In the name of GOD

EPILEPSY

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SEIZURE

- ***TRANSITORY AND SIMULTANEUSLY SEVER DISCHARGE OF CEREBRAL NEURONS THAT CREAT INVOLUNTARY MOTOR,SENSORY,PSYCHIC AND BEHAVIOR PRESENTATION.***

EPILEPSY

- Epilepsy defined as recurrent (2 or more) seizure.
- For example recurrent (2 or more) partial seizure defined as partial epilepsy.

EPIDEMIOLOGY (seizure)

- Studies have estimated that 1.5-5.0% of any population will have a seizure at some time.

EPIDEMIOLOGY (epilepsy)

- In most developed countries, incidence rates of epilepsy range from 40-70 per 100,000, but in developing countries, the rates may be as high as 100-190 per 100,000 (Sander 2003).

EPIDEMIOLOGY

- **The prevalence of active epilepsy, defined as *persons who take anticonvulsant drugs* or *who have had a seizure in the past* 5 *years,* ranges from 4-10 per 10,000 in developed countries and up to 57 per 10,000 in developing countries.**

Factors contributing to the higher incidence and prevalence of epilepsy in developing countries

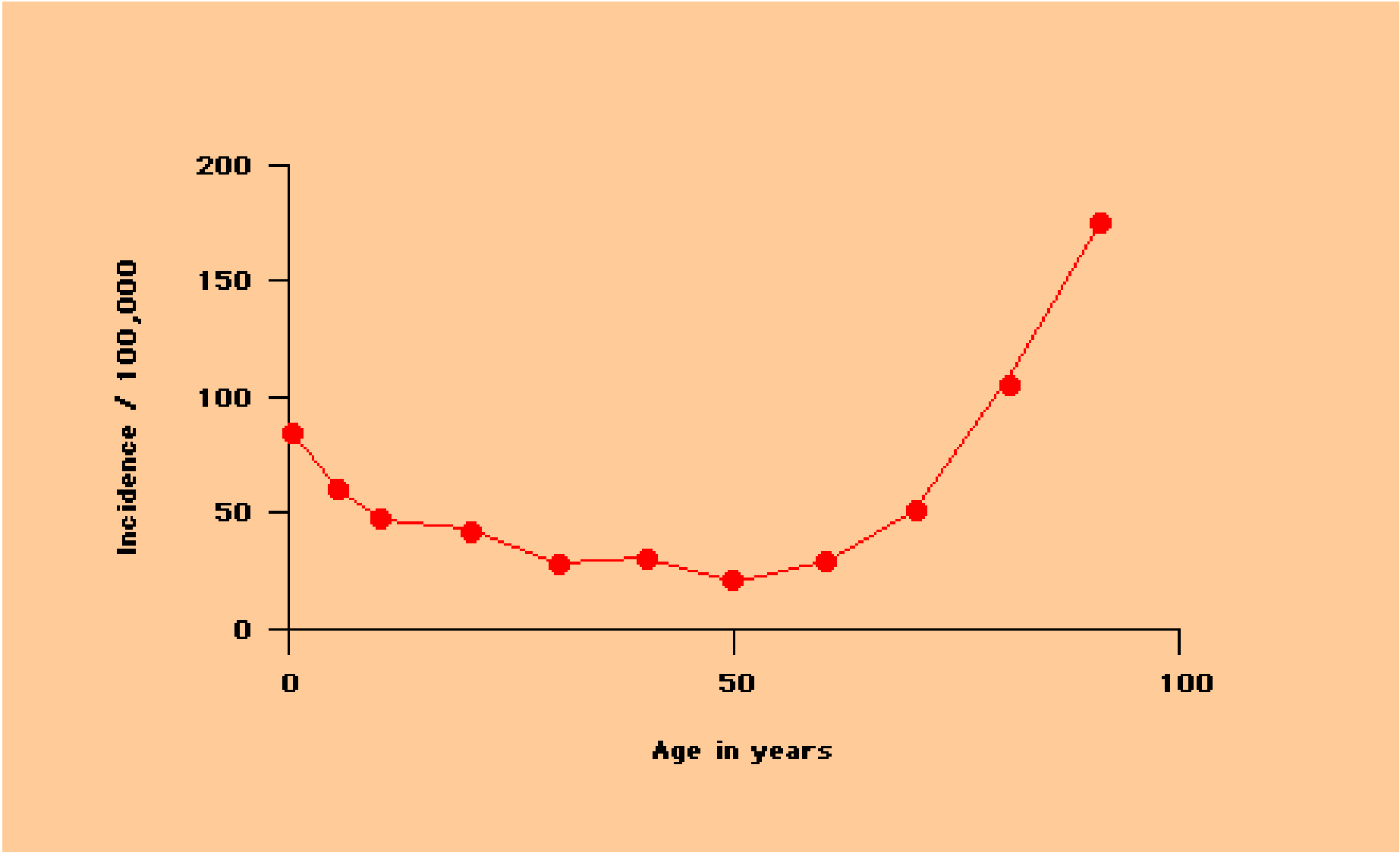
- Birth injury, head trauma, poor sanitation, infectious disorders, poverty and illiteracy, alcohol and substance abuse.

EPIDEMIOLOGY

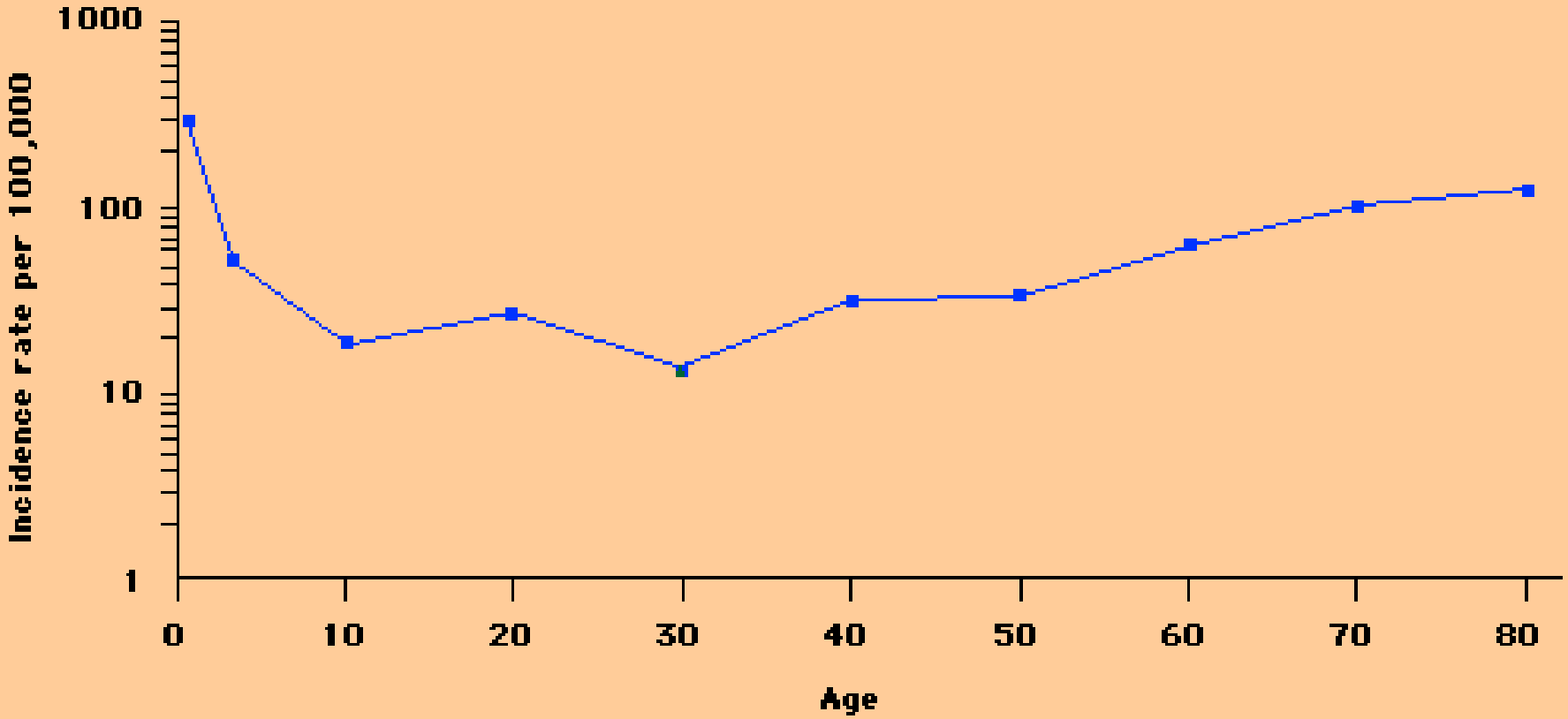
- Epilepsy has been more common in children than in adults.
- Men are 1.0-2.4 times more likely to have epilepsy than women.

EPIDEMIOLOGY

- Rates are high in the first decade, particularly under the age of 1 year, with a decline during the first decade.
- Rates are low during most of adulthood, and a secondary increase occurs after age 60 years.



Age-related incidence of epilepsy Data from: Hauser, WA, Annegers, JF, Kurland, LT. The incidence of epilepsy and unprovoked seizures in Rochester, Minnesota, 1935-1984. Epilepsia 1993; 34:453.



Acute symptomatic seizures; rates by age, Rochester, Minnesota, 1975-1984 Data from: Annegers, JF, Hauser, WA, Lee, RJ, Rocca, WA. Incidence of acute symptomatic seizures in Rochester, Minnesota, 1935-1984. Epilepsia 1995; 36:327.

Etiology of epilepsy

- The etiology for epilepsy can be identified in only approximately one fourth to one third of cases.

Table 8–1. Common causes of seizures of new onset.

Primary neurologic disorders
Benign febrile convulsions of childhood
Idiopathic epilepsy
Head trauma
Stroke or vascular malformations
Mass lesions
Meningitis or encephalitis
HIV encephalopathy
Systemic disorders
Hypoglycemia
Hyponatremia
Hyperosmolar states
Hypocalcemia
Uremia
Hepatic encephalopathy
Porphyria
Drug overdose
Drug withdrawal
Global cerebral ischemia
Hypertensive encephalopathy
Eclampsia
Hyperthermia

ETIOLOGY IN PEDIATRICS

In whom an etiology can be determined

- Congenital brain malformations, inborn errors of metabolism, perinatal disorders, mental retardation, cerebral palsy, cerebral degeneration.
- High fevers, head trauma, brain tumors, stroke, intracranial infection, alcohol or heroin use and withdrawal states, iatrogenic drug reactions.

ETIOLOGY IN ADULTS

In whom an etiology can be determined

- Perinatal disorders, mental retardation, cerebral palsy, head trauma, infections of the CNS, cerebrovascular disease, brain tumors, Alzheimer's disease, and alcohol or heroin use all are associated with an increased risk for epilepsy.

Causes of Seizures and Epilepsy in the Elderly

	Relative proportion, percent
Acute Seizures	
Acute Stroke	50
Metabolic Encephalopathy	6-30
Drugs	10
Others (trauma, infections)	5-20
Epilepsy	
Cerebrovascular disease	30-50
Dementia	9-17
Others (tumors, trauma)	5-15
Cryptogenic	30-50

Prognosis

- The risk of seizure recurrence after the first seizure ranges from 27% to 80% (Sander 2003).
- Most recurrences happen within 6 months of the first seizure.

Prognosis

- The risk for further seizures decreases with longer interval from the initial event.
- Seizures associated with CNS insults, particularly those in the neonatal period, have a high rate of recurrence.

Excellent prognosis

- *Excellent prognosis* is expected in approximately 20-30% of individuals who have one of a number of genetic conditions, such as benign neonatal seizures, benign childhood epilepsy with centrotemporal spikes, or benign myoclonic epilepsy of childhood.
- Often, remission occurs without AED treatment.

Good prognosis

- A *good prognosis* is characteristic in approximately 30-40% of people with epilepsy whose seizures are easily controlled with AEDs.
- Remission is often permanent when medications are discontinued.
- Some of the conditions with good prognosis include childhood absence epilepsy, epilepsy with generalized tonic-clonic seizures on awakening, and even a small subset of localization-related epilepsies.

Uncertain prognosis

- In an *uncertain prognosis* group, comprising approximately 10-20% of people with epilepsy, AEDs are suppressive rather than curative: medication must be continued for seizure control.
- Individuals with juvenile myoclonic epilepsy (]ME) and the majority of those with localization-related epilepsy fall into this category.
- A subset of the latter group may benefit from epilepsy surgery.

Bad prognosis

- As many as 20 percent of individuals with epilepsy have a *bad prognosis,* meaning that most treatments, including surgery, reduce seizures only partially.
- Individuals in this group often have a history of infantile spasms, Lennox- Gastaut syndrome, or localization-related seizures associated with extensive structural brain damage or congenital disorders such as tuberous sclerosis.

Classifications and Definitions

Seizure

- Seizures result from electrical hypersynchronization of neuronal networks in the cerebral cortex that lead to sudden change in behavior, sensory and motor function that is the consequence of brain dysfunction.

Epilepsy

- Epilepsy is characterized by recurrent seizures due to a genetically determined or acquired brain disorder.

Table 73.1: The International League Against Epilepsy classification of epileptic seizures

I. Partial (focal, local) seizures
  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
    2. With no other features
    3. With features as in simple partial seizures
    4. With automatisms
  C. With impairment of consciousness at onset
    1. With no other features
    2. With features as in simple partial seizures
    3. With automatisms
  D. Partial seizures evolving to secondarily generalized seizures
    1. Simple partial seizures evolving to generalized seizures
    2. Complex partial seizures evolving to generalized seizures
    3. Simple partial seizures evolving to complex partial seizures to generalized seizures

II. Generalized seizures (convulsive or nonconvulsive)
  A. Absence seizures
    1. Absence seizures
    2. Atypical absence seizures
  B. Myoclonic seizures
  C. Clonic seizures
  D. Tonic seizures
  E. Tonic-clonic seizures
  F. Atonic seizures (astatic seizures)

III. Unclassified epileptic seizures (includes all seizures that cannot be classified because of inadequate or incomplete data and some that defy classification in hitherto described categories. This includes some neonatal seizures, such as rhythmic eye movements, chewing, and swimming movements.

TYPES OF SEIZURE

- PARTIAL SEIZURES(SPS,CPS)
- GENERALIZED SEIZURES (Generalized tonic-clonic seizure, Absence seizure and Clonic, Myoclonic, Tonic, and Atonic seizures).

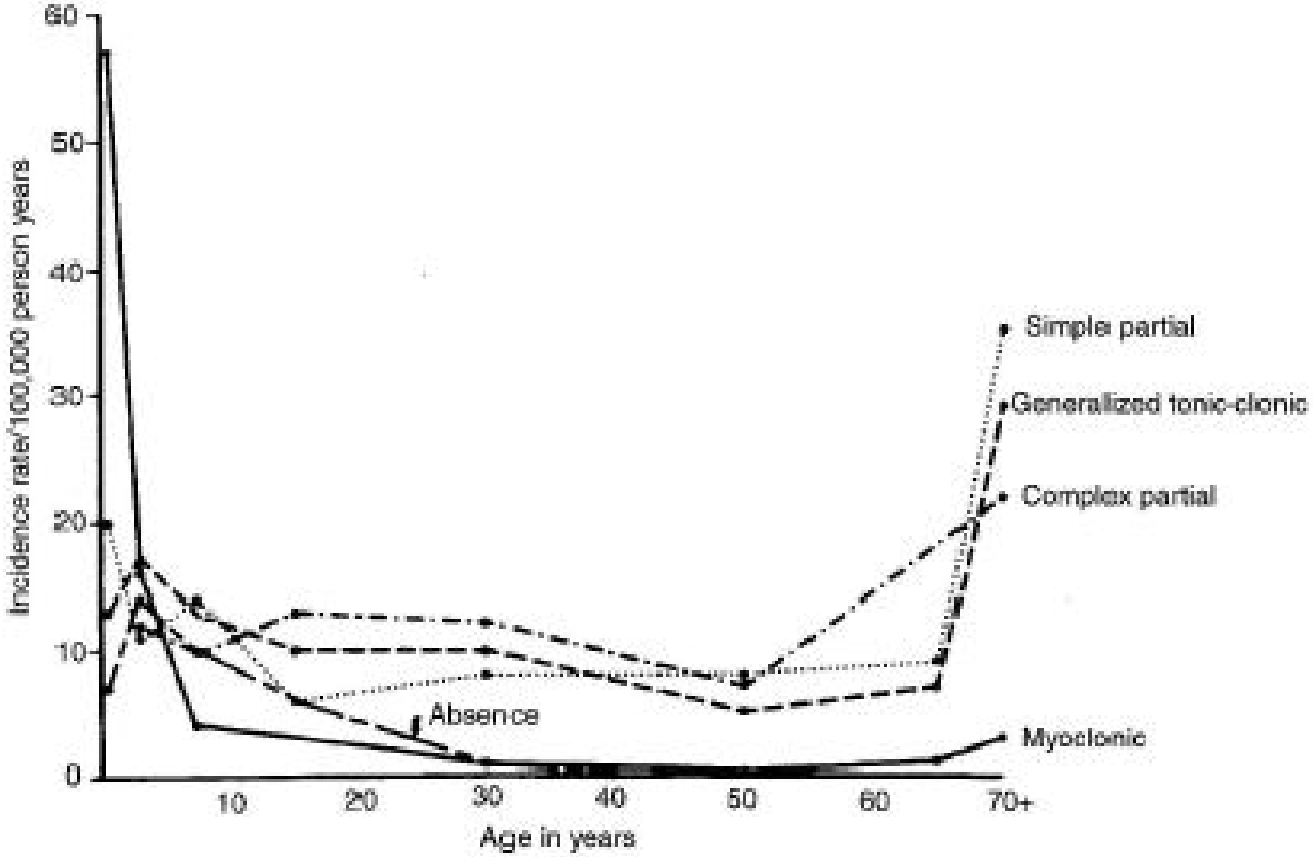


FIGURE 43.4 Epilepsy. Average annual age-specific incidence rates per 100,000 population by clinical type of seizure (absence, myoclonic, generalized, simple per complex partial). (Reprinted with permission from Kurtzke, J. F. & Kurland, L. T. 1983, "The epidemiology of neurologic disease," in *Clinical Neurology*, vol. 4, eds A. B. Baker & L. H. Baker, Harper & Row, Philadelphia.)

Table 86.1: Types of neonatal seizures

Neonatal seizure types	*Clinical manifestations*	*Age distribution*
Subtle	Eye deviation, blinking, fixed stare Repetitive mouth and tongue movements Apnea Pedaling, tonic posturing of limbs	Premature and term
Tonic: focal or generalized	Tonic extension of limbs Tonic flexion of upper limbs, extension of legs	Primarily premature
Clonic: multifocal or focal	Multifocal, clonic, synchronous, or asynchronous limb movements Nonordered progression Localized clonic limb movements Consciousness often preserved	Primarily term
Myoclonic: focal, multifocal, or generalized	Single or several synchronous flexion jerks of upper more than lower limbs	Rare

Table 86.3: Treatment of neonatal seizures

I. Ensure adequate ventilation and perfusion		
II. Begin therapy for specific metabolic disturbances (if present)		
	Acute therapy	**Maintenance therapy**
Hypoglycemia: glucose (10% solution)	2 mL/kg IV (0.2 g/kg)	Up to 8 mg/kg/min IV
Hypocalcemia: calcium gluconate (5% solution)	4 mL/kg IV (Note: monitor cardiac rhythm)	500 mg/kg/24 hr PO
Hypomagnesemia: magnesium sulfate (50% solution)	0.2 ml/kg IM	0.2 ml/kg/24 hr IM
Pyridoxine deficiency: pyridoxine	50–100 mg IV	100 mg PO daily for 2 wk
III. Begin anticonvulsant therapy		
	Acute therapy	**Maintenance therapy (begin 12 hr after loading dose)**
Phenobarbital	20 mg/kg IV if necessary, additional 5–25 mg/kg IV in 5 mg/kg aliquots (Note: monitor blood pressure and respiration)	4–6 mg/kg/24 hr IV/IM/PO
Phenytoin*	2 doses of 10 mg/kg IV, diluted in normal saline (Note: monitor cardiac rate and rhythm)	5–10 mg/kg/24 hr IV
Lorazepam	0.05–0.10 mg/kg IV	

*Fosphenytoin may be the preferred form of phenytoin.
IV = intravenous; IM= intramuscular; PO= orally.

Table 86.2: Major causes of neonatal seizures: clinical features and outcome

Cause	*Most common age at onset*	*Relative incidence*		*Outcome (% of normal development)*
		Premature	*Full-term*	
Hypoxic-ischemic encephalopathy	<3 days	+++	+++	50
Intracranial hemorrhage				
Intraventricular hemorrhage	<3 days	++		<10
Primary subarachnoid hemorrhage	<1 day			90
Hypoglycemia	<2 days	+	+	50
Hypocalcemia				
Early-onset	23 days	+	+	50
Late-onset	>7 days		+	100
Intracranial infection				
Bacterial meningitis	>3 days	++	++	50
Intrauterine viral	>3 days	++	++	<10
Developmental defects	Variable	++	++	0
Drug withdrawal	<3 days	+	+	Unknown

Note: +++ = most common; ++ = less common; + = least common.

Source: Reprinted with permission from Volpe, J. J. 2000, *Neurology of the Newborn*, 4th ed., WB Saunders, Philadelphia.

Simple partial seizures (SPS)

- Seizures are usually stereotyped.
- Visible manifestations, such as jerking of a limb.
- Subjective experiences perceived only by the patient, such as epigastric discomfort, fear, or an unpleasant smell.
- No clouding of consciousness.

Complex partial seizure (CPS)

- Subjective experiences perceived only by the patient, such as epigastric discomfort, fear, or an unpleasant smell.
- Clouding of consciousness, staring.
- Repetitive motor behaviors, termed automatisms, such as swallowing, chewing, or lip smacking.
- After a CPS, the patient may experience confusion, fatigue, and a throbbing headache.

Table 2.3: Comparison of absence and complex partial seizures

Feature	*Absence seizure*	*Complex partial seizure*
Age at onset	Childhood or adolescence	Any age
Aura or warning	No	Common
Onset	Abrupt	Gradual
Duration	Seconds	Up to minutes
Automatisms	Simple	More complex
Provocation by hyperventilation	Common	Uncommon
Termination	Abrupt	Gradual
Frequency	Possibly multiple seizures per day	Occasional
Postictal phase	No	Confusion, fatigue
Electroencephalogram	Generalized spike and wave	Focal epileptic discharges or nonspecific lesions
Neuroimaging	Usually normal	May demonstrate focal lesions

Generalized seizures

- In contrast to partial seizures, generalized seizures originate virtually in all the regions of the cortex.
- Absence seizures and generalized tonic-clonic seizures are types of generalized seizures.
- Other subtypes of generalized seizures are clonic, myoclonic, tonic, and atonic seizures.

Generalized tonic-clonic seizure

- It begins with an abrupt loss of consciousness, often in association with a scream or shriek. All of the muscles of the arms and legs as well as the chest and back then become stiff. The patient may begin to appear cyanotic during this tonic phase. After approximately one minute, the muscles begin to jerk and twitch for an additional one to two minutes. During this clonic phase the tongue can be bitten, and frothy and bloody sputum may be seen coming out of the mouth. The postictal phase begins once the twitching movements end. The patient is initially in a deep sleep, breathing deeply, and then gradually wakes up, often complaining of a headache.

Absence seizure

- Usually occur during childhood and typically last between 5 and 10 seconds. They frequently occur in clusters and may take place dozens or even hundreds of times a day. Absence seizures cause sudden staring with impaired consciousness. If an absence seizure lasts for 10 seconds or more, there may also be eye blinking and lip smacking.

Clonic seizure

- Cause rhythmical jerking muscle contractions that usually involve the arms, neck, and face.

Myoclonic seizure

- Consist of sudden, brief muscle contractions that may occur singly or in clusters and that can affect any group of muscles, although typically the arms are affected. Consciousness is usually not impaired.

Tonic seizure

- Tonic seizures cause sudden muscle stiffening, often associated with impaired consciousness and falling to the ground.

Atonic seizure

- Atonic seizures (also known as drop seizures or drop attacks) produce the opposite effect of tonic seizures — a sudden loss of control of the muscles, particularly of the legs, that results in collapsing to the ground and possible injuries.

DIFFERENTIAL DIAGNOSIS

- Syncope and faint
- Nonepileptic seizures (NES)
- Transient ischemic attacks (TIAs)
- Transient global amnesia (TGA)
- REM behavior disorder
- Migraine
- Others

SYNCOPE

- **Syncope is the abrupt and transient loss of consciousness associated with absence of postural tone, followed by a rapid and usually complete recovery.**

Table 2.2: Classification of syncope

Cardiac arrhythmias
Bradyarrhythmias
Tachyarrhythmias
Reflex arrhythmias
Decreased cardiac output
Cardiac outflow obstruction
Inflow obstruction
Cardiomyopathy
Hypovolemia
Hypotension
Drug use
Dysautonomia
Carotid sinus
Vertebrobasilar disease
Vasospasm
Takayasu's arteritis
Metabolic
Hypoglycemia
Anemia
Anoxia
Hyperventilation
Vasovagal (vasodepressor, neurocardiogenic; neural mediated)
Cardiac syncope
Cough, micturition
Multifactorial

FAINT

- A simple faint is usually precipitated by emotional stress, unpleasant visual stimuli, prolonged standing, or pain.
- Although the duration of unconsciousness is brief, it may vary from seconds to minutes.
- As the fainting episode corrects itself (e.g., by the patient becoming horizontal), the color returns, breathing becomes more regular, and the pulse and blood pressure return to normal.

DIFERRENTIATE SIEZURE FROM SYNCOPE

Table 2.1: Comparison of clinical features of syncope and seizures

Features	*Syncope*	*Seizure*
Relation to posture	Common	No
Time of day	Diurnal	Diurnal or nocturnal
Precipitating factors	Emotion, injury, pain, crowds, heat	Sleep loss, drug/alcohol withdrawal
Skin color	Pallor	Cyanosis or normal
Aura or premonitory symptoms	Long	Brief
Convulsion	Rare	Common
Injury	Rare	Common (with convulsive seizures)
Urinary incontinence	Rare	Common
Postictal confusion	Rare	Common
Postictal headache	No	Common
Focal neurological signs	No	Occasional
Cardiovascular signs	Common (cardiac syncope)	No
Abnormal electroencephalogram recording	Rare (may show generalized slowing during the event)	Common

Nonepileptic seizures (NES)

- NES are subdivided into two major types:
  - physiological
  - psychogenic

Psychogenic NES (Pseudoseizure)

- Are sudden changes in behavior that resemble epileptic seizures but are not associated with the typical neurophysiological changes that characterize epileptic seizures.
- Are thought to result from stressful psychological conflicts or major emotional trauma and are more challenging to recognize and diagnose.

Physiological NES

- Physiological NES are caused by a sudden alteration of neuronal function due to metabolic derangement or hypoxemia.
- Causes of physiological NES include cardiac arrhythmias, syncope, and severe hypoglycemia

DIFERRENTIATE

Pseudoseizure from seizure

Table 2.4: Comparison of psychogenic and epileptic seizures

Feature	*Psychogenic seizure*	*Epileptic seizure*
Stereotypy of attack	May be variable	Usually stereotyped
Duration	May be prolonged	Brief
Diurnal variation	Daytime	Nocturnal or daytime
Injury	Rare	Can occur with tonic-clonic seizures
Tongue biting	Rare	Can occur with tonic-clonic seizures
Urinary incontinence	Rare	Common
Motor activity	Prolonged, uncoordinated; pelvic thrusting	Automatisms or coordinated tonic-clonic seizures
Postictal confusion	Rare	Common
Relation to medication changes	Unrelated	Usually related
Interictal EEG	Normal	Frequently abnormal
Ictal EEG	Normal	Abnormal
Presence of secondary gain	Common	Uncommon
Psychiatric disturbances	Common	Uncommon

EEG = electroencephalogram.

DIAGNOSIS

- The diagnostic evaluation of seizure begins with the accurate description of the seizure.

Table 8–3. Evaluation of a new seizure disorder in a stable patient.

History (including medications or drug exposure)
General physical examination
Complete neurologic examination
Blood studies
Fasting glucose
Serum calcium
Serum FTA-ABS
Serum electrolytes
Complete blood count
Erythrocyte sedimentation rate
Renal function studies
Hepatic function studies
EEG (positive in 20–59% of first EEGs; 59–92% with repeated EEGs)
Brain MRI (especially with abnormal examination, progressive disorder, or onset of seizures after 25 years of age)

DIAGNOSIS

- Medication history
- Family history
- Past medical history
- Physical and neurologic examination

DIAGNOSIS

- **Laboratory screening:**

  Laboratory evaluations that are appropriate for the evaluation of a first seizure include glucose, calcium, magnesium, hematology studies, renal function tests, and toxicology screens.

DIAGNOSIS

- The serum prolactin concentration may rise shortly after generalized tonic- clonic seizures and some partial seizures.
- Typically, a level is drawn 10 to 20 minutes after the event and compared with a baseline level drawn six hours later.
- Criteria for abnormality are not well established; many investigators use twice the baseline level.

DIAGNOSIS

- A lumbar puncture is essential if the clinical presentation is suggestive of an acute infectious process that involves the central nervous system or the patient has a history of cancer that is known to metastasize to the meninges.

DIAGNOSIS

- When the EEG is abnormal, it is useful to localize the epileptogenic region in patients with partial seizures or to distinguish seizures types, particularly in the case of genetic epilepsies, such as absence versus complex partial seizures.
- Routine EEGs should be recorded during wakefulness and sleep to maximize the chance of seeing epileptiform activity.

DIAGNOSIS

- Neuroimaging has become increasingly important in the diagnosis and management of epilepsy, especially in patients with intractable seizures who are being considered for surgery.
- Obtaining a CT-Scan or MRI is necessary.

SEIZURE

EMRGENCIES AND TREATMENT

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FIRST IMPORTANT STEP

- IS IT A CORRECT SUGGESTION.

Which possibility

- Seizure
- Pseudoseizure
- Syncope or Faint
- Transient Ischemic Attacks (TIAs)
- Transient Global Amnesia (TGA)
- REM Behavior Disorder (RBD)
- Migraine and others

DIFERRENTIATE SIEZURE FROM OTHER POSSIBILITY

- OBTAIN A CAREFUL HISTORY
- PERFORM A BRIEF EXAM

SECOND STEP

EVALUATION OF PATIENTS FOR EMERGENT MEASURES

EVALUATION OF PATIENTS

- CHECKING OF AIRWAY.
- CHECKING OF CIRCULATION.
- CHECKING OF SYMPTOMS AND SIGN OF HERNIATION FOR EARLY SURGERY.

EMERGENT MEASURES

- DIAZEPAM FOR ACTIVE SEIZURE.
- CONTROL OF STATUS EPILEPTICUS
- ADMINASTRATION OF PHENYTOIN.
- INJECTION OF GLUCOSE AND CALCIUM OR OTHER DRUGS.
- COTROL OF VIOLENT BEHAVIORS.

Table 73.3: A suggested timetable for the treatment of status epilepticus*

Time (min)	*Action*
0–5	Diagnose status epilepticus by observing continued seizure activity or one additional seizure. Give oxygen by nasal cannula or mask; position patient's head for optimal airway patency; consider any abnormalities as necessary; initiate ECG monitoring. Obtain and record vital signs at onset and periodically thereafter; control any abnormalities as necessary; initiate ECG monitoring. Establish IV access; draw venous blood samples for glucose level, serum chemistries, hematology studies, toxicology screens, and determinations of antiepileptic drug levels. Assess oxygenation with oximetry or periodic arterial blood gas determinations.
6–10	If hypoglycemia is established or a blood glucose determination is unavailable, administer glucose; in adults, give 100 mg of thiamine first, followed by 50 mL of 50% glucose by direct push into the IV line; in children, the dose of glucose is 2 mL/kg of 25% glucose.
5–20	Administer either lorazepam, 0.1 mg/kg IV at 2 mg/min, or diazepam, 0.2 mg/kg IV at 5 mg/min. If diazepam is given, it can be repeated if seizures do not stop after 5 minutes; if diazepam is used to stop the status, phenytoin should be administered next to prevent recurrent status.
10–30	If status persists, administer phenytoin, 15–20 mg/kg IV, no faster than 50 mg/min in adults and 1 mg/kg/min IV in children; monitor ECG and blood pressure during the infusion; phenytoin is incompatible with glucose-containing solutions; the IV line should be purged with normal saline before the phenytoin infusion. Alternatively, fosphenytoin, 20 mg/kg phenytoin equivalents at 150 mg/min in adults or 3 mg/kg/min in children, can be used.
20–40	If status does not stop after 20 mg/kg of phenytoin or fosphenytoin, give additional doses of 5–10 mg/kg of phenytoin or fosphenytoin to a maximal dose of 30 mg/kg.
40–60	If status persists, give phenobarbital, 20 mg/kg IV at 50–100 mg/min; when phenobarbital is given after a benzodiazepine, the risk of apnea or hypopnea is great, and assisted ventilation usually is required. If seizures continue, give an additional 5–10 mg/kg of phenobarbital.
>60–70	If status persists, give anesthetic doses of drugs such as midazolam (loading dose of 0.2 mg/kg by slow intravenous bolus, then 0.75–10.00 μg/kg/min), propofol (loading dose of 12 mg/kg IV, followed by 2–10 mg/kg/hr), or pentobarbital (5–15 mg/kg IV bolus over 1 hour, followed by 0.5–3.0 mg/kg/hr); ventilatory assistance and vasopressors are virtually always necessary. Continuous EEG monitoring is indicated throughout therapy, with the primary endpoint being suppression of EEG spikes or a burst-suppression pattern with short intervals between bursts.

Table 73.4: Major drugs used to treat status epilepticus: intravenous doses, pharmacokinetics, and major toxicity

	Diazepam	*Lorazepam*	*Phenytoi n*	*Phenobarbital*
Adult IV dose in mg/kg (range [total dose])	0.15–0.25 [10 mg]	0.1 [48 mg]	15–20	20
Pediatric IV dose in mg/kg (range [total dose])	0.1–1.0 [10 mg]	0.05–0.50 [14 mg]	20	20
Pediatric per rectum dose in mg/kg	0.2–0.5 [20 mg maximum]			
Maximal administration rate in mg/min	5.0	2.0	50	100
Time to stop status in minutes	13	610	1030	2030
Effective duration of action in hours	0.25–0.50	>12–24	24	>48
Potential side effects				
Depression of consciousness	10–30 min	Several hours	None	Several days
Respiratory depression	Occasional	Occasional	Infrequent	Occasional
Hypertension	Infrequent	Infrequent	Occasional	Infrequent
Cardiac arrhythmia			In patients with heart disease	

EARLY STUDIES

- SAMPLING OF BLOOD FOR ELECTROLYT, BIOCHEMESTRY, AND TOXOLGIC STUDIES.
- ECG, CT-Scan.
- EEG, MRI, LP, VDRL, RENAL AND LIVER FUNCTION TESTS, AND OTHER COMPLEMENTARY LAB TESTS IN A STABLE SITUATION.

Table 8–5. Emergency evaluation of serial seizures, or status epilepticus.

Treatment with anticonvulsants should be instituted immediately (Table 8–6), while the following measures are taken.
Vital signs:
Blood pressure: exclude hypertensive encephalopathy and shock
Temperature: exclude hyperthermia
Pulse: exclude life-threatening cardiac arrhythmia
Draw venous blood for serum glucose, calcium, electrolytes, hepatic and renal function blood studies, complete blood count, erythrocyte sedimentation rate, and toxicology
Insert intravenous line
Administer glucose (50 mL of 50% dextrose) intravenously
Obtain any available history
Rapid physical examination, especially for:
Signs of trauma
Signs of meningeal irritation or systemic infection
Papilledema
Focal neurologic signs
Evidence of metastatic, hepatic, or renal disease
Arterial blood gases
Lumbar puncture, unless the cause of seizures has already been determined or signs of increased intracranial pressure of focal neurologic signs are present
ECG
Calculate serum osmolality: 2 (serum sodium concentration) + serum glucose/20 + serum urea nitrogen/3 (normal range: 270–290)
Urine sample for toxicology, if indicated

HOSPITALIZATION

- Prolonged postictal state
- Incomplete recovery.
- Status epilepticus.
- The presence of a systemic illness that may require treatment.
- Trauma or other neurological diseases.
- Questions regarding compliance.
- Violent behavior.
- For complete evaluation of causes.

Classification of patients

- First time seizure.
- History of seizure:
  - No previous treatment.
  - History of treatment:
    - regular drug consumption.
    - irregular drug consumption.

Treatment of first time seizure

- **Symptomatic seizure:**

1. **Trauma**
2. **Infection**
3. **Metabolic**
4. **Hypoxic ischemic**
5. **Drug and toxin**

- **Non-symptomatic seizure (single unprovoked seizure).**

Treatment of first time seizure
(symptomatic seizure)

- Usually in acute phase of disease or up to six month.
- Occasionally longer period (3-5 years):

1. MRI ABNORMALLITY
2. EEG ABNORMALLITY
3. FND
4. Febrile convulsion
5. Family history
6. Status epilepticus
7. Sever underlying disease
8. Stroke , abscess, tumor and other instances with cortical insult
9. Other possibilities

Treatment of first time seizure
(non-symptomatic seizure)

- Usually no treatment or up to six month.
- Long term treatment:

- Age <16 or >59
- positive FH
- FC
- Previous trauma and CVA
- Onset with more than one attack
- Onset in night
- Onset with status
- Focal or focal onset

- Absence, partial, myoclonic
- Existence of FND
- Todd's paralysis
- Major developmental anomaly
- Abnormal EEG
- Abnormal MTI or CT-Scan
- Violent behavior
- Low socioeconomic

Treatment with history of seizure

- **Not previously treated:**
  treatment with adequate drug
- **History of treatment but irregular drug consumption:**
  temporary second drug and recommendation to regular consumption

Treatment with history of seizure

- **History of treatment and regular drug consumption:**

- Inadequate drug, Inadequate dose, and wrong interval (special food)
- Drug interactions AND consumption of drugs that cause seizure
- Alcohol and elicited drug
- Inadequate sleep, fatigue, stress, computer, hungry
- Recent metabolic and infectious diseases
- Menstruation, puberty, pregnancy, alternation in weight
- Another type of seizure and altered pattern of seizure
- Ultimately no response to one drug

Table 8–2. Major categories of drugs reported to cause seizures.

Anticholinesterases (organophosphates, physostigmine)
Antidepressants (tricyclic, monocyclic, heterocyclic)
Antihistamines
Antipsychotics (phenothiazines, butyrophenones, clozapine)
β-Adrenergic receptor blockers (propranolol, oxprenolol)
Chemotherapeutics (etoposide, ifosfamide, cisplatinum)
Cyclosporine, FK 506
Hypoglycemic agents (including insulin)
Hypoosmolar parenteral solutions
Isoniazid
Local anesthetics (bupivacaine, lidocaine, procaine, etidocaine)
Methylxanthines (theophylline, aminophylline)
Narcotic analgesics (fentanyl, meperidine, pentazocine, propoxyphene)
Penicillins
Phencyclidine
Sympathomimetics (amphetamines, cocaine, ephedrine, MDMA[1] "ecstasy," phenylpropanolamine, terbutaline)

[1] Methylenedioxymethamphetamine.

TREATMENT

- The management of patients with epilepsy is focused on three main goals:
- Controlling seizures.
- Avoiding side effects of treatment.
- Maintaining or restoring quality of life.

The following basic principals increase the likelihood of achieving seizure control without drug toxicity:

1. Use a single drug whenever possible.
2. Increase the dose of that drug to either seizure control or toxicity (decreasing the dose if toxicity occurs).
3. If a drug fails to control seizures without toxicity, switch to another appropriate drug used alone and again increase the dose until seizure control occurs or toxicity intervenes.
4. Remember that the "therapeutic drug range" is a guideline and not an absolute. Some patients achieve seizure control with blood concentrations below the range, and others tolerate concentrations above the range without toxicity.
5. Use two drugs only when monotherapy has failed. Some patients may have more seizures when taking two drugs, compared with one drug, because of drug interactions.
6. Be aware that the ability to metabolize anticonvulsant drugs is different in the young, the elderly, pregnant women, and people with certain chronic diseases, especially hepatic and renal disease, compared with healthy nonpregnant adults.
7. Routine schedules of laboratory monitoring are recommended for all antiepileptic medications in common use. Routine testing, however, does not detect or prevent severe reactions, most of which are idiosyncratic.

Table 73.5: Antiepileptic drugs approved for use in North America, Europe, or Japan

Drug	F%	Tmax (hr)	Protein binding (%)	Route of elimination	T½ (hr)	T ss (day)	Dose range (mg/kg)	Target plasma drug concentration (range)	
								mg/L	μmol/L
Carbamazepine	75–85	4–12	75	Hepatic	20–50† 5–20†	20–30	10–30	3–12	12–50
Clobazam	>90	1–4	85	Hepatic	10–30	10	0.5–2	NA	NA
Norclobazam					36–46				
Clonazepam	>90	1–4	85	Hepatic	20–40	6	0.1–0.15	NA	NA
Ethosuximide	>90	1–4	<10	Hepatic	30–60	7	10–40	40–100	300–700
Felbamate	>90	2–6	25	Renal 90%	14–23	4	40–80	30–100	120–400
Gabapentin	35–60	2–3	0	Renal	5–9	1–2	30–40	4–16	20–100
Lamotrigine	>90	1–3	55	Hepatic	15–60	3–10	1–15	2–20	8–80
Levetiracetam	>90	0.6–1.3	<10	Renal	7	2	20–60	20–60	115–350
Lorazepam	>90	1.5–2	90	Hepatic	15	3	0.03	NA	NA
Oxcarbazepine	>95	1–2		Hepatic	2	2	15–30	5–50*	20–200*
MHD*		3–5	40		10–15				
Phenobarbital	>90	0.5–4	45	Hepatic	65–110	15–20	2–5	10–30	40–130
Phenytoin	>90	2–12	90	Hepatic	10–60§	15–20	5–10	3–20	12–80
Primidone	>90	2–4	<20	Hepatic	8–15		10–20		
Tiagabine	>90	1–2	96	Hepatic	2–9	1–2	0.1–1	5–70	12–170
Topiramate	>80	1–4	15	Renal 70%	12–30	3–5	5–9	2–25	6–75
Valproic acid	>90	1–8‡	70–93	Hepatic	5–15	2	15–30	50–100	350–700
Vigabatrin	80	0.5–2	0	Renal	5–7	2	40–100		
Zonisamide	>90	2–5	55	Hepatic	50–70	10–15	4–8	10–40	45–180

F = fraction absorbed, bioavailability; Tmax = time interval between ingestion and maximal serum concentration; T½ = elimination half life; T ss = steady-state time.

*Monohydroxy derivative (MHD) 10-OH-carbamazepine.

†Concentration dependent.

‡Absorption of enteric-coated tablet is delayed.

§Steady state values for half-life and serum levels are reached only after complete autoinduction.

NA – not applicable

Source: Modified with permission from Glauser, T. A. & Pippenger, C. E. 2000, "Controversies in blood-level monitoring: reexamining its role in the treatment of epilepsy," *Epilepsia*, vol. 41, pp. S6-S15.

Drug	Dose Related	Idiosyncratic
Phenytoin	Diplopia Ataxia Gingival hyperplasia Hirsutism Coarse facial features Polyneuropathy Osteomalacia Megaloblastic anemia	Skin rash Fever Lymphoid hyperplasia Hepatic dysfunction Blood dyscrasia Stevens-Johnson syndrome
Carbamazepine	Diplopia Ataxia Gastrointestinal distress Sedation	Skin rash Blood dyscrasia Hepatic dysfunction Stevens-Johnson syndrome SIADH
Oxcarbazepine	Hyponatremia	Skin rash
Phenobarbital	Sedation Insomnia Behavioral disturbance Diplopia Ataxia	Skin rash Stevens-Johnson syndrome
Valproic acid	Gastrointestinal distress Tremor Sedation Weight gain Hair loss Thrombocytopenia	Hepatic dysfunction Peripheral edema Pancreatitis
Ethosuximide	Gastrointestinal distress Sedation Ataxia Headache	Skin rash Blood dyscrasia
Clonazepam	Sedation Diplopia Ataxia Behavioral disturbance Hypersalivation	
Gabapentin	Drowsiness Fatigue Drugged sensation Loss of libido	
Lamotrigine	Dizziness Ataxia	Skin rash in 1–2% (frequency increased by concomitant valproic acid therapy and reduced by gradual build-up of dose) Stevens-Johnson syndrome
Vigabatrin	Sedation Vertigo Psychosis	Peripheral visual constriction (irreversible)
Topiramate	Ataxia Confusion	Renal stones Glaucoma
Tiagabine	Dizziness Sedation Nausea	Rash
Zonisamide	Drowsiness Ataxia Anorexia Headache	Nephrolithiasis Skin rash

Benzodiazepines

- Clonazepam and nitrazepam are effective as prophylactic therapy for several seizure types but are used commonly, in combination with other drugs, for the treatment of Lennox- Gastaut syndrome, myoclonic epilepsy, and infantile spasms.
- Clorazepate usually is ineffective by itself and is used for adjunctive therapy.
- Clobazam originally was expected to be more effective, to be less sedating, and to have decreased tendency toward the development of tolerance, but its spectrum of activity and side effects may be similar to the other benzodiazepines (Henriksen 1998).

Benzodiazepines

- Adverse effects are drowsiness, ataxia, diplopia, blurred vision, personality changes, irritability, memory disturbances, hypotonia, and hypersecretion in children.
- Additionally, tolerance may develop to the anticonvulsant effects as well as to the side effects. Cross-tolerance can occur between different benzodiazepines.
- Finally, dependence occurs, and abrupt discontinuation of benzodiazepines can cause withdrawal symptoms and seizures.
- In general, no clear correlation exists between plasma levels of these compounds and their therapeutic effect (Henriksen 1998).

Carbamazepine

- Carbamazepine is related structurally to tricyclic antidepressants.
- In the United States, it originally was approved
- for treatment of trigeminal neuralgia, but its antiepileptic
- activity has been well established for treatment of partial and
- generalized tonic-clonic seizures. It is not effective against
- and may even exacerbate absence and myoclonic seizures.
- Carbamazepine acts by preventing repetitive firing of action
- potentials in depolarized neurons through blockade of
- voltage-dependent sodium channels (Brodie and Dichter1996).

PREGNANCY

- Folic acid 2-4 mg daily for all women with epilepsy who are taking anticonvulsants, beginning as long as 3 months before conception until 12 weeks' gestation.
- A deficiency of vitamin K-dependent clotting factors occurs in some neonates born to women who take phenobarbital, primidone, carbamazepine, ethosuximide, or phenytoin.

EPILEPSY AND PREGNANCY

- Women with epilepsy have approximately 15% fewer
- children than expected.
- Women who have less than one seizure in 9 months usually do not experience an increase in
- seizure rate during pregnancy.
- Most studies suggest that approximately one fourth of
- women experience an increase in seizure rate during
- gestation,
- Others recommend 2-4 mg daily for all women with
- epilepsy who are taking anticonvulsants, beginning as long
- as 3 months before conception until 12 weeks' gestation.

A deficiency of vitamin K-dependent clotting factors occurs in some neonates born to women who take phenobarbital, primidone, carbamazepine, ethosuximide, or phenytoin. Although rarely reported, neonatal intracerebral hemorrhage may be attributable to this vitamin K deficiency. In an attempt to lower this risk, physicians prescribe oral vitamin KI 10-20 mg daily beginning 2-4 weeks before expected delivery and until birth. Often, the neonate receives a single 1- to 2-mg intramuscular injection of vitamin KI immediately after delivery.

- Nearly 90% of epileptic women deliver healthy, normal
- babies, but risks of miscarriage, stillbirth, prematurity,
- developmental delay, and major malformations are
- increased in epileptic mothers. Maternal seizures; AEDs;
- and socioeconomic, genetic, and psychological aspects of
- epilepsy affect outcome.

However, even when blood levels of drugs are maintained adequately, approximately 10% of women can expect worsened seizure control during pregnancy. During labor, approximately 1-2% of epileptic women have a convulsive seizure, and another 1-2% have a seizure within 24 hours of delivery.

Other factors that may contribute to an increase in seizure rate include hormonal changes, sleep deprivation, mild chronic respiratory alkalosis, the use of folic acid supplements, and emotional factors. Seizure type did not play a role in some studies, but in others, partial complex epilepsy worsened more often during gestation.

- Controversy continues over whether seizures increase
- risks for developing eclampsia, preeclampsia, hlood loss,
- placental abruption, and premature labor. For studies
- that claim increased risk, these risks are calculated to
- be approximately 1.5-3.0 times the risk of women
- without epilepsy.

In previous studies, the rate of major birth defects in the general population has been estimated to be approximately 2.0-4.8%, depending on the population studied and methodology used. The risk of birth defects increases for infants of women with epilepsy to a rate of 3.5-6.0%, independent of the effect of medication. In general, use of a single AED increases the risk of congenital malformations to 4-8%. Researchers found a 5.5% incidence of malformations with two anticonvulsant drugs, 11% with three anticonvulsant drugs, and 23% with four AEDs.