

Seizures and Epilepsy: Current Concepts

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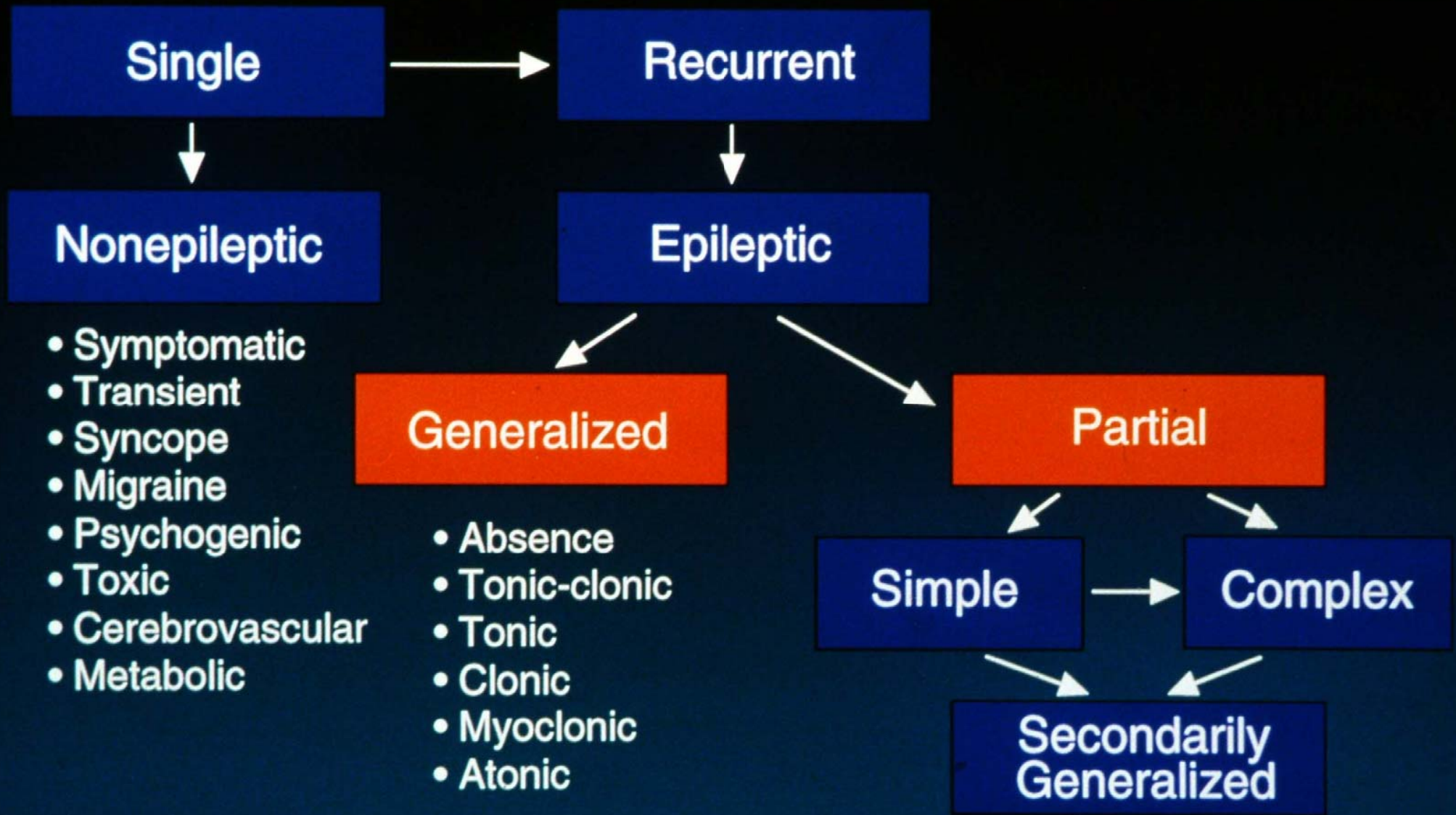
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Comprehensive Epilepsy Program

Epilepsy: Definition

- Epilepsy:** Chronic brain disorder of various etiologies characterized by *recurrent* unprovoked sz
- Epileptic Sz:** Discrete epileptic events due to transient, hypersynchronous, abnormal neuronal behavior
- Epilepsy Syndromes:** Grouping of similar epileptic patterns according to sz type, EEG, age of onset, familial episodes, prognosis, other clinical signs

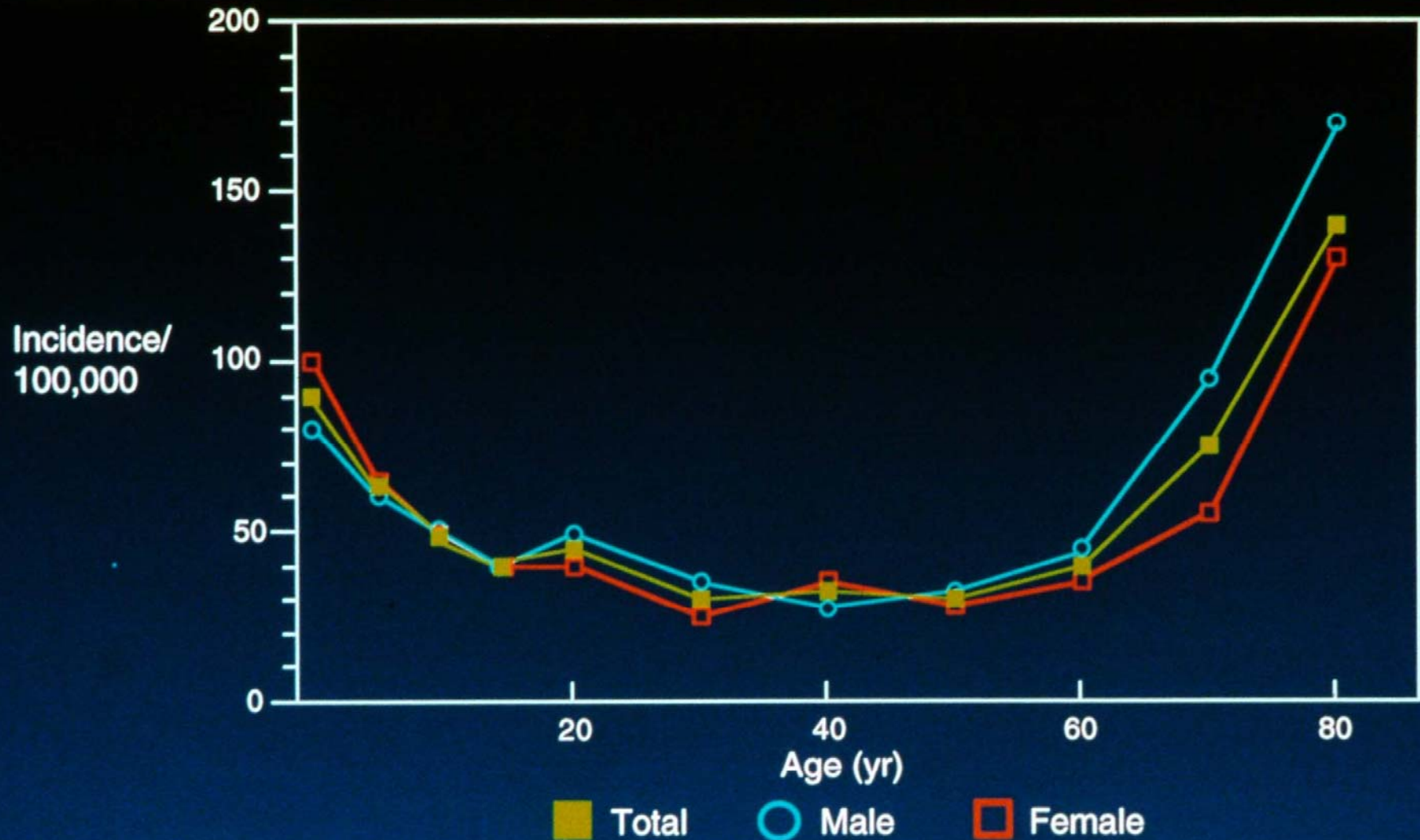
Seizure Types



EPILEPSY EPIDEMIOLOGY I

- Incidence 50 per 100,000 population per year (150,000 cases per year)
- Prevalence 1% of population (2.5 million in USA)
- Cumulative Incidence
 - 10% of population will have at least one seizure in their lifetime
 - 4% of population will have diagnosis of epilepsy
 - 1% will have a single unprovoked seizure
 - 3% will have a seizure due to an acute brain or metabolic insult
 - 2-5% will have febrile convulsion(s)

Incidence of Epilepsy in Rochester, Minnesota, 1935 to 1984



Adapted with permission from Hauser WA, Annegers JF, Kurland LT. *Epilepsia*. 1993;34:453-468.

EPILEPSY EPIDEMIOLOGY II

- 60-65% of all patients with epilepsy can be controlled with one or two AEDs
 - Only 40% of patients with partial seizures (with or without secondary generalization) are seizure-free *
- 35-40% are medically intractable
 - 60-80% of patients with partial seizures are medically intractable*
 - 20-30% of patients with intractable seizures are surgical candidates

*VA I and II Studies

EPILEPSY EPIDEMIOLOGY III: Detroit Metropolitan Area

- Population 5,000,000
- All patients with epilepsy (1%) 50,000
 - Patients with partial seizures (60%) 30,000
- Medically intractable epilepsy (40%) 20,000
 - Patients with partial seizures (60%) 18,000
 - Surgical Candidates (25%) 5,000

CLASSIFICATION

Partial seizures

- Simple
- Complex

Generalized seizures

- Absence
- Myoclonic
- Tonic-clonic
- Atonic

Continual seizures: status epilepticus



OLD vs NEW TERMINOLOGY

Former

Focal motor;
Jacksonian “march”

Psychomotor;
temporal lobe

Major motor;
grand mal

Petit mal

Current

Simple partial

Complex partial

Generalized
tonic-clonic

Absence



Simple Partial Seizures

("Focal Motor"/"Focal Sensory")

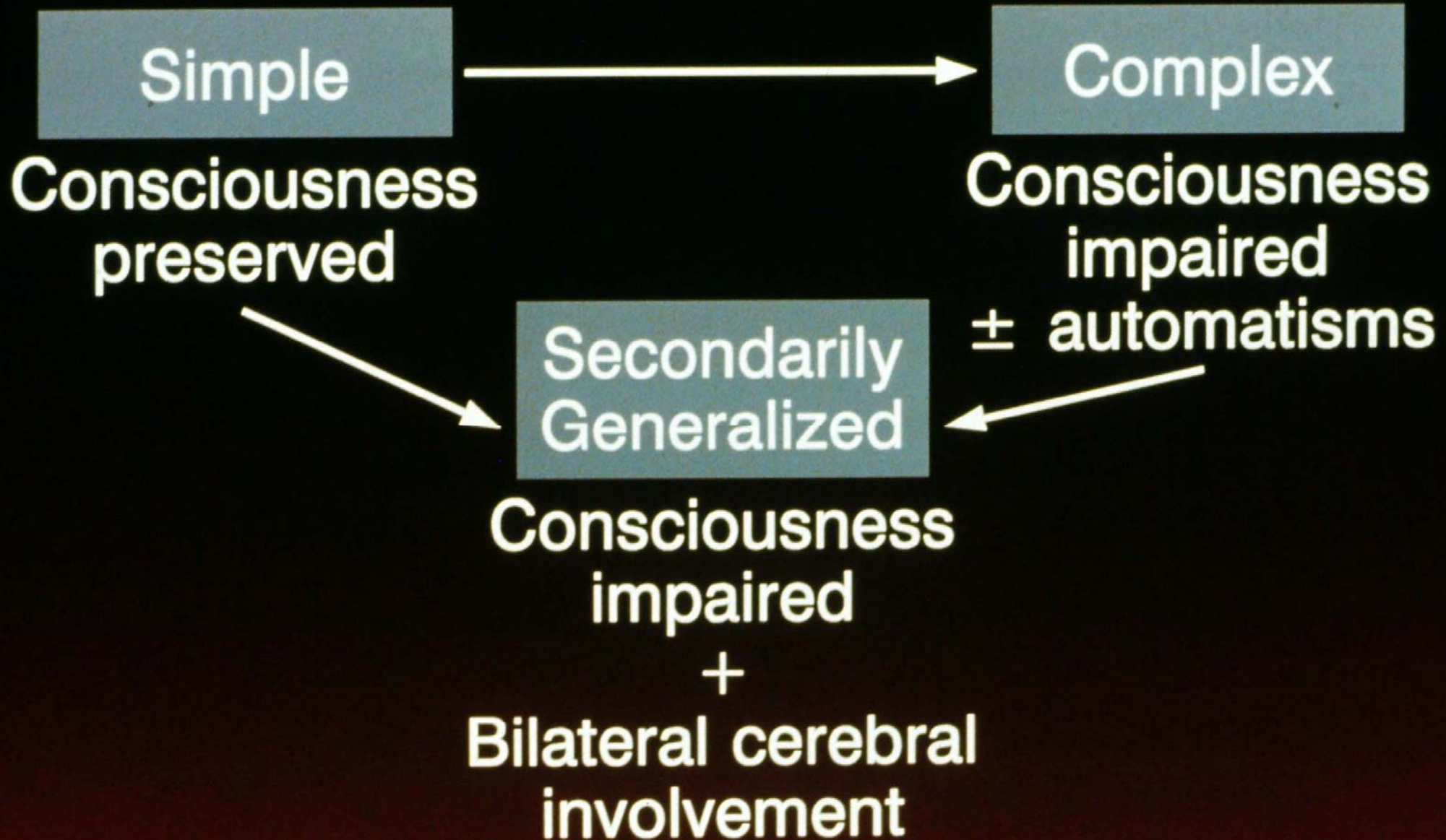
- **Consciousness intact**
- **Signs/symptoms variable**
 - Motor
 - Sensory
 - Autonomic
 - Psychic
- **Focal EEG abnormality**

Complex Partial Seizures

("Temporal Lobe"/"Psychomotor")

- Clouding, without loss of consciousness
- Ictus duration, 1 min.
- Staring spells
- Automatisms
- Amnesia for ictal event
- Focal EEG abnormality
- Postictal confusion generally present

Partial Seizures



Generalized Seizures

- Absence (typical / atypical)
- Tonic-clonic / clonic-tonic-clonic
- Clonic
- Tonic
- Myoclonic
- Atonic

Absence Seizures

("Petit Mal")

- Childhood / adolescence onset
- Sudden onset, without aura
- Momentary loss of consciousness / staring spell
- Duration, 10-20 sec.
- Nonconvulsive
- Ictal EEG, 3 cps S&W (typical)
- Abrupt recovery postictally
- Amnesia for ictal event

Diagnostic Differentiation

	Absence Seizures	Complex Partial Seizures
Aura	None	In the majority
Automatisms	Seen in more prolonged seizures, somewhat simpler	Common, almost always more complex
Clonic component	45%	15%
Postictal confusion	No	Yes
Mean duration	10 sec.	1-2 min.
EEG	Generalized spike-wave	Focal spikes

Tonic-Clonic Seizures*

("Grand Mal" / "Convulsive")

- Loss of consciousness
- Ictus
 - Fall
 - Muscular rigidity (tonic)
 - Respiration inhibited (cyanosis)
 - Rhythmic jerking (clonic)
 - 1-5 min duration
 - Tongue-biting / injury common
 - Bladder/ bowel incontinence
- Postictal confusion

*Primary or secondarily generalized seizures

Diagnostic Differentiation

Primary GTCS

- Abrupt onset, without localizing aura
- Tonic, clonic, or tonic-clonic
- Genetic component highly likely
- Onset early in life

Secondarily GTCS

- May begin abruptly, usually follows partial seizure
- Tonic-clonic
- Subjective aspects of partial seizure (visual, auditory, tactile components)
- Onset later in life

Myoclonic Seizures

("Minor Motor")

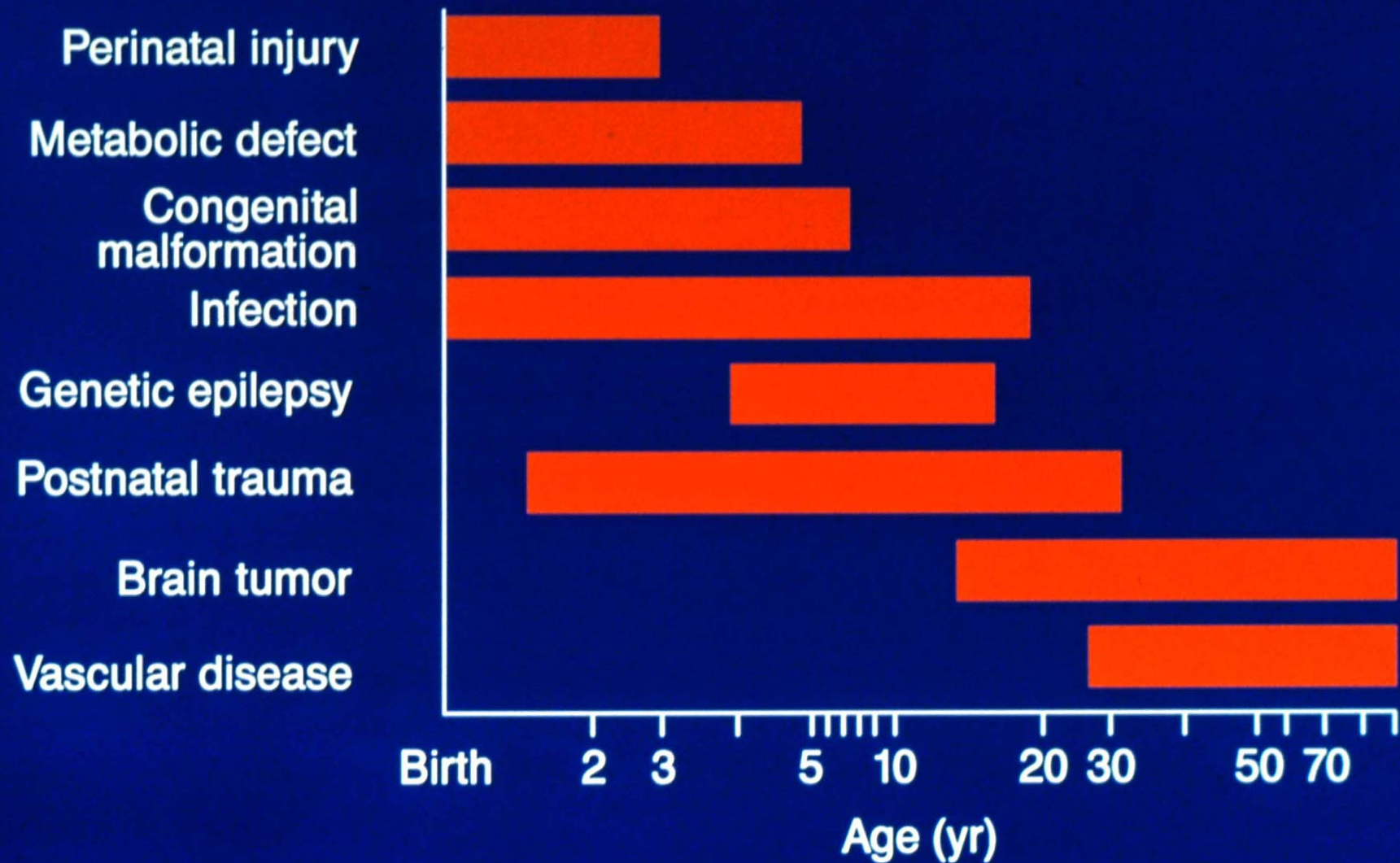
- **Brief, shocklike muscle contractions**
 - Head
 - Upper extremities
- **Bilaterally symmetrical**
- **Consciousness preserved**
- **Precipitated by awakening or falling asleep**
- **May progress into clonic or clonic-tonic seizures**

Atonic Seizures

(Drop Attacks, Astatic Seizures)

- **Sudden loss of tone in postural muscles**
- **Person falls to ground suddenly**
- **Duration, usually only a few seconds**
- **Brief impairment of consciousness**
- **Abrupt recovery postictally**
- **Ictal EEG, polyspike and wave or suppression of EEG activity**
- **Frequent falls result in injury**
- **Corpus callosotomy may be necessary if medically intractable**

Epilepsy: Etiology vs Age of Onset



Seizure Diagnosis

- **History**
 - Patient
 - Witness
- **Physical/neurological exam**
- **EEG**
 - Photic stimulation
 - Hyperventilation
 - Sleep deprivation
- **Anatomic studies**
 - CT
 - MRI
- **Special studies**
 - SPECT
 - PET
- **Intensive CCTV/EEG monitoring**

CONCEPTS IN ANTICONVULSANT PHARMACOTHERAPY

- Initiate treatment with single drug
- Nonsedating drugs preferable
- Assess treatment based on clinical response with lab monitoring



INDIVIDUALIZING THERAPY

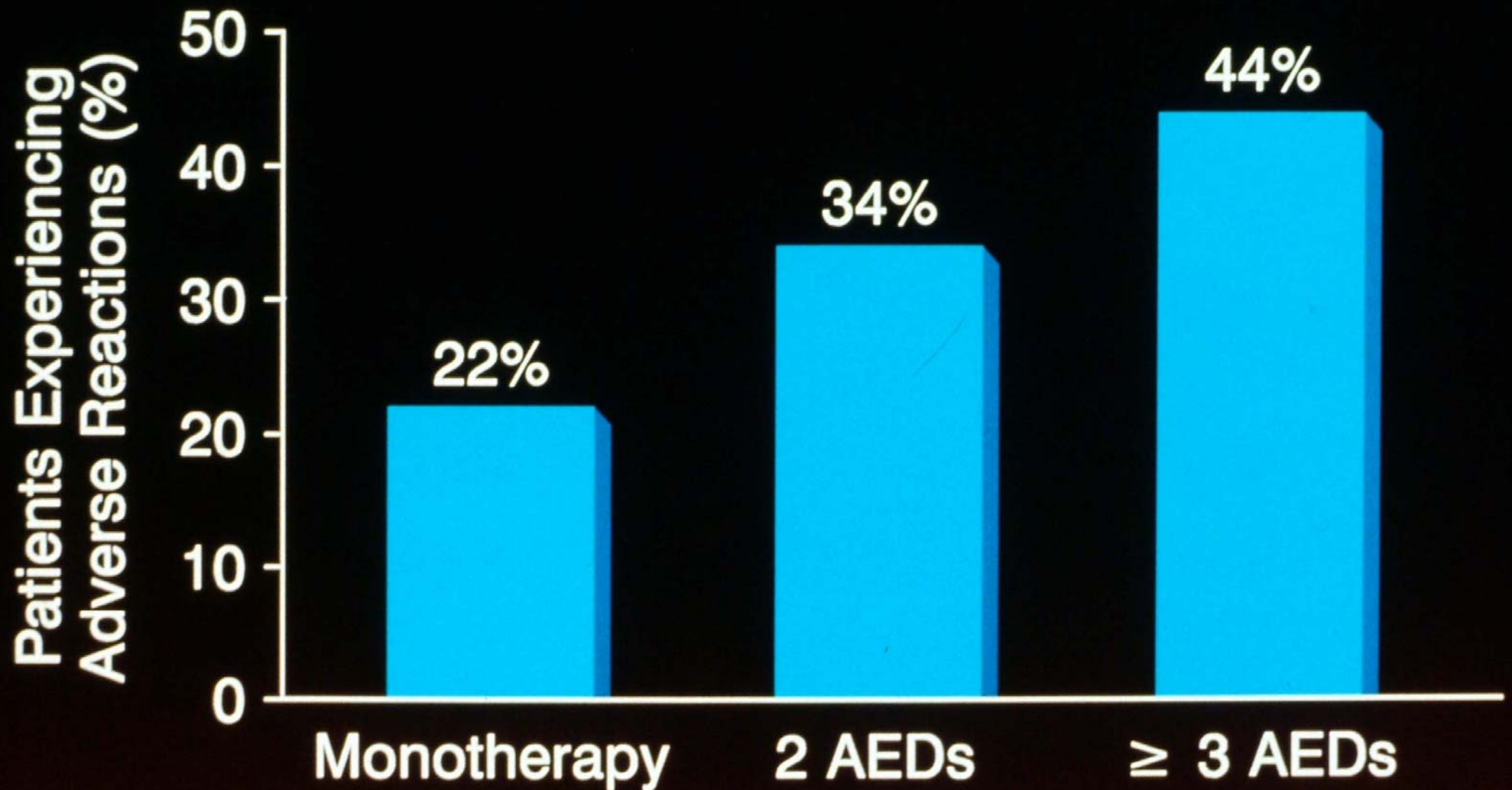
- Use drug most appropriate for patient's seizure disorder
- Titrate to effective level
- In case of treatment failure or toxicity, *substitute* an alternative agent
- If necessary, combine two nonsedating agents
- If necessary, consider adding phenobarbital or primidone



Why Monotherapy?

- Enhanced seizure control
- Reduction of side effects
 - Reduction of idiosyncratic reactions
 - Reduction of teratogenic effects
- Absence of drug interactions
- Cost effective
- Improved quality of life
- Improved patient compliance

Adverse Drug Reactions (N = 509)



Collaborative Group for Epidemiology of Epilepsy. *Epilepsia* 27:323, 1986

Which AEDs to Use: Partial Seizures w/wo GTCS

Drugs of choice

- CBZ
- PHT

Second line AEDs

- VPA
- PB
- PRM

Newer AEDs

- LTG
- TPM
- OXC
- LEV
- ZNS
- PGB
- LCM

Second line AEDs

- GBP
- TGB

Which AEDs to Use: Primary Generalized Epilepsy

Drugs of choice

- Simple absence (CAE)
 - VPA
 - ESM
- GTCS
 - VPA
 - CBZ
 - PHT
- Mixed PGE
 - VPA

Newer AEDs

- LTG
- TPM
- LEV
- ZNS

Identification and Treatment of Refractory Epilepsy

- **Goal:** Maintenance of normal lifestyle by complete seizure control with no side effects (65% of patients with newly diagnosed epilepsy)
- Accurate classification of seizure type(s) and epilepsy syndrome
- Failure to respond to 1st AED (only 11% become Sz-free)
- Failure to respond to 2 first line AEDs (only 4% become Sz-free)
- Consider (“synergistic”) dual AED therapy (only 3% become Sz-free)
- Consider resective epilepsy surgery (especially if HS or lesion present)
- Consider VNS if not a surgical candidate

Kwan & Brodie. NEJM 342:314-319, 2000

Brodie & Kwan. Neurology 58 (suppl 5):S2-S8, 2002

Kwan & Brodie. Seizure 11:77-84, 2002

AED Acronyms

Established AEDs

- Phenytoin (PHT)
- Carbamazepine (CBZ)
- Valproic acid (VPA)
- Phenobarbital (PB)
- Primidone (PRM)
- Ethosuximide (ESM)

Newer AEDs

- Gabapentin (GBP)
- Lamotrigine (LTG)
- Topiramate (TPM)
- Tiagabine (TGB)
- Oxcarbazepine (OXC)
- Levetiracetam (LEV)
- Zonisamide (ZNS)
- Pregabalin (PGB)
- Lacosamide (LCM)