Neurological Emergencies

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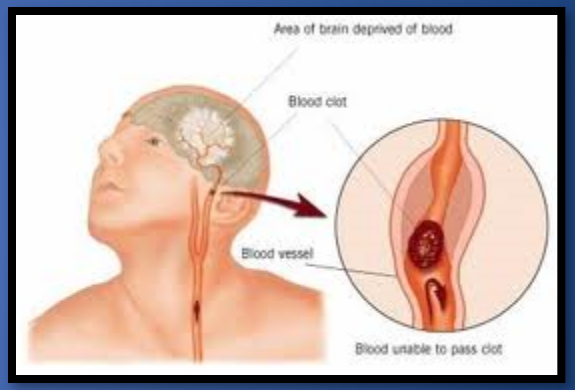
Neurological Emergencies

- Cerebrovascular Disease (Stroke)
- Increased intracranial pressure
- Status epilepticus
- CNS infections
- Neuromuscular disorders with respiratory failure

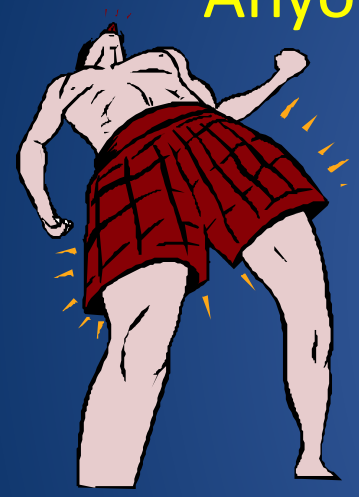
Cerebrovascular Disease (Stroke)



The STROKE SOCIETY of the PHILIPPINES

What is a Stroke?

Anyone should consider stroke if they experience…



- Sudden numbness or weakness in the face, arm, or leg especially on one side of the face or body
- Sudden confusion, trouble speaking or understanding
- Sudden trouble seeing in one or both eyes
- Sudden trouble walking, dizziness, loss of balance or coordination
- Sudden severe headache with no known cause

Evolving Definitions of Stroke

- Stroke is a **heterogenous disease** and manifestations are highly variable
- 1970s – defined by WHO as *"a neurological deficit of cerebrovascular cause that persists beyond 24 hrs, or is interrupted by death within 24 hrs"*
- May be attributed to ischemic stroke, hemorrhagic stroke, or vascular anomalies
- If neurological deficits last <24 hrs, it was defined to be a transient ischemic attack (TIA)

Evolving Definitions of Stroke

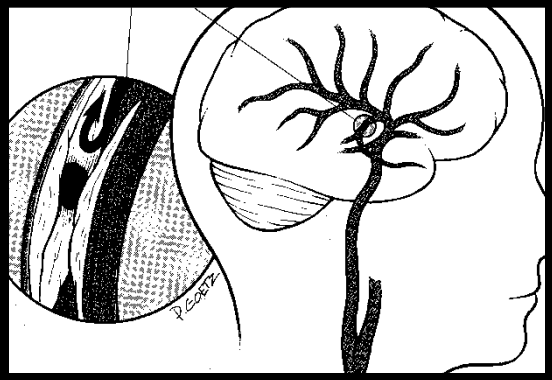
- Advent of MRI and thrombolytic therapy: old definitions are challenged
  - *Shift from time-based definition to a pathology-based one*
- Working definitions by the Stroke Society of the Philippines (Sept 2010):
- **TIA**: *a **transient** episode of neurological **dysfunction** caused by focal brain or spinal or retinal ischemia, **without evidence of acute infarction** in which clinical symptoms typically last less than an hour*

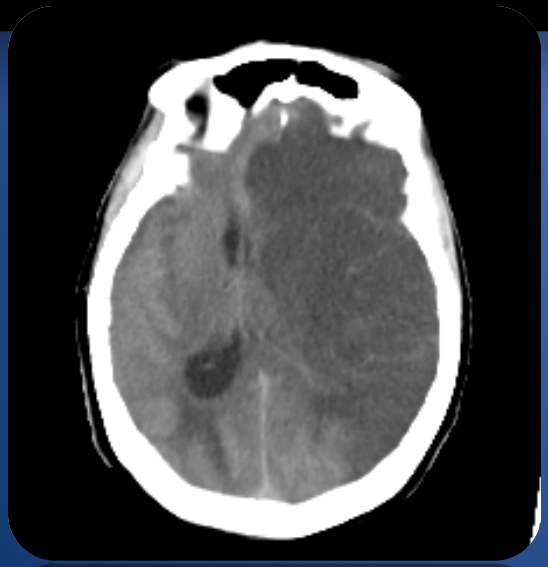
Evolving Definitions of Stroke

- Stroke: ***sudden*** *onset of focal (or global) neurologic* ***deficit*** *due to* ***an underlying vascular pathology***
- Two major types:
  - **Ischemic stroke** – *an infarction of CNS tissue*
    - *Symptomatic*
    - *Silent – seen only on neuroimaging*
  - **Hemorrhagic** – *results from a rupture of a blood vessel or an abnormal vascular structure directly into and around the brain*

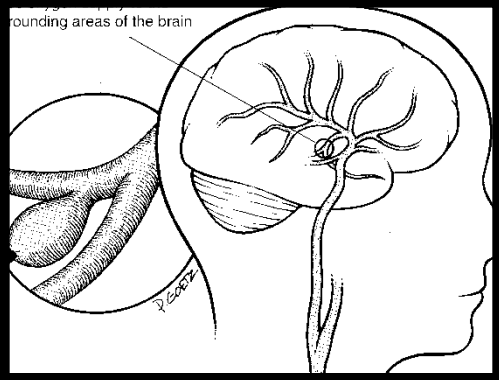
2 Types of Stroke

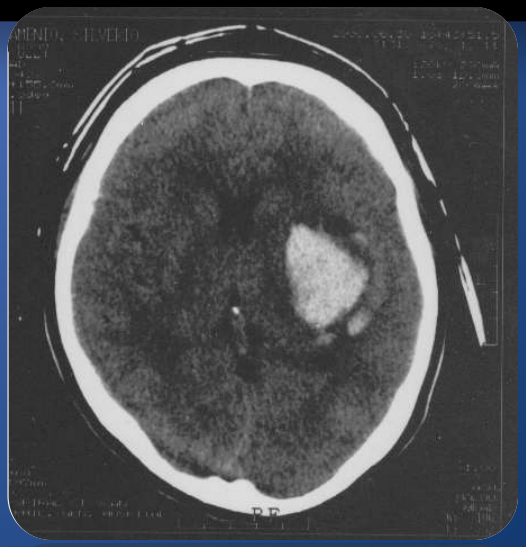
Infarction





Intracerebral Hemorrhage



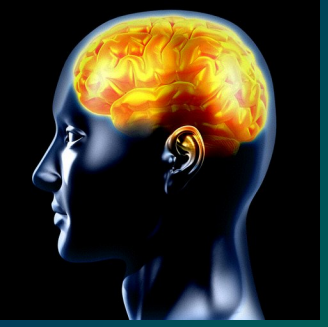


The Role of Physicians in Acute Stroke Care

- **Confirm** that the diagnosis is STROKE and **not mimickers**; that stroke is ISCHEMIC versus HEMORRHAGIC
- Determine if acute treatment with **thrombolytic** agent is advisable
- Do diagnostics to **screen** for acute medical or neurologic **complications** of stroke
- Determine vascular distributions of the stroke and provide clues on likely **pathophysiology** and etiology

SSP Classification of Acute Stroke Based on Clinical Severity

- Transient Ischemic Attack
- Mild Stroke
- Moderate Stroke
- Severe Stroke



Transient Ischemic Attack

- **NOT** a “ministroke” or “warning stroke” or “transient stroke”
- Stroke and TIA are on a **spectrum** of serious conditions involving **brain ischemia** and are both markers of reduced cerebral blood flow and increased **risk of disability and death**
- TIAs offer an opportunity to **initiate treatment** that can forestall the onset of permanent disabling injury

Guidelines for TIA

Management Priorities

Ascertain clinical diagnosis of TIA (history and physical exam are very important

- Exclude common stroke mimickers
- Provide basic emergent supportive care (ABCs of resuscitation)
- Monitor neuro vital signs, BP, MAP, RR, temp, pupils
- Perform stroke scales (NIHSS, GCS)
- Perform risk stratification using the ABCD2 scale
- Monitor and manage BP, treat if MAP >130

Precautions:

- Avoid precipitous drop in BA (not > 15% of baseline MAP). Do not use rapid-acting sublingual agents; when needed use easily titratable IV or short-acting oral antihypertensive medication
- Ensure appropriate hydration

Guidelines for TIA

Emergent Diagnostics

- Complete blood count
- Blood sugar
- Electrocardiogram
- PT/PTT

Cranial MRI-DWI is preferred
May do Noncontrast CT if MRI is not possible

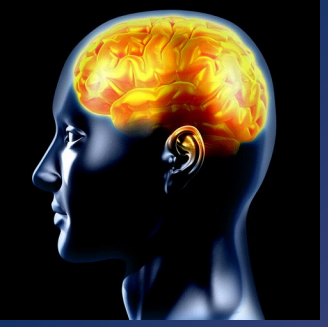
Early Specific Treatment

Non-cardioembolic	Cardioembolic
Aspirin 160-325 mg/day as early as possible Neuroprotection	Consider anticoagulation with IV heparin or LMWH for those high risk for early recurrence (e.g. AF with thrombus, VHD, or MI) **OR** Aspirin 160-325 mg/day (if anticoagulants not possible) If infective endocarditis is suspected, give antibiotics and do not anticoagulate!

Guidelines for TIA

Delayed Management and Secondary Prevention

Non-cardioembolic	Cardioembolic	Others
Antiplatelets (aspirin, clopidrogrel, cilostazol, triflusal, dipyridamole) **Control of risk factors** **Vascular studies:** Carotid UTZ TCD or MRA or CTA Neuroprotection	**Echocardiography** If age <75 and PT/INR available, anticoagulate with **warfarin** (INR 2-3) If age >75, INR 2.0 (1.6-2.5) **Aspirin** 160-325 mg/ day (if anticoagulants not possible/ contraindicated)	Specialized **coagulation tests** (protein C & S, antithrombin III, fibrinogen, homocysteine) and **drug screening** (e.g. MAP, cocaine) in young patients with no vascular risk factors If vasculitis is suspected: **ESR, ANA, Lupus anticogulant** Transesophageal Echo (TEE) to rule out PFO



Mild Stroke

- **Alert patients** with any or a combination of the following:
  - **Mild pure motor** weakness of one side of the body, defined as: can raise arm above shoulder, has clumsy hand, or can ambulate without assistance
  - **Pure sensory** deficit
  - **Slurred** but intelligible speech
  - Vertigo with **incoordination** (e.g., gait disturbance, unsteadiness or clumsy hand)
  - **Visual** field defects alone
  - **NIHSS score 0 – 5**

Guidelines for Mild Stroke

Management Priorities

Ascertain clinical diagnosis of TIA (history and physical exam are very important

- Exclude common stroke mimickers
- Provide basic emergent supportive care (ABCs of resuscitation)
- Monitor neuro vital signs, BP, MAP, RR, temp, pupils
- Perform stroke scales (NIHSS, GCS)
- Provide O2 support to maintain O2 sat >95%
- Monitor and manage BP, treat if MAP >130

Precautions:

- Avoid precipitous drop in BA (not > 15% of baseline MAP). Do not use rapid-acting sublingual agents; when needed use easily titratable IV or short-acting oral antihypertensive medication
- Ensure appropriate hydration.
  IVF: 0.9% NaCl

Guidelines for Mild Stroke

Emergent Diagnostics

- Complete blood count
- Blood sugar
- Electrocardiogram
- PT/PTT

Cranial MRI-DWI is preferred
May do Noncontrast CT if MRI is not possible
If ICH, compute for hematoma volume

Early Specific Treatment for Ischemic Stroke

Non-cardioembolic	Cardioembolic
Aspirin 160-325 mg/day as early as possible Neuroprotection Early rehabilitation once stable within 72 hrs	Consider anticoagulation with IV heparin or LMWH for those high risk for early recurrence **OR** Aspirin 160-325 mg/day (if anticoagulants not possible) If infective endocarditis is suspected, give antibiotics and do not anticoagulate! Early rehabilitation

Guidelines for Mild Stroke

Delayed Management and Secondary Prevention

Non-cardioembolic	Cardioembolic
Antiplatelets (aspirin, clopidrogrel, cilostazol, triflusal, dipyridamole) **Control of risk factors** **Vascular studies:** Carotid UTZ – if with >70% stenosis, refer to neurosurgeon or TCVS for possible CEA or stenting TCD or MRA or CTA Neuroprotection	**Echocardiography** If age <75 and PT/INR available, anticoagulate with **warfarin** (INR 2-3) If age >75, INR 2.0 (1.6-2.5) **Aspirin** 160-325 mg/day (if anticoagulants not possible/ contraindicated)

Guidelines for Mild Stroke

Early Specific Treatment for CT or MRI-confirmed Hemorrhagic Stroke

- Early neurology/neurosurgery consult for all ICH
- Monitor and maintain BP: Target **MAP of 110**
- Neuroprotection
- Early **rehab within 72 hrs** if stable
- Give **anticonvulsants** for clinical seizures and proven subclinical or electrographic seizures. Prophylactic AEDS not recommended
- Steroids not recommended
- Monitor and correct laboratory parameters
- Correct coagulation/bleeding abnormalities

Delayed Management and Treatment (Secondary Prevention)

- Long-term **strict BP control** and monitoring
- **Consider** contrast CT scan, 4 vessel angiogram, MRA or CTA if the patient is:
  - Less than 45 years old
  - Normotensive
  - Has lobar ICH
  - Uncertain cause of ICH
  - Suspected to have aneurysm, AV malformation or vasculitis

Moderate and Severe Stroke

- **Moderate Stroke**
  - Awake patient with **significant motor** and/or **sensory** and/or **language** and/or **visual** deficit
  - **Disoriented, drowsy or light stupor** with purposeful response to painful stimuli
  - NIHSS score **6-21**
- **Severe Stroke**
  - **Deep stupor or comatose** patients with non-purposeful response, decorticate, or decerebrate posturing to painful stimuli
  - NIHSS score **>22**

Guidelines for Moderate Stroke

Management Priorities

Ascertain clinical diagnosis of TIA (history and physical exam are very important)

- Exclude common stroke mimickers
- Provide basic emergent supportive care (ABCs of resuscitation)
- Monitor neuro vital signs, BP, MAP, RR, temp, pupils, O2 sat
- Perform stroke scales (NIHSS, GCS)
- Provide O2 support to maintain O2 sat >95%
- Monitor and manage BP, treat if MAP >130

Precautions:

- Avoid precipitous drop in BA (not > 15% of baseline MAP). Do not use rapid-acting sublingual agents; when needed use easily titratable IV or short-acting oral antihypertensive medication
- Ensure appropriate hydration. IVF: 0.9% NaCl

Identify comorbidities (cardiac, DM, hepatic, ulcers, etc)

Recognize and treat early signs and symptoms of inc ICP

Guidelines for Moderate Stroke

Early Specific Treatment for CT or MRI-confirmed Ischemic Stroke

Non-cardioembolic	Cardioembolic
If **within 3 hours** of stroke onset, consider IV recombinant tissue plasminogen activator **(rTPA)**. May give within 4.5 hrs in selected patients In specialized centers: intraarterial (IA) thrombolysis within 6 hrs **Aspirin** 160-325 mg/day - 24 hrs after rTPA - if rTPA ineligible Neuroprotection Early rehabilitation once stable Consider early decompressive hemicraniectomy for large malignant MCA infarction	If within 3 hours of stroke onset, consider IV rTPA. In specialized centers: intraarterial (IA) thrombolysis within 6 hrs If ineligible for rTPA: 1. Consider anticoagulation with IV heparin or LMWH for those high risk for early recurrence **OR** Aspirin 160-325 mg/day (if anticoagulants not possible) If infective endocarditis is suspected, give antibiotics and do not anticoagulate! Early rehabilitation

Guidelines for Moderate Stroke

Early Specific Treatment for CT or MRI-confirmed Hemorrhagic Stroke

- Early neurology/neurosurgery consult for all ICH
- Monitor and maintain BP: Target **MAP of 110**
- Neuroprotection
- Early **rehab within 72 hrs** if stable
- Give **anticonvulsants** for clinical seizures and proven subclinical or electrographic seizures. Prophylactic AEDS not recommended
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Delayed Management and Treatment (Secondary Prevention)

- Long-term **strict BP control** and monitoring
- **Consider** contrast CT scan, 4 vessel angiogram, MRA or CTA if the patient is:
  - Less than 45 years old
  - Normotensive
  - Has lobar ICH
  - Uncertain cause of ICH
  - Suspected to have aneurysm, AV malformation or vasculitis

Guidelines for Severe Stroke

Management Priorities

Ascertain clinical diagnosis of TIA (history and physical exam are very important)

- Exclude common stroke mimickers
- Provide basic emergent supportive care (ABCs of resuscitation)
- Monitor neuro vital signs, BP, MAP, RR, temp, pupils, O2 sat
- Perform stroke scales (NIHSS, GCS)
- Provide O2 support to maintain O2 sat >95%
- Monitor and manage BP, treat if MAP >130

Precautions:

- Avoid precipitous drop in BA (not > 15% of baseline MAP). Do not use rapid-acting sublingual agents; when needed use easily titratable IV or short-acting oral antihypertensive medication
- Ensure appropriate hydration. IVF: 0.9% NaCl

Identify comorbidities (cardiac, DM, hepatic, ulcers, etc)

Recognize and treat early signs and symptoms of inc ICP

Guidelines for Severe Stroke

Early Specific Treatment

Non-cardioembolic Infarct	Cardioembolic Infarct	Hemorrhagic
May give aspirin 160-325 mg/day Strokes within 12 hrs of onset: possible thrombolytic therapy Neuroprotection	May give aspirin 160-325 mg/day Strokes within 12 hrs of onset: possible thrombolytic therapy Neuroprotection	Supportive treatment: 1. Mannitol 20% 0.5-1 g/kg BW q 4-6 hrs for 3-7 days 2. Neuroprotection 3. AEDs for clinical seizures only
If cerebellar infarct, consult neurosurgeon ASAP Early supportive rehab	If cerebellar infarct, consult neurosurgeon ASAP Early supportive rehab	Neurosurgery consult if: 1. Patient NOT herniated and family is willing to accept consequences of coma or PVS. Goal is reduction of morbidity 2. ICP monitoring

BP Management in Acute Stroke

CPP = MAP-ICP

$$\textbf{MAP} = \frac{\textbf{SBP} + 2\,\textbf{DBP}}{3}$$

Target MAP 110 – 130

- *Hypotension may result in cerebral hypoperfusion.*
- *Sustained hypertension may alter cerebral autoregulation increase edema and in CVD bleeds, promote progression of bleeding.*

- In acute CVD infarction, allow **permissive hypertension.**
- Antihypertensive agents should be withheld unless:
  - SBP >220, DBP > 120, or MAP > 130
  - Hypertensive encephalopathy
  - Aortic dissection
  - Acute renal failure
  - Acute pulmonary edema
  - Acute myocardial infarction
- In **CVD bleed**, the absence of a ischemic penumbra allows for a **more aggressive BP management**

IV AntiHPN Drugs for Stroke

- **Nicardipine**
  - 1 to 15 mg/hr as 10 mg/10 ml solution
  - Onset: 5-10 mins, Duration of Action: 1-4 hrs
  - Inhibits Ca ion from entering slow channel, producing smooth muscle relaxation and vasodilatation
- **Hydralazine**
  - 10-20 mg IV push q 4-6 hrs as needed, up to 40 mg/dose
  - Onset: 10-20 mins; Duration: 3-8 hrs
  - Direct vasodilatation of arterioles & decreased resistance
- Labetalol
- Esmolol

Neuroprotective Interventions

- **Avoid 5 "H":** hypotension, hypoxemia, hypoglycemia or hyperglycemia, hyperthermia
- Avoid Hypotension and **allow permissive HPN**
  - Aggressive BP lowering is detrimental in acute stroke
- **Avoid hypoxemia**
- **Avoid hypoglycemia or hyperglycemia**
  - Ensure glycemic control at **110-180 mg/dL**
  - May start insulin if CBG > 180
  - Avoid glucose-containing IV fluids. Use **isotonic saline (0.9%)**
- **Avoid hyperthermia**
  - Hyperthermia increases relative risk of **1 yr mortality by 3.4x**
- **Neuroprotectant drugs** (Citicoline, Cerebrolysin)

Management of Subarachnoid Hemorrhage

- Clinical diagnosis:
  - **"worst headache of my life"** in 80% of patients
  - May be associated with **vomiting, stiff neck, loss of consciousness** or focal neurologic deficits, **seizures** in 20%
  - PE: signs of **meningeal irritation**, decreased consciousness, CN III or IV palsy, may or may not have focal deficits

Management of SAH

Neurodiagnostic Examinations

Noncontrast cranial CT scan ASAP

- Hyperdense blood in the basal cisterns are diagnostic
- Suggestive of SAH: parenchymal clot in temporal, basal frontal or ventricles
- Sensitivity depends on timing of imaging

Lumbar Tap with CSF Analysis

- Recommended if CT scan is negative or unavailable
- Considerations: RBC and WBC, xanthochromia, timing of LT in relation to ictus
- Multiple specimens (at least 3 tubes) should be collected to rule out traumatic tap

Cerebral Angiography

- Gold standard in determining cause of SAH
- If negative, repeat angiogram may be performed after 7-14 days

Good quality CT Angiography (CTA) or Magnetic Resonance Angiography (MRA)

- Good options in the ff. situations:
  1. Poor grade patients
  2. When 4VA cannot be done in a timely fashion
  3. When initial angiogram is negative

Management of SAH

General Symptomatic Treatment

- Absolute bed rest in a quiet and comfortable environment
- Monitor neuro-vital signs closely
- NPO if with immediate neurosurgical intervention
- Analgesics for headache. Avoid NSAIDs and aspirin
- Give gastrointestinal prophylaxis for stress gastritis
- Give anti-emetics if with nausea and vomiting
- Maintain euthermia: give antipyretics and cooling blankets
- Maintain euglycemia
- Give sedatives for restlessness or agitation
- Give stool softeners
- Start DVT prophylaxis using pneumatic compression devices or antiembolic stockings. No heparin until aneurysm has been secured

Early Specific Treatment

- Calcium channel blockers
  - **Nimodipine** 60 mg every 4 hrs for 3 weeks
- **Anticonvulsants**
  - prophylactic AEDs in immediate post-bleed period
  - in high risk for sz: prior seizures, parenchymal hematoma, infarct, or MCA aneurysm
- Antifibrinolytic agents are NOT recommended
- Manage increased ICP
  - patient positioning at **30 degrees**
- BP Management
  - **IV nicardipine to target SBP of <150** in pre-op phase
- Maintain **euvolemia**. Avoid large amounts of hypotonic fluids
- Manage hyponatremia
- Steroids have NO role and are NOT recommended

Prevention and Management of Vasospasm

- Monitoring
  - Serial/daily **transcranial Doppler (TCD)**
  - CT and MRI perfusion studies
- **Triple H therapy**
  - Volume expansion, induction of hypertension, hemodilution once aneurysm is secured
- **Magnesium sulfate & statins** (i.e. Atorvastatin/ simvastatin)
- Endovascular angioplasty

- Obliteration of aneurysm ASAP from the circulation is the MAIN GOAL of treatment!

Timing of Surgery

- Definitions:
  - **Early surgery** is surgery IDEALLY performed within **72 hrs** from ictus
  - Late surgery: performed more than 3 days post ictus
- Indications:
  - Early surgery is recommended for good to moderate grade aneurysmal SAH to minimize chances of rebleed
  - For poor grade patients, early surgery for:
    - Hematoma
    - Hydrocephalus
    - **Delay surgery** if with **ischemia/infarction** or **severe angiographic vasospasm**
  - Advanced age is NOT a contraindication for early surgery in the absence of organ failure

Coiling

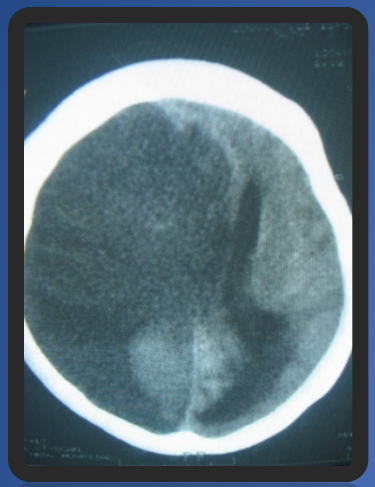
- Can be performed early in both good and poor grade patients
- Reduces rate of rebleed for poor grade SAH
- **Vasospasm is NOT a contraindication** and can be dealt with endovascular coiling
- Under local anesthesia

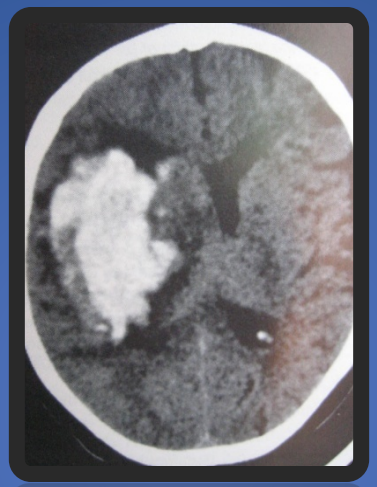
Increased Intracranial Pressure

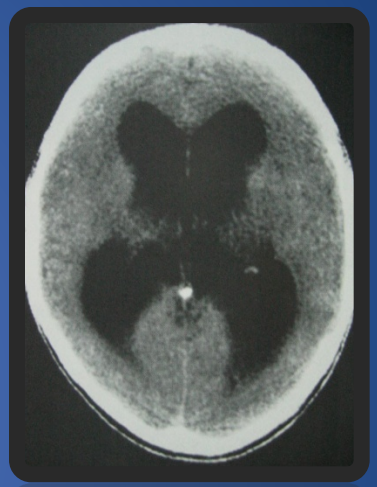
Sources:
1 Guidelines for Management of Stroke by the Stroke Society of the Philippines
2 Neurocritical Care by Zeng, et al. 2010

Causes of Increased ICP

- Large infarcts
- Intracranial hemorrhage

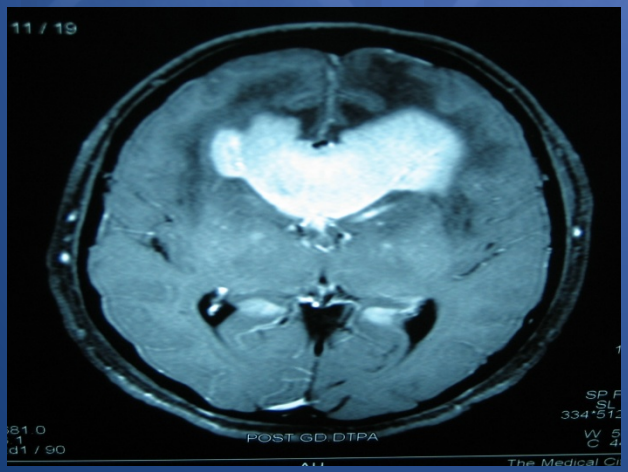


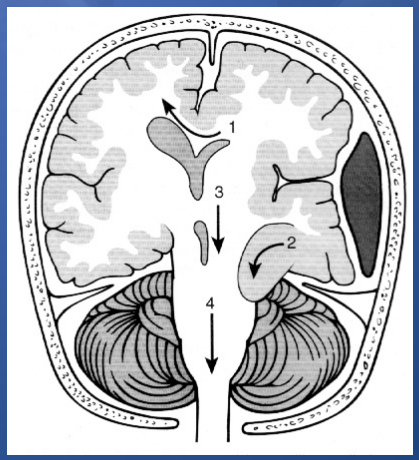




- Hydrocephalus

- Brain Tumors





- Subdural/ Epidural Hematoma

Symptoms of Increased ICP

Headache

Diplopia

Agitation

Nausea and vomiting

Decreased sensorium

Clinical Features of Increased ICP

- History
  - Rapid onset: hemorrhage, acute hydrocephalus, trauma
  - Gradual onset: tumor, long-standing hydrocephalus, abscess
  - Previous history of cancer, weight loss, smoking, drug use, coagulopathy, trauma, ischemic disease may point its etiology
- Physical Examination
  - Breathing patterns can help localize the level of injury
  - Vital Signs: Cushing's triad (hypertension, bradycardia, respiratory irregularity/ bradypnea) implies elevated ICP

Breathing Pattern

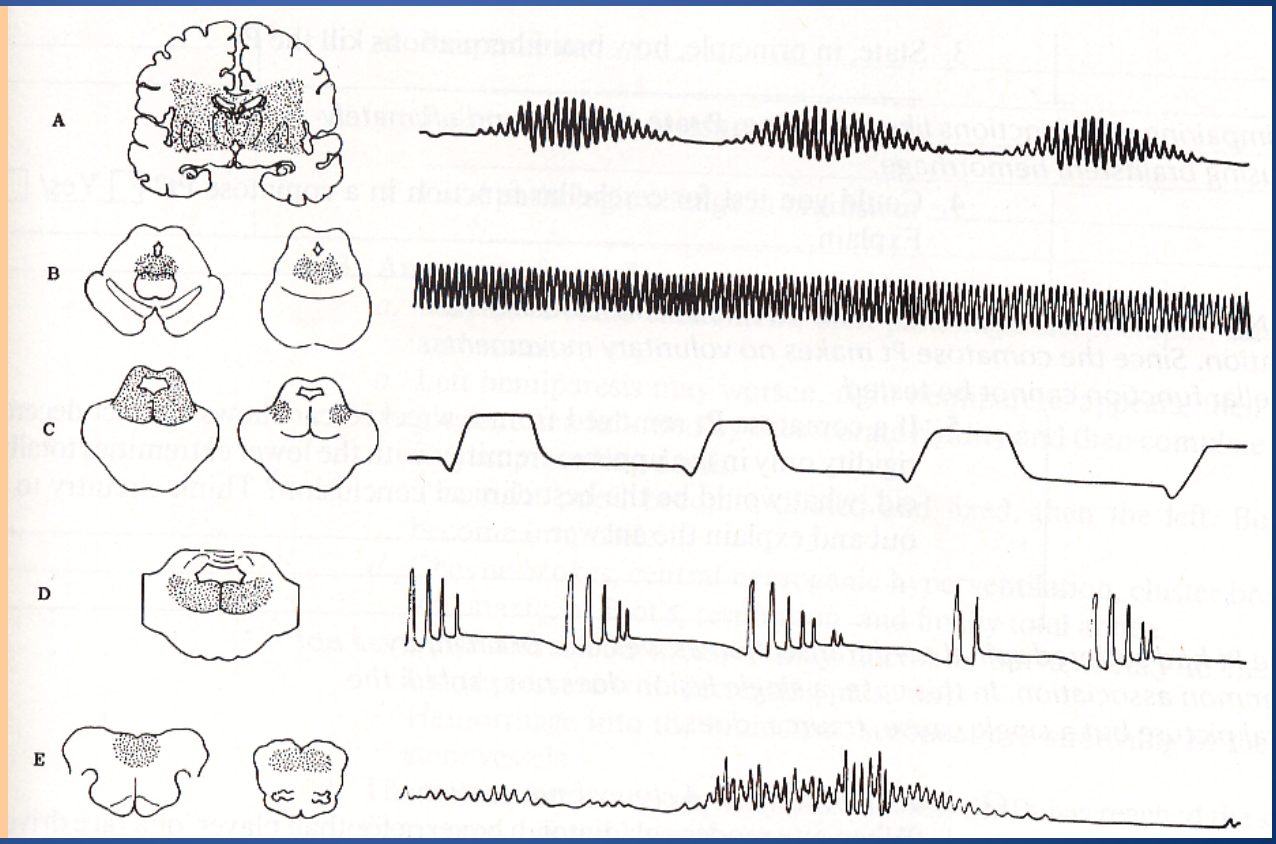
Cheyne Stokes

Central Neurogenic hyperventilation

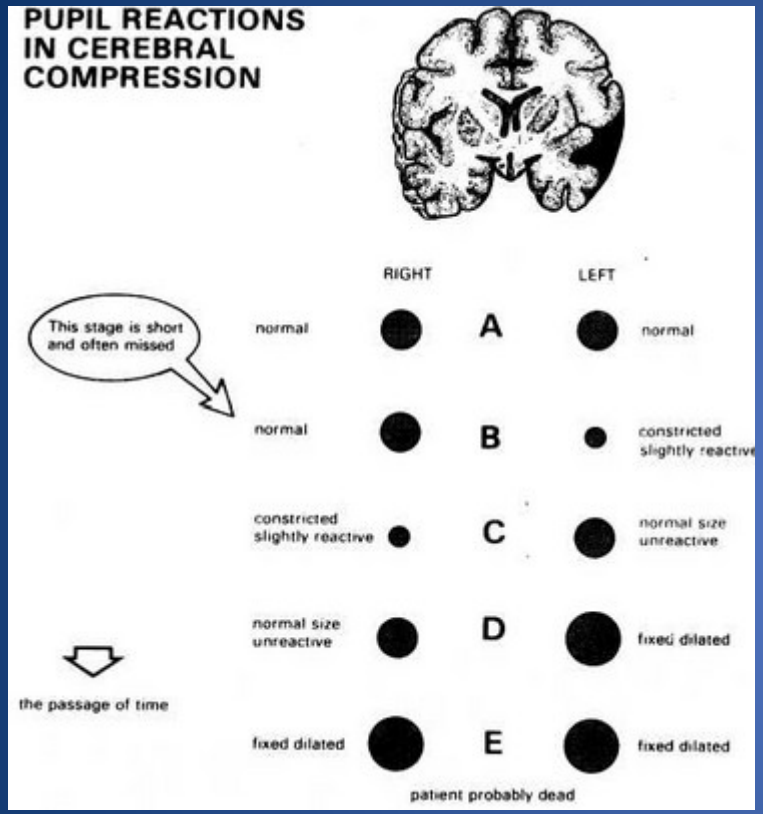
Apneustic breathing

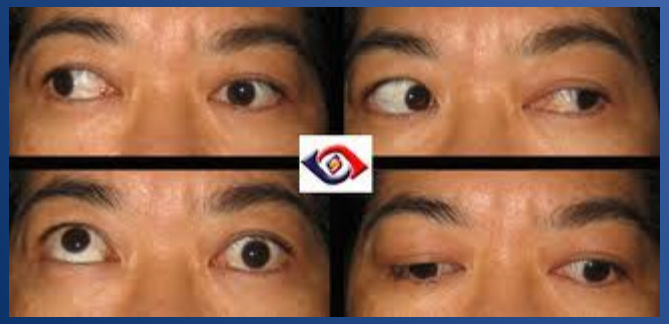
Cluster breathing

Ataxic breathing

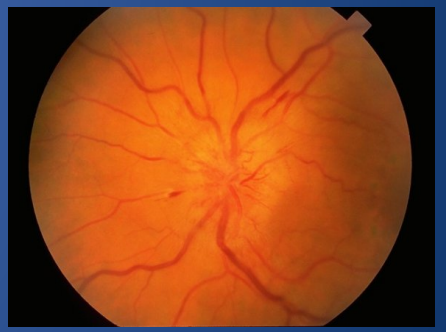


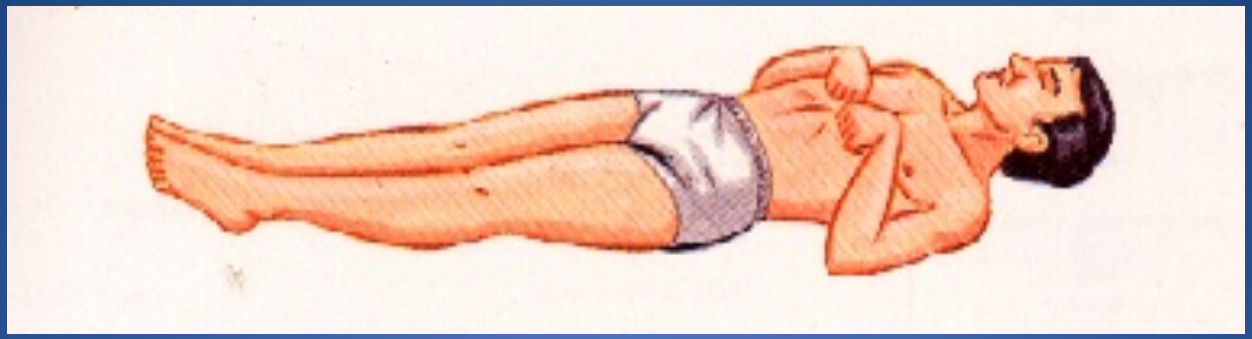
Neurologic Examination





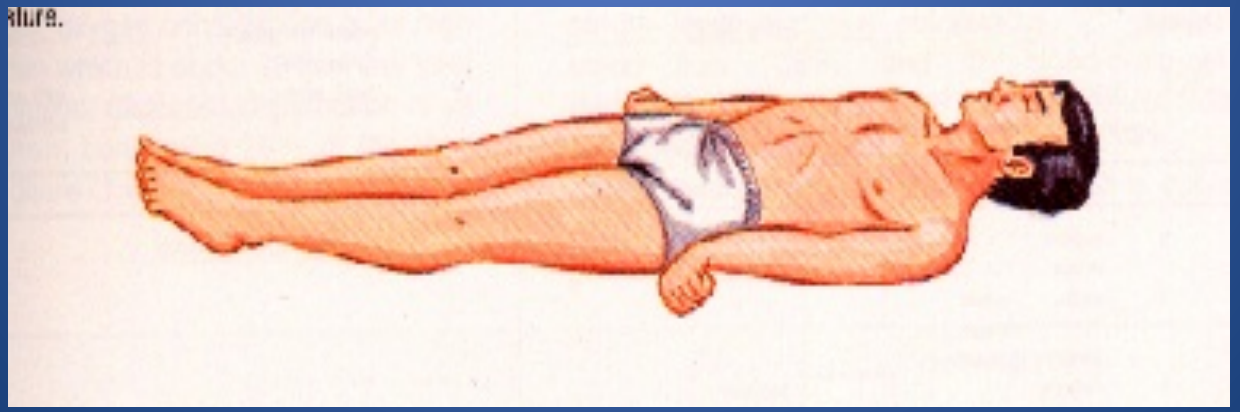
- A full neurologic examination must be done
- Mental status changes range from **inattention to coma**
- Cranial nerve examination
  - Pupillary findings may be localizing
  - CN III palsy
  - CN VI palsy
  - Papilledema
- Motor examination



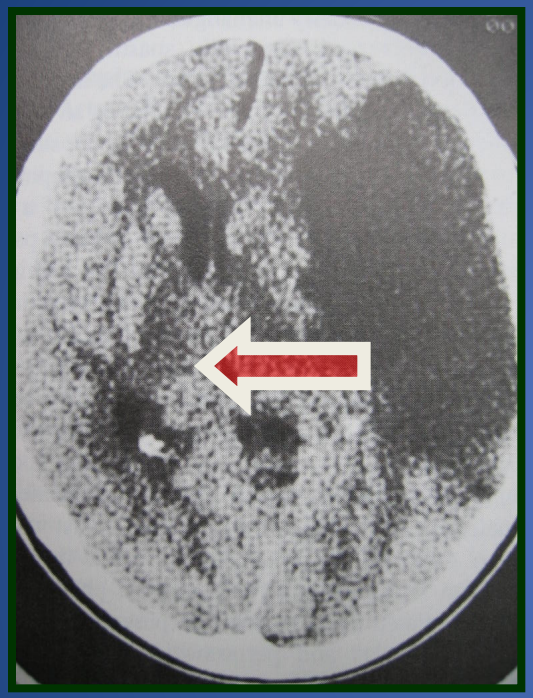


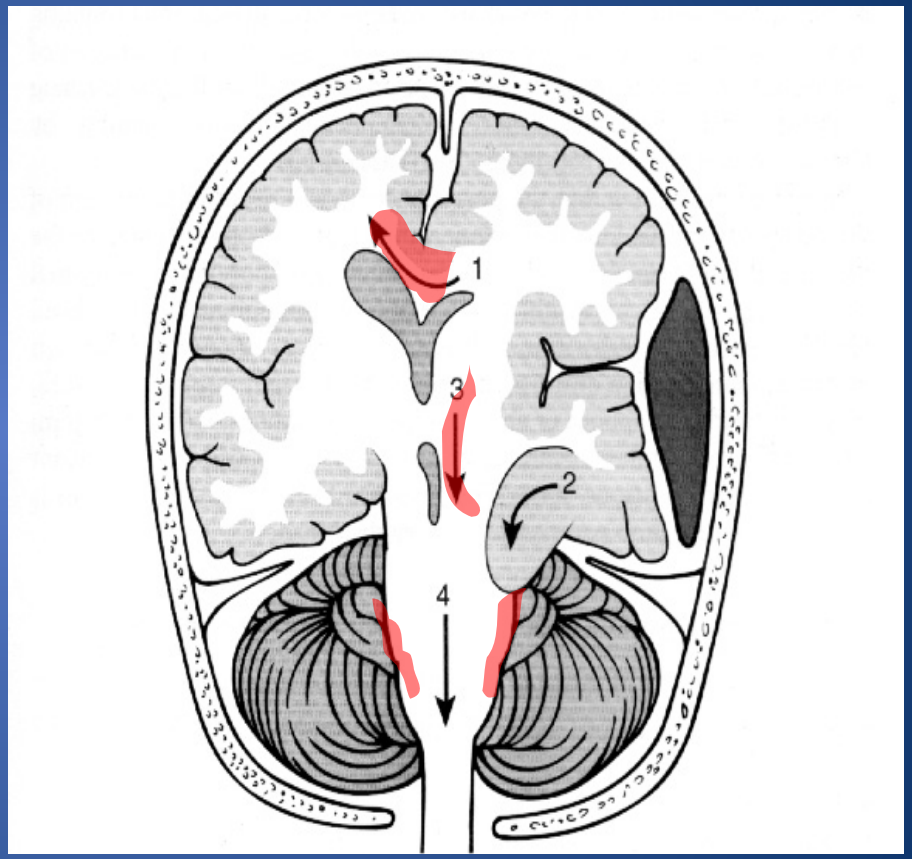
DECORTICATE POSTURING

DECEREBRATE POSTURING



Brain Herniation





- Dreaded complication of ↑ICP
- Shifting of brain tissue from one compartment where the pressure is high to another where it is low.

Herniation and ICP

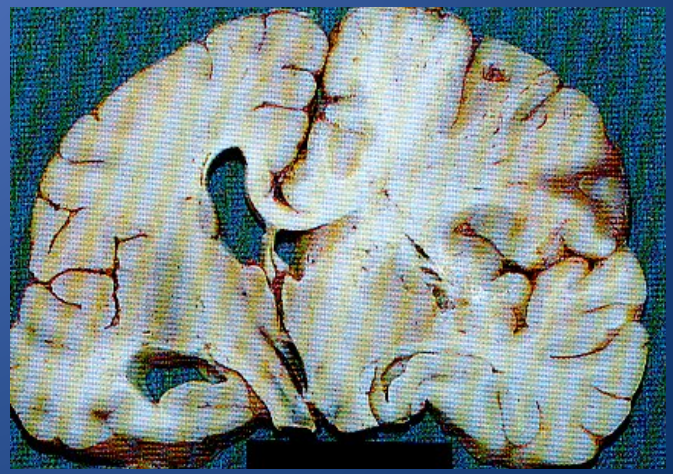
Neurological features associated with progressive elevation of intracranial pressure

Reduction in level of consciousness

Dilation of pupil ipsilateral to mass lesion

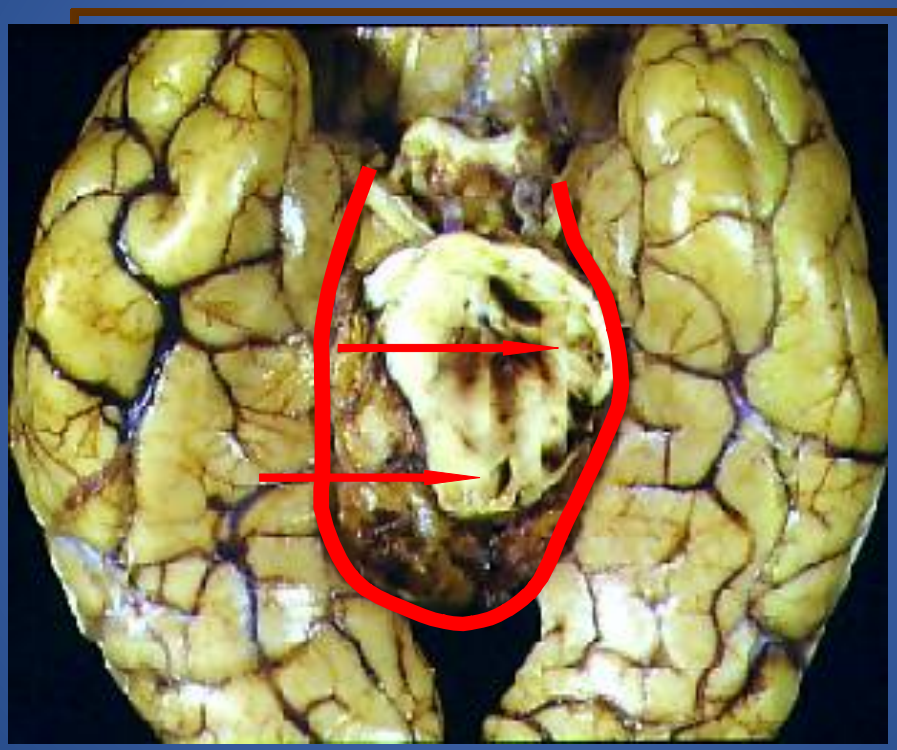
Bradycardia, increase in pulse pressure and increased mean arterial pressure (Cushing's Triad)

Cheyne - Stokes respiration



Kernohan Phenomenon

Ipsilateral
Dilated pupils



Initial contralateral
Motor weakness

Subsequent
ipsilateral motor
weakness

Brain Herniation leads to worsening of deficits

- Compression of blood vessels → Infarction
- Compression of the diencephalon and brainstem → Deterioration in sensorium, compression on the medullary centers of respiration

Glasgow Coma Scale (GCS)

Eye Opening

Spontaneous	4
To verbal command	3
To pain	2
None	1

Best Verbal Response

Oriented Speech	5
Confused conversation	4
Inappropriate speech	3
Incomprehensible sounds	2
No speech	1

Best Motor Response

Obeys commands	6
Localizes pain	5
Withdrawal	4
Abnormal Flexion	3
Abnormal Extension	2
None	1

TOTAL **15**

Highest score 15
Lowest score 3
Poor prognosis <8

Emergency Measures for ICP Reduction in an Unmonitored Comatose Patient with Clinical signs of Herniation

- ABCs of resuscitation
- Neuroprotection (5H)
- Elevate head of bed 15 – 30°
  - – Displaces CSF & enhances CSF reabsorption & cerebral venous outflow
- Hyperventilate (target PCO_2 26 – 30 mm Hg)
  - → Cerebral vasoconstriction
- Normal saline (avoid hypotonic fluids)
- Mannitol and other Hyperosmolar Agents
- Neurosurgical consult

Head Positioning

- Optimal ICP reduction occurs with head elevation of 15 – 30 degrees.
- This displaces CSF & enhances CSF reabsorption & cerebral venous outflow:
- Midline head positioning is recommended.

Hyperventilation

- Use only during impending herniation by adjusting tidal volume to achieve PCO2 levels of 30-35 mm Hg
- Short term only as its effect on cerebral blood flow and ICP is short lived (≈ 6 hrs)

PCO_2

↓

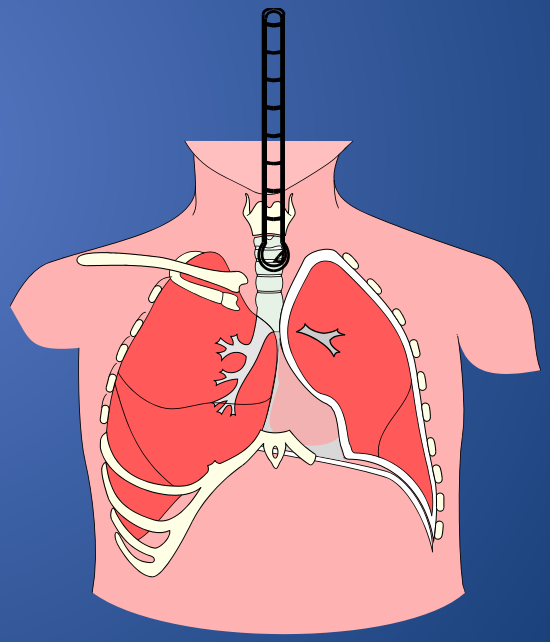
Vasoconstriction

↓

CBF/CBV

↓

ICP

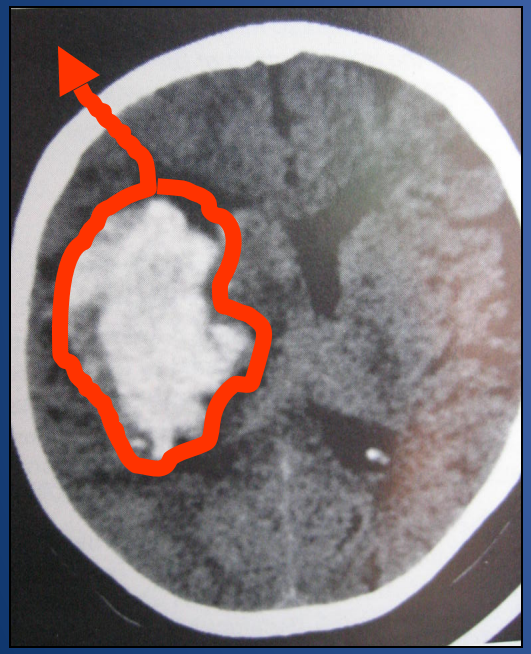


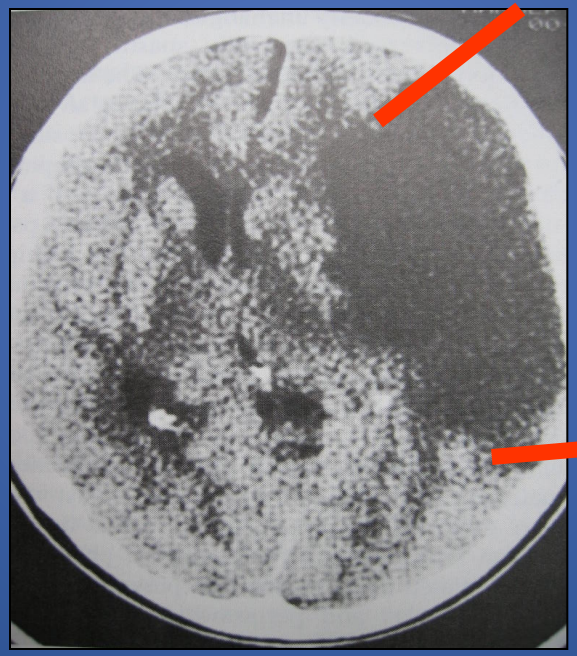
PCO_2: 30-35 mm Hg

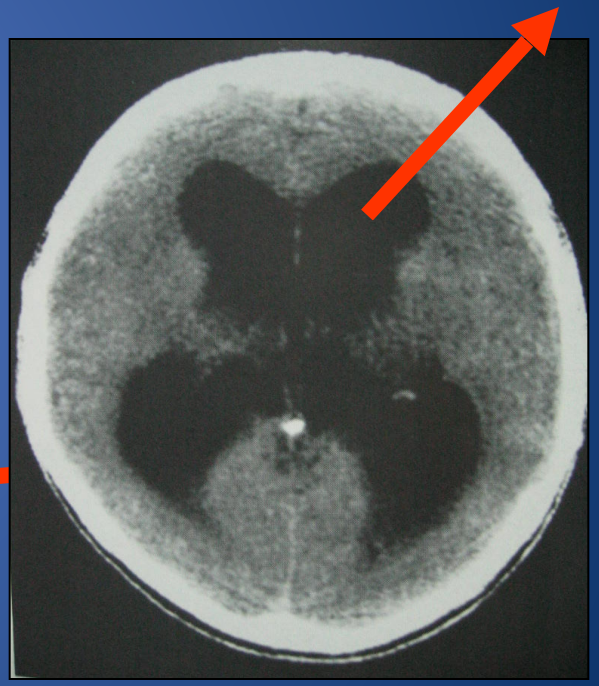
Hyperosmolar Agents

- Mannitol 20%
  - 0.5-1.5 g/kg every 3-6 hrs. Doses up to 1.5 g/kg are appropriate when deterioration is due to mass effect
- Hypertonic saline
  - Ideally via a central line, with maintenance dose of 3% saline 1 mg/kg/hr
  - Titrated to a serum sodium of 145-155, checked every 6 hrs
  - Advantages: reduce ICP faster and for a longer period of time than mannitol. Also used for mannitol-refractory cases
- Always maintain serum osmolality at 300-320 mOsmol/kg
  - Serum osmolality = 2 (Na) + glucose/18 + BUN/2.8

Surgical Management

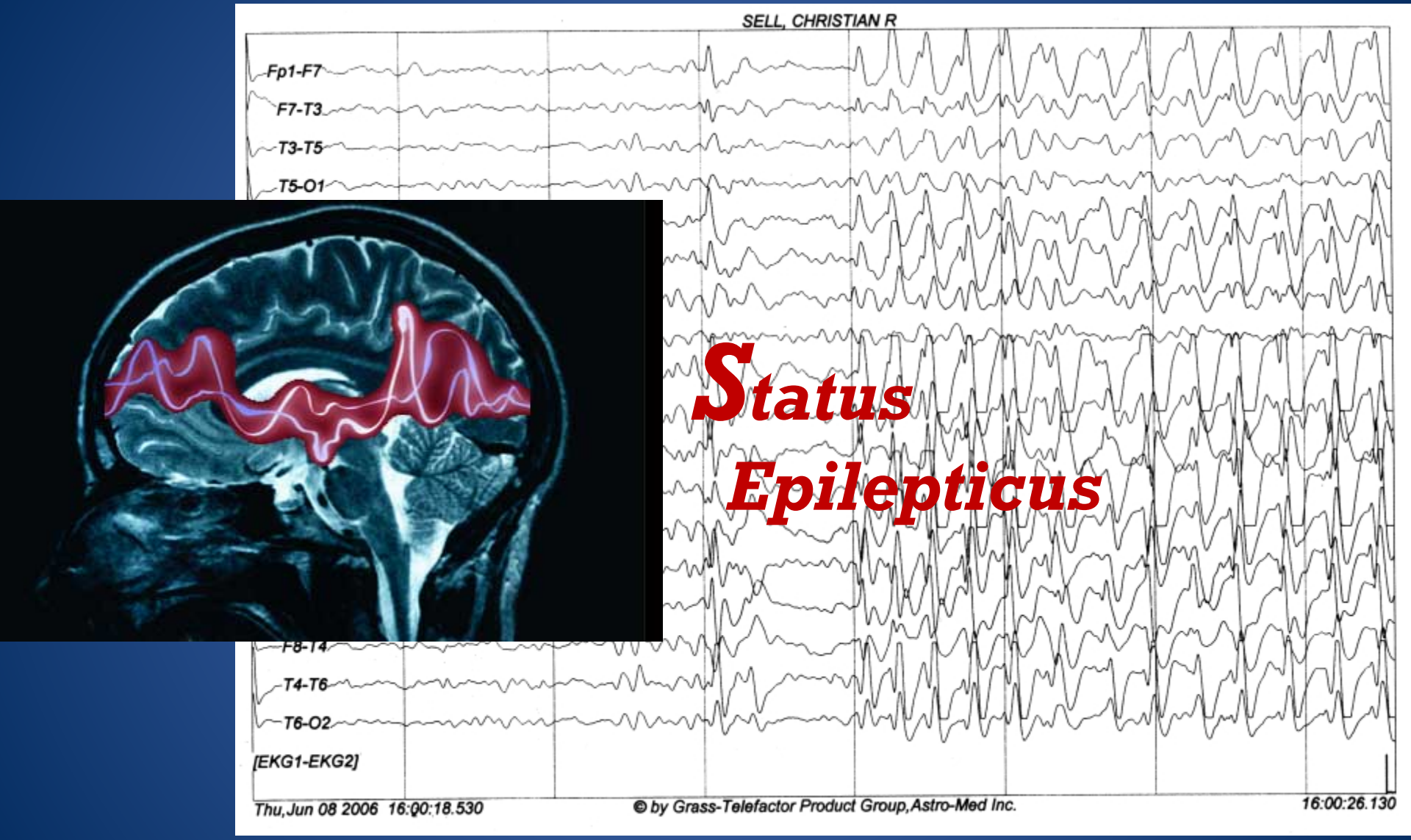




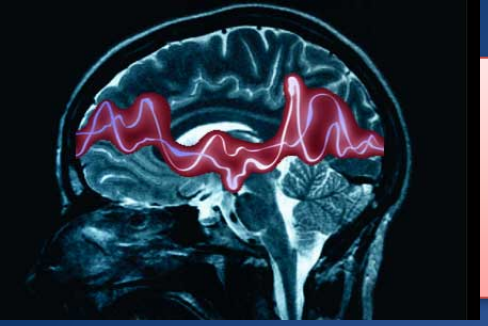


General Measures

- Control agitation and pain
- Treat fever aggressively
- Control seizures if present
  - Phenytoin LD 18-20 mg/kg IV then maintained at 3-5 mg/kg
  - Levetiracetam 500 mg IV q 12 hrs
  - Status epilepticus should be managed accordingly
- Strict glucose control between 110-180 mg/dL
- Normal fluid and electrolyte balance
  - Avoid excessive free water or hypotonic fluids (ie. D5W)
- Stool softeners to prevent straining

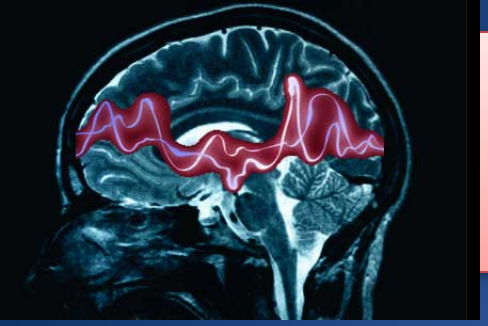


Source: PNA Epilepsy Council Guidelines for the Management of Status Epilepticus. 2009



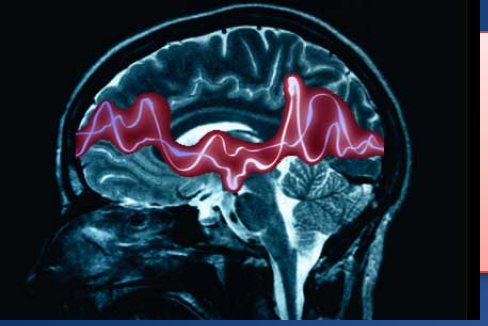
Status Epilepticus

- **Status epilepticus** (SE) especially if generalized tonic-clonic SE (GTCSE) is **a medical emergency** associated with significant **mortality** and **morbidity**.
- **Mortality rate: 10%!**
  - related with the underlying cause of the prolonged seizures.
  - The Richmond Study: overall mortality rate of **6% in children** (Morton et al)...



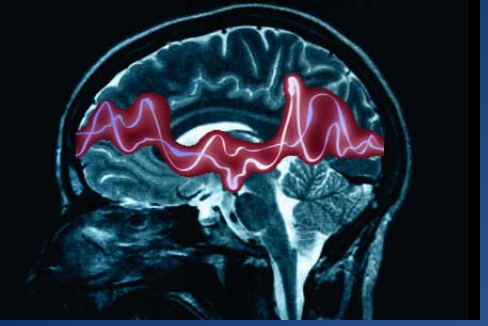
Status Epilepticus

- **Mortality rate: 10% !**
  - The overall mortality rate is **17.8% in the first year** of life
  - Lowenstein et al ,1998: frequency of SE is between **102,000-152,000 per year** and about **55,000 deaths were associated with SE**.
  - Hauser has recently estimated that 60,000 cases occur each year in the US



Status Epilepticus

- Barnard and Wirrell: 34% of 40 children with SE lasting from 30-720 mins had subsequent developmental deterioration
- The **outcome** depends largely on the **etiology**, but prompt and appropriate management both therapeutic and supportive can reduce significant morbidity and mortality

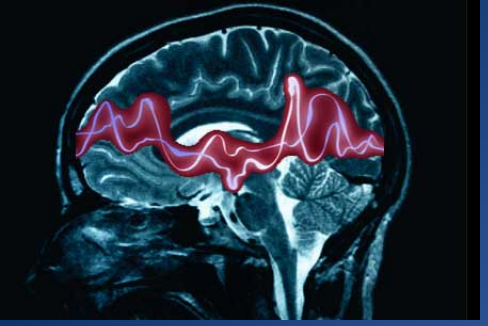


Definitions

- **Although the popular definition of status epilepticus is recurrent or continuous seizures lasting at least 30 minutes, the group recommends initiating treatment with the status epilepticus protocol when seizures persist for more than 5 minutes.**
- This operational definition is based on studies of seizure durations by Gastaut and Broughton, (Level IIC) and Theodore et al, (Level III), Lowenstein, Bleck and Macdonald, 1999 (Level III).

Definitions

- **Status epilepticus** may be classified as follows (Riviello AAN 2003):
- **Generalized SE**
  - Convulsive (tonic-clonic, myoclonic)
  - Nonconvulsive (Absence)
- **Partial SE**
  - Simple (no alteration of consiousness)
    - Somatomotor (epilepsia partialis continua)
  - Complex (alteration of awareness)



Generalized Convulsive SE

- Treiman defines **generalized convulsive SE** as…
  "***paroxysmal or continuous*** *tonic and/or clonic* ***motor*** *activity which may be symmetrical or asymmetrical and overt or subtle, associated with marked impairment of consciousness and with bilateral, although frequently asymmetrical****, ictal discharges on the EEG***"
- **A medical emergency!!!**
  - Adverse consequences can include hypoxia, hypotension, acidosis and hyperthermia
- **Goal: stop seizures as soon as possible**

Causes of Seizures

Vascular (SAH, venous sinus thrombosis, hypertensive enceph)

Infectious

Traumatic

Autoimmune (SLE)

Metabolic/Toxic (hypo-/hypernatremia, hypo-/hyperglycemia, alcohol intoxication/withdrawal, INH)

Idiopathic

Neoplastic

Structural/congenital

Pathophysiology

- Early compensation meets increased CNS metabolic needs (SBP, CBF ↑↑)
- Failure at 40-60 minutes, (SBP, CBF ↓↓)
- CNS tissue necrosis, adverse sequelae
- Glutamate toxic mediator
- CNS necrosis even if systemic complications fully mitigated
- HPN, fever, rhabdomyolysis, hypercarbia, hypoxia, infection

Pharmacologic Recommendations for the Treatment of SE

- **First Line Drugs**
  - Drugs used to stop GSCE as fast as possible
  - First line drug is a benzodiazepine
  - **Diazepam 5-10 mg IV bolus** at a rate of 2-5mg/min until seizure stops or a total of 20mg has been given (Grade A)
    - *Level I: Alldredge 2001; Leppik 1983; Prasad 2007*
  - **Lorazepam 4mg IV bolus** at a rate of 1 mg/min until seizures stops or a total of 8 mg has been given (Grade A)

Pharmacologic Recommendations for the Treatment of SE

- **Second line drugs**
  - Drugs to use if the first line drugs fail to control the SE and as maintenance to prevent recurrence
  - If the initial second line drug fails, try another second line drug

1. **PHENOBARBITAL – 15-20 mg/kg IV** loading dose at a rate of <100 mg per minute (Grade A)[1]
2. **PHENYTOIN – 18-20 mg/kg IV** loading dose at a rate not exceeding 50 mg/min (Grade A)[2]

Pharmacologic Recommendations for the Treatment of SE

- **Second line drugs**
  3. **VALPROIC ACID – 20-30 mg/kg IV** loading dose bolus over 15 minutes or at a rate of 40 mg/min (Grade A)
  4. **LEVETIRACETAM – 20 mg/kg IV** loading dose then 15 mg/kg every 12 hrs starting 6 hours after loading dose (Grade B)

Pharmacologic Recommendations for the Treatment of SE

- **Drugs for Refractory SE**
  - Evidence-based data from controlled double blind trials are lacking

  1. **MIDAZOLAM** (Grade B Recommendation)

     Bolus: 0.2 mg/kg IV

     Infusion: start at 1 ug/kg/min. May increase by 1 ug/kg/min every 15 minutes until seizures are controlled. Mean infusion rate: 8 ug/kg/min (range 3-21 ug/kg/min)

Pharmacologic Recommendations for the Treatment of SE

- **Drugs for Refractory SE**

  2. PHENOBARBITAL (Grade B Recommendation)

  Daily dose: 40-140 mg/kg/day

  (level 35-218 ug/ml)

  3. **PROPOFOL** (Grade B Recommendation)

  Initial bolus: 1-2 mg/kg to terminate seizure

  Infusion: 2-15 mg/kg/hr, titrate by

  1 mg/kg/hr

Pharmacologic Recommendations for the Treatment of SE

- **Drugs for Refractory SE**

  4. THIOPENTAL (Grade B Recommendation)

  Bolus: 5 mg/kg

  Infusion: 0.5-6 mg/kg/hr (adjusted based on observation of clinical seizure activity)

Non Pharmacologic Recommendation

1. ABCs (airway, breathing, circulation).
   Monitoring of BP, temp, HR and rhythm, RR
2. Hook to cardiac monitor – 58% with SE had potentially fatal arrythmias
3. When to consider intubation?

   - at any point during SE when respiratory compromise develops

   - treatment with AEDs that cause respiratory depression (e.g. phenobarbital, midazolam)

Non Pharmacologic Recommendation

4. When to admit to Neuro ICU?

- when seizures persist after loading the initial 2nd line drug
- when patient is intubated
- unstable vital signs

5. What should be done after SE has resolved?

- close monitoring
- maintenance of antiepileptic drugs
- underlying cause of SE should be searched and adequately treated

Recommended diagnostic procedures

- Should be based on:

  1. different identified etiologies of status epilepticus from various epidemiologic studies

  2. effects and pathophysiology of generalized convulsive SE

  3. review of articles on management of SE

  4. AAN and CNS Practice Parameter

Recommended Diagnostic Procedures

- Blood Tests
  - Glucose, creatinine, BUN, electrolytes, CKs
  - Liver function tests, CBC, ABG, blood culture
  - AED levels
- Blood and Urine Toxicologic and Metabolic Screens
- Chest X ray, urinalysis
- Electroencephalogram
- Other tests: CT scan/ MRI, lumber puncture

Protocol Summary

0-5 minutes 	**Determination of generalized convulsive status** **Short History** **ABCs** **Insert IV line** **Extract blood for chemistries (i.e. glucose, electrolytes)** **Save blood for other tests** **Diazepam 5-10 mg IV at a rate of 2-5 mg/min until seizure stops or a total of 20 mg**
5-30 minutes 	If seizures persist **Phenobarbital 15-20 mg/kg IV LD** at <100mg/min (intubate patient before giving LD) OR **Phenytoin 18-20 mg/kg IV LD** at rate ≤ 50 mg/min (hook to cardiac monitor) OR **Valproic Acid 20-30 mg/kg IV LD** over 15 mins

30-40 minutes	**Additional 5-10 mg/kg IV of the 2nd line AED started, with the same infusion rate**
40-60 minutes	Use one of the **2nd line AED that was not selected initially** **INTUBATE** PATIENT CONTINUOUS **EEG MONITORING** IF AVAILABLE
>60 MINUTES **Refer to Anesthesiology**	May use any of the following **anesthetic agents**: **1.) Midazolam** 0.2 mg/kg IV bolus followed by infusion at a rate of 1 ug/kg/min. May increase by 1 ug/kg/min q 15 minutes until seizures are controlled. Mean infusion rate: 8 ug/kg/min (Range 3-21 ug/kg/min) Preparation: dilute 3 mg/kg in 50 ml D5W wherein 1 ug/kg/min is equivalent to 1 ugtt/min **2.) Propofol** 1-2 mg/kg IV bolus to terminate seizure Infusion 2-15 mg/kg/hr titrated by 1 mg/kg/hr. used for max of 48 hrs **3.) Thiopental** 5 mg/kg IV bolus Infusion 0.5-6 mg/kg/hr

CNS Infections

Cardinal Manifestations of CNS Infections

- **Fever**
- Headache
- Alteration of Sensorium
- ± Seizures
- Meningismus
- ± Other focal neurologic signs

Main CNS Infection Syndromes

Acute Meningitis (Days)	Bacterial meningitis Viral meningitis
Subacute to Chronic meningitis (Days to Weeks)	Tuberculous meningitis Cryptococcal meningitis Partially treated bacterial meningitis
Space-Occupying Lesions	Brain/Spinal Abscess Subdural empyema Cysticercosis
Chronic CNS Infection (Months to Years)	Neurosyphilis Prion diseases

Diagnostics in CNS Infection

- CSF analysis
  - Lumbar puncture
  - Cisternal puncture
  - Ventricular tap
  - Q/Q, GS/CS,AFB, CALAS
- Neuroimaging
  - CT scan
  - MRI

CSF Profiles

	WBCs/ mm^3	Cell Type	Protein (mg/dl)	Glucose (mg/dl)	Opening Pressure (cm H_2O)
Normal	≤5	Lymphos and monos only	15 – 45	45 – 80	8 – 18
Bacterial meningitis	5 – 10,000	PMNs	↑	↓	↑
Viral meningitis	5 – 1,000	Lymphos	↑	N	N, occ'l ↑
Tuberculous meningitis	5 – 500	Lymphos	↑	↓	↑
Cryptococcal meningitis	5 – 100	Lymphos	↑	N, occ'l ↓	↑

Treatment

- Bacterial Meningitis
  - Antibiotics
- TB Meningitis
  - Anti-Koch's
  - VPS for hydrocephalus
  - Steroids for arteritis

Empiric Antibiotic Treatment for Bacterial Meningitis

Risk Group	Etiologies	Antibiotic Coverage
Neonates (< 1 mo)	Group B or Group D streptococci Gram-negative rods (*E. coli*) *Listeria monocytogenes*	Ampicillin 50 mg/kg IV q 6-8 Cefotaxime 50 mg/kg IV q 8
Children (3 mos - 7 y.o.)	*Haemophilus influenzae* *Streptococcus pneumoniae* *Neiserria meningitidis*	Ceftriaxone 50 mg/kg IV q 12 h
Young adults (7 - 50 y.o.)	*S. pneumoniae* *N. meningitidis*	Vancomycin 1 g IV q 12 h Ceftriaxone 2 g IV q 12 h
Adults > 50 y.o. alcoholics, Pts with debilitating medical condition	*S. pneumoniae* *L. monocytogenes* Gram-negative rods	Ampicillin 2 gm IV q 4 h Ceftriaxone 2 g IV q 12 h
Patients w postneurosurgical procedure or head trauma	*S. aureus* *S. pneumoniae* Gram-negative rods	Vancomycin 1 gm IV q 12 Ceftazidime 2 gm IV q 8 h

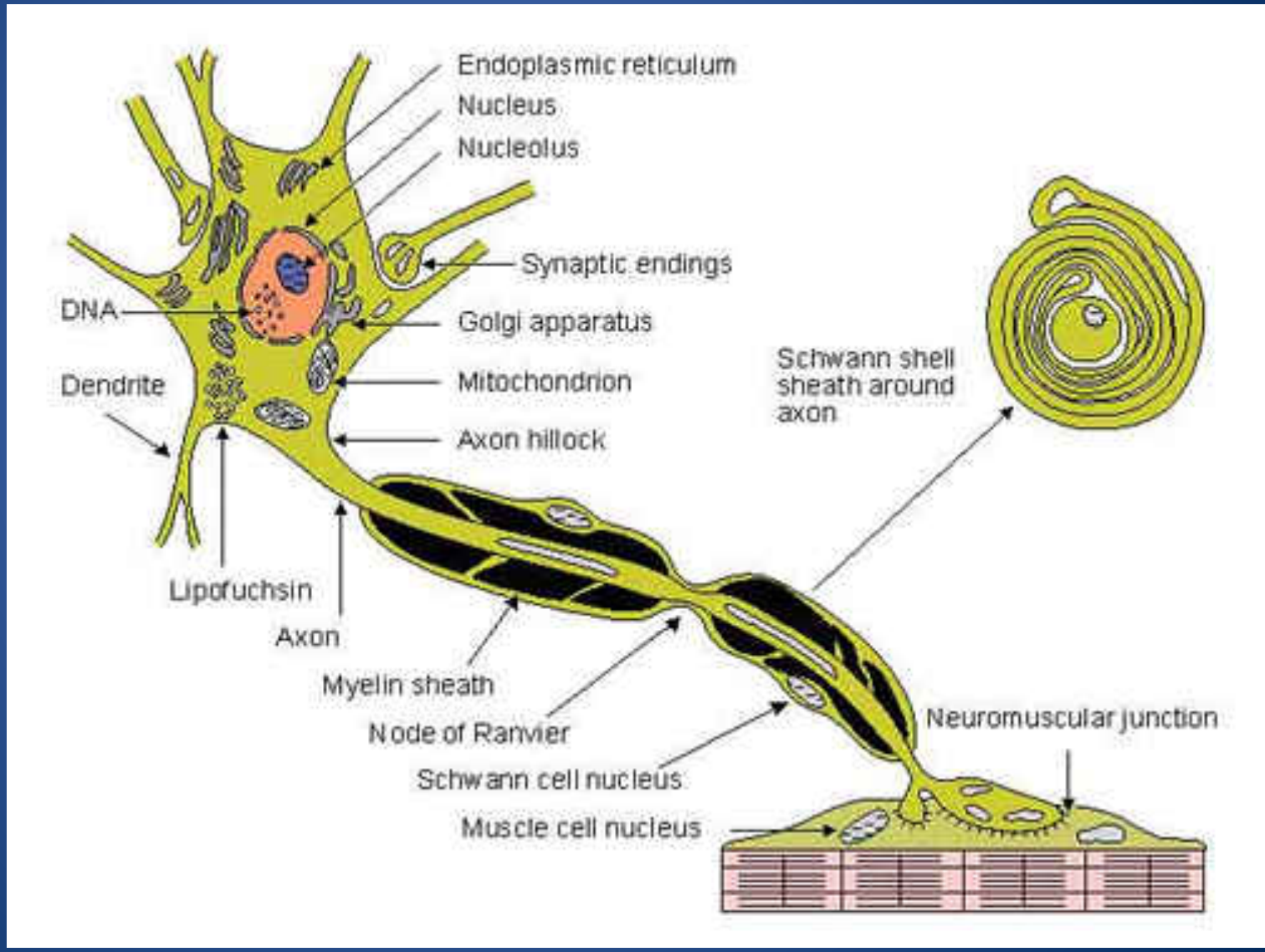
Acute Weakness Resulting from Lower Motor Neuron Lesions

Causes of Acute Weakness in Previously Healthy Patients

- Anterior Horn Cell
  - Poliomyelitis
- Nerve
  - Acute Inflammatory Demyelinating Polyneuropathy (GBS)
  - Diphtheria
  - Tick paralysis
  - Heavy metal intoxication
- Neuromuscular
  - Myasthenia gravis
  - Lambert Eaton syndrome
  - Botulism
  - Organophosphate poisoning
- Muscle
  - Polymyositis
  - Periodic paralysis (hypokalemia, thyrotoxic)
  - Toxic myopathy
  - Rhabdomyolysis
  - Malignant hyperthermia

Guillain-Barre Syndrome

Peripheral Nerves



Acute Inflammatory Demyelinating Polyneuropathy (AIDP,GBS)

- History
  - Antecedent infection or immunization
  - Progressive relatively symmetrical weakness
  - Bulbar weakness and ataxia or respiratory muscle dysfunction may predominate
- Examination
  - Hypo-/areflexia
  - Motor weakness
  - Facial diplegia
  - Minimal objective sensory deficits
  - Normal mentation

- Laboratory
  - Lumbar tap and CSF analysis with elevated protein and less than 10 WBC (albumino-cytologic dissociation)
  - Electromyography with prolonged F waves, decreased nerve conduction velocity or conduction block

Acute Inflammatory Demyelinating Polyneuropathy

- Management
  - Consider plasmapheresis or IVIG
  - Evaluate respiratory function, ventilate if necessary
  - Monitor cardiac rhythm and hypotension

Acute Weakness Resulting from Neuromuscular Junction Disorder (Myasthenia Gravis)

Clinical Manifestations

- Fluctuating weakness and muscular fatigue, affecting ocular, bulbar, and peripheral (skeletal) muscles
  - 50-60% will present with diplopia and ptosis as early primary features
  - Isolated extraocular and palpebral muscle weakness may be the only initial manifestation in some patients (Ocular Myasthenia Gravis).
  - 85% to 90% of patients presenting with ocular symptoms will eventually develop more generalized weakness

- With generalized disease, extremity weakness, usually involving the proximal upper and lower extremities and the extensor muscles, is common and typically worsens with exertion
- Most serious complication is respiratory muscle weakness, which may progress to hypoventilation and respiratory failure

Classification

I : Ocular myasthenia (14% stay at this stage)

IIA: Mild generalized myasthenia with ocular signs

IIB: Moderately severe generalized myasthenia with mild bulbar and ocular involvement

III: Acute severe, with bulbar and respiratory complications (Myasthenic Crisis)

IV: Late severe, developing from other groups within 2 years

Diagnostic Methods

- Tensilon (Edrophonium) test:
  - Sensitivity is 90%, seen also in other neuromuscular diseases
  - WOF hypotension, syncope, respiratory failure
- AChR antibodies
  - Sensitivity 90%, specificity 100%
- Electrodiagnostic
  - RNS Sensitivity 50%
  - SFEMG Sensitivity 90% (also in other diseases)

Treatment of MG

- Acetylcholinesterase inhibitors
  - Reversible binding to AchE, accumulation of Ach at post-synaptic membrane
  - Pyridostigmine (Mestinon): Onset 15-30m, Peak effect 1-2h; Wearing off 3-4 H
  - WOF: Cholinergic crisis
- IVIG
- Plasmapharesis

Steroids in MG

- Sustained improvement appears in most patients within 2 weeks, with improvement in 90% of patients within 3 weeks
- Mild exacerbation within 1 to 17 days after starting glucocorticoids (most commonly starting on day 5), but lasts only 4 days on average
- Induces effective remission in up to 80% of patients

Thymectomy in MG

- Has been incompletely studied and most patients in trials were also treated with additional immunosuppressive therapies
- Lasting improvement following thymectomy is delayed for 6 to 12 months and may not appear for several years
- Up to 60% to 70% of patients with onset before 40 years of age and no thymoma may improve after surgery