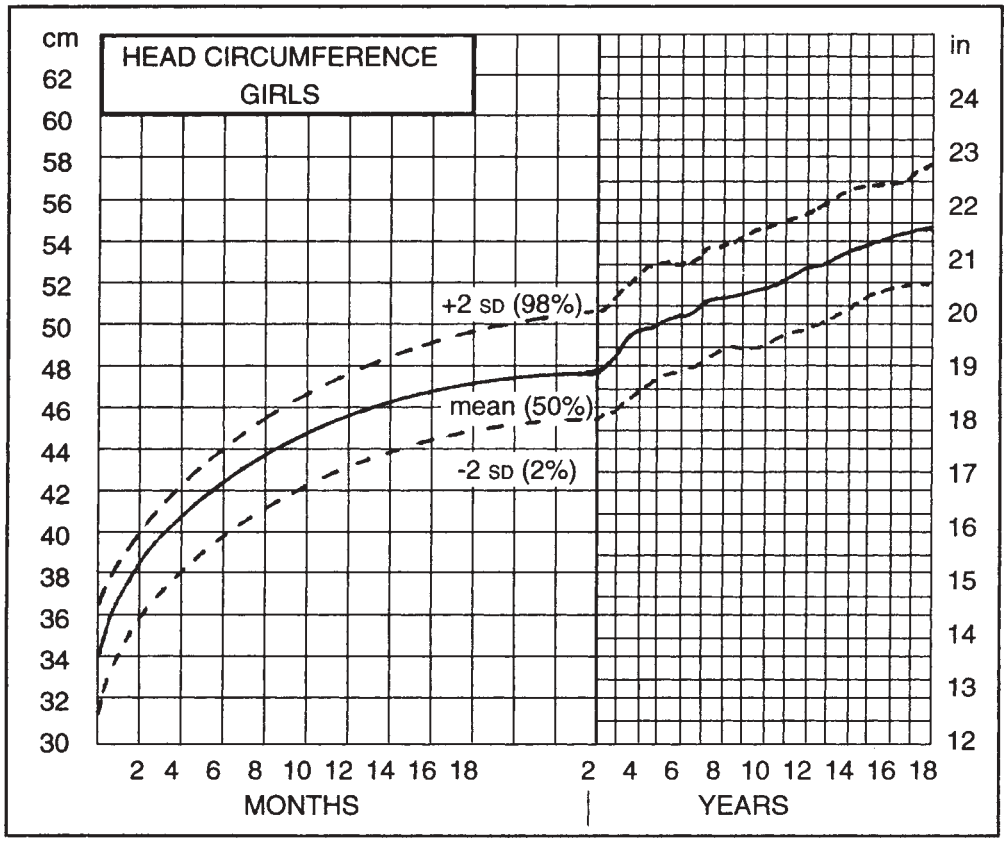
	Phenobarbitone	Phenytoin	Carbamazepine	Valproate	Ethosuximide	Clonazepam
Indications	GTCS febrile convulsions daytime seizures	partial seizures sec GTCS nocturnal seizures	partial seizures complex partial seizures, sec GTCS	absences myoclonic seizures awakening seizures	absences	GTCS, idiopatic or symptomatic myoclonic seizures
Main side-effects	drowsiness, hyperactivity in children	drowsiness, gum hypertrophy allergy: rash + lymphadenopathy	drowsiness, ataxia skin rash	nausea, vomiting, diarrhoea, increased weight, hair loss	drowsiness, hallucinations	drowsiness, weakness, ataxia, increased bronchial secretion, aggressiveness
Main interactions						
decreases	vitamin D, folates phenytoin, carbamazepine, valproate, oral contraceptives	vitamin D, folates carbamazepine, clonazepam, oral contraceptives	folates, oral contraceptives			
decreased by			phenytoin phenobarbitone	phenytoin phenobarbitone	carbamazepine	carbamazepine, phenytoin, phenobarbitone
increases		phenobarbitone	effect of alcohol	phenobarbitone phenothiazines antidepressants		effect of alcohol
increased by	phenytoin valproate frusemide	INH rifampicin	INH erythromycin		INH phenytoin valproate	

APPENDIX C

Head circumference graphs



Head circumference graph: boys
(adapted from G. Nellhaus 1968)



Head circumference graph: girls
(adapted from G. Nellhaus 1968)

APPENDIX D

Record cards

Date first visit — Clinic location
Name — Patient's registration No.
Date of birth — Patient's address
Sex — Location
Ethnic origin — Sublocation
Village

Age ay onset of seizures
Seizure type or description

Epilepsy type
- idiopathic — febrile convulsions
- known/suspected symptomatic — others

Aetiology of symptomatic epilepsy
- birth injury/asphyxia — accident
- meningitis/encephalitis — tumour
- measles/malaria — following febrile convulsions
- other or unknown disease — others

Frequency of seizures before treatment
Number of seizures before treatment

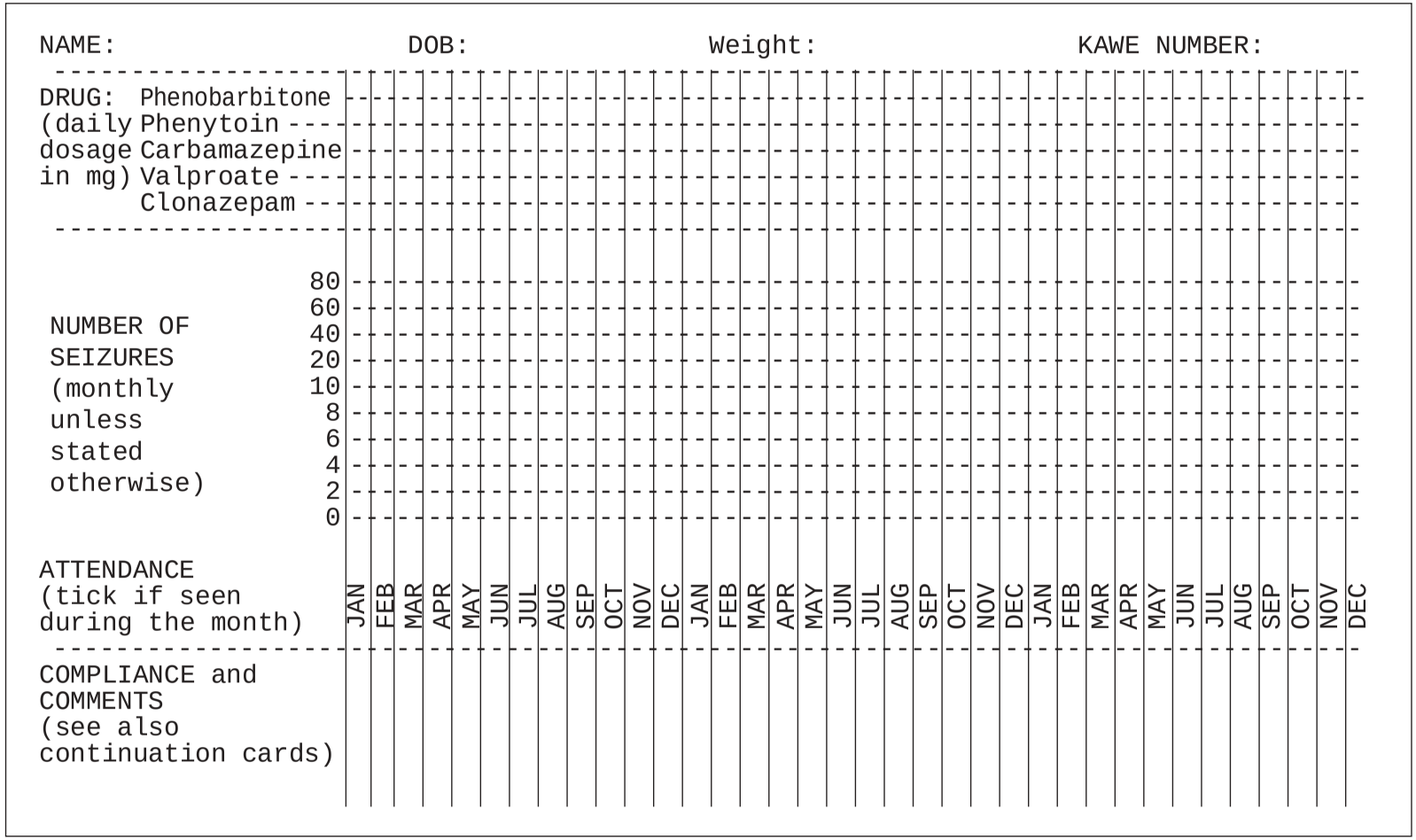
Usual time of seizures
- while awake — on awakening
- while asleep — mixed

Trigger to seizures
- alcohol — fever/stress
- pregnancy — photostimulation
- menstruation — others

Birth order
Epilepsy in family
Pregnancy
Delivery
Milestones
Physical examination
- Eyes — Weight
- ENT — Height
- Skin — Head circumference
- Chest — Investigations
- Abdomen
- Reflexes — If on treatment
  - medicines
  - dosage
  - effect

Physical handicaps
Mental retardation
General impression — Management up till now
Schooling — Diagnosis
Job — Plan

Epilepsy treatment record card



Seizure record card

Epilepsy register, first visit

Clinic's name:

Reporting year:

Registration number							
sex							
date first visit							
date of birth							
age first seizure							
seizure type							
epilepsy type							
aetiology							
frequency seizure before treatment							
number of seizures before treatment							
time of seizures							
trigger							
birth order							
epilepsy in family							
physical handicaps							
occupation							
mental retardation							
on treatment now before							
new treatment							

Epilepsy register, first visit

Epilepsy register, follow up Clinic's name: Reporting year:

No.	31 Dec first calender year condition			31 Dec one year later			31 Dec two years later			
	condition	attendance	treatment	condition	attendance	treatment	condition	attendance	treatment	

condition: c.c. = complete control, no seizures in last year
w.c. = well controlled, 1–12 seizures last year
improved = >12 seizures, but better than before

not improved: = no change or worse

died

attendance: yes or no
if not attending because
– discharged from treatment
– transferred
– moved out of area
– defaulted
– died

Epilepsy register, follow up

Annual report form

Clinic: ..... Calender year: .....

A. Number of patients under treatment 1 January .....

B. Added to register: new patients .....
transfer from other clinics .....
resumed treatment .....

male
female
age: 0–1 year .....
1–5 years .....
6–10 years .....
11–15 years .....
16–20 years .....
21–30 years .....
31–40 years .....
41–50 years .....
>50 years .....

C. Treatment discontinued
discharged from treatment .....
transferred to other clinic .....
moved out of area .....
died .....
defaulted .....

D. Number of patients on treatment 31 December (= A + B – C) .....

E. Number of tablets used
phenobarbitone 30 mg .....
phenytoin 50 mg .....
phenytoin 100 mg .....
carbamazepine 200 mg .....
valproate 150 mg .....
valproate 200 mg .....
valproate 300 mg .....
clonazepam 0.5 mg .....
clonazepam 2 mg .....
others .....
.....
.....

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Useful addresses.

It is important to offer patients and their families support from people who have gone through similar experiences or for other reasons have a special interest in epilepsy. In many countries these people have formed organisations for this purpose and to guard the interests of people with epilepsy. In a number of countries there are also professional organisations whose members wish to improve care and knowledge about epilepsy through research, study, education and networking. These national organisations are members (chapters) of umbrella organisations that act on a global scale, respectively the International Bureau for Epilepsy (IBE) and the International League Against Epilepsy (ILAE).

In 1997 ILAE, IBE, and the World Health Organization started a joint initiative to bring epilepsy “Out of the Shadows” by improving the diagnosis, treatment, prevention and social acceptability of the disorder world-wide. This initiative has the alias: Global Campaign Against Epilepsy.

Addresses are presented of national organisations as known at the time of printing of this book. National organisations often do not have a permanent office. If the address is not functional, the office of IBE or ILAE may provide an update. From IBE and ILAE it is also possible to obtain addresses of people with an interest in epilepsy in countries that have not yet established a formal organisation. Furthermore IBE and ILAE have websites with useful information.

http://www.ibe-epilepsy.org and http://www.ilae-epilepsy.org

International organisations

Offices IBE
IBE Dublin Office
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