# Practical Neurocritical Care

*Lori Shutter, MD*
*shutterla@upmc.edu*
*Director, Neurocritical Care Fellowship Program*
*Visiting Professor, Critical Care Medicine, Neurology & Neurosurgery*
*University of Pittsburgh Medical Center*

# Topics

- Acute unresponsiveness
- Increased ICP / Cerebral Edema
  - Herniation
  - Brain Death
- Status Epilepticus
- Neuromuscular (respiratory) Crisis
- Pearls
  - Stroke: Ischemic / Hemorrhagic
  - Critical Illness Myopathy / Neuropathy

# Altered Mental Status

# AMS: Coma

- Absence of awareness of self and environment
- State of unresponsiveness with eyes closed
  - Depressed brainstem reflexes
  - No responses of limbs, except for reflex movements
  - No response to painful stimuli, except for reflex movements
  - Irregular breathing

- Multiple potential causes
- Usually transient state

# AMS: Other Terms

- Encephalopathy
  - Any disorder of the brain
- Confusion
  - Alert but confused, disoriented
- Delirium
  - Hyperactive OR hypoactive; irritable, agitated
- Drowsy
  - Easily aroused, alert for short periods
- Lethargy
  - Slow responses
- Abulia
  - Lack of will / initiation; extreme form - akinetic mutism
- Locked-in Syndrome
  - Top of the basilar; preserved eye movements and cognition

# General Causes

- Damage to both hemispheres
- Suppression of function
  - Extrinsic – drugs, toxins, hypoxia
  - Intrinsic – metabolic abnormalities
- Brainstem lesion
  - Midbrain: RAS vs ascending arousal

# Causes of Altered Mental State

- Traumatic brain injuries
- Hypoxia / Anoxia *
- Stroke
  - Brainstem
  - Hemorrhagic (SAH)
  - Mass effect
- Tumors
  - Cerebral edema
- Electrolyte Abnormalities
  - Hepatic
  - Renal
  - Glucose
  - Sodium
- Infections
  - Meningitis / encephalitis
  - Ventriculitis
  - Sepsis
- Seizures
  - Non-convulsive
- Endocrine
  - Thyroid
- Toxins
  - Drugs / alcohol
- Medications
- Hypothermia
- Psychogenic

# Causes of altered mental state

- Toxic reactions
  - Carbon monoxide poisoning
  - Alcohol poisoning
  - Acetaminophen overdose
  - Ethylene glycol poisoning
- Medication side effects
  - Reye's syndrome
  - Neuroleptic malignant syndrome
  - Central anticholinergic syndrome
  - Serotonin syndrome
  - Isoniazid intoxication
  - Baclofen Withdrawal

# Assessment

- ABCs
  - Protect the airway
  - Assess need for resuscitation
- Physical exam
  - Look for signs that would explain AMS
- Neurological Exam
  - GCS
  - NIHSS
- Etiology

# General Caveats

- Supratentorial
  - Initially with focal signs & a rostral to caudal progression
  - Asymmetrical motor signs
- Infratentorial
  - Sudden onset of coma
  - Cranial nerve palsies & strange respiratory patterns
- Systemic
  - Confusion, delirium, AMS often precede motor signs
  - Pupillary responses preserved & motor signs symmetrical
  - Asterixis, myoclonus, seizures
- Psychogenic
  - Active avoidance on exam

# Neurological Examination

- Level of Consciousness
  - GCS; FOUR score
  - Signs of arousal: visual fixation, tracking, forced eye closure
- Brainstem
  - Cranial nerve examination
- Motor response
  - Purposeful or reflexive
- Breathing pattern
  - Localizing

# Glasgow Coma Score (GCS)

- Eye opening
- Motor response
- Verbal response
- Scale from 3 to 15

| | Eye | Verbal | Motor |
|---|---|---|---|
| 1 | None | None | Flaccid |
| 2 | With pain | Incoherent | Extension |
| 3 | To verbal | Mumbles | Flexion |
| 4 | Spontaneous | Confused | Withdraws |
| 5 | | Oriented | Localizes |
| 6 | | | Follows commands |

# Pearls of Scoring the GCS

- Eyes:
  - General rule: patient should be spoken to before they are touched
  - Patients can only get “4” if regarding
- Voice:
  - Intubated patients get a “1”, documented as a 1T
- Motor:
  - Always ask the patient to follow commands
  - Movement to central pain
  - Look at what the elbow does!
    - Elbows toward the core is abnormal and represents abnormal flexion or extensor posturing.
    - Elbows away from the body is typically seen when a patient is withdrawing from pain.

# Full Outline of UnResponsiveness: FOUR Score

| Points | Eye response | Motor response | Brainstem reflexes | Respiration |
|---|---|---|---|---|
| 4 | Eyelids open or opened, tracking, or blinking to command | Thumbs-up, fist, or peace sign | Pupil & corneal reflexes present | Not intubated, regular breathing pattern |
| 3 | Eyelids open but not tracking | Localizing to pain | One pupil wide and fixed | Not intubated, Cheyne–Stokes breathing pattern |
| 2 | Eyelids closed but open to loud voice | Flexion to pain | Pupil or corneal reflexes absent | Not intubated, irregular breathing |
| 1 | Eyelids closed but open to pain | Extension to pain | Pupil & corneal reflexes absent | Breathes above ventilator rate |
| 0 | Eyelids remain closed with pain | No response to pain/generalized myoclonus status | Absent pupil, corneal, and cough reflex | Breathes at ventilator rate or apnea |

- Scores range from 0 – 16, higher is better
- Rationale: can be used to assess consciousness in patients with or without intubation (no verbal measure)

*Wijdicks EF, et al. Annals of Neurology. 2005;58: 585–93*

# Pupil Findings

| Lesion Location | Clinical Findings |
|---|---|
| Optic nerve | Dilated pupil, APD, visual acuity |
| Thalamic | Constricted, reactive pupil |
| Hypothalamic region | Ipsilateral constricted pupil, ptosis, face & body anhydrosis |
| Midbrain – CN III | Dilated pupil, ptosis, ophthalmoplegia |
| Midbrain – Nuclear | Midposition, irregular, asymmetrical, non-reactive |
| Midbrain – Dorsal tectal | Midposition, round, symmetrical, non-reactive but accommodates, spontaneous size fluctuations |
| **Pons** | **Pinpoint, reactive** |
| Transtentorial herniation | Initially – sluggish, reactive<br>Late – widely dilated, round, symmetrical, nonreactive |
| Metabolic | Small, symmetrical, reactive, hippus |
| **Drugs** | **Opiates – pinpoint; Barbiturates – dilated; Atropine – widely dilated, nonreactive** |

# Ocular motility

- Metabolic coma
  - Symmetrical
  - Roving eye movements
  - Upward gaze
- Herniation
  - Downward gaze
- Cranial Nerves
  - 3rd nerve palsy: lateral & slight downward deviation
  - 6th nerve palsy: medial deviation

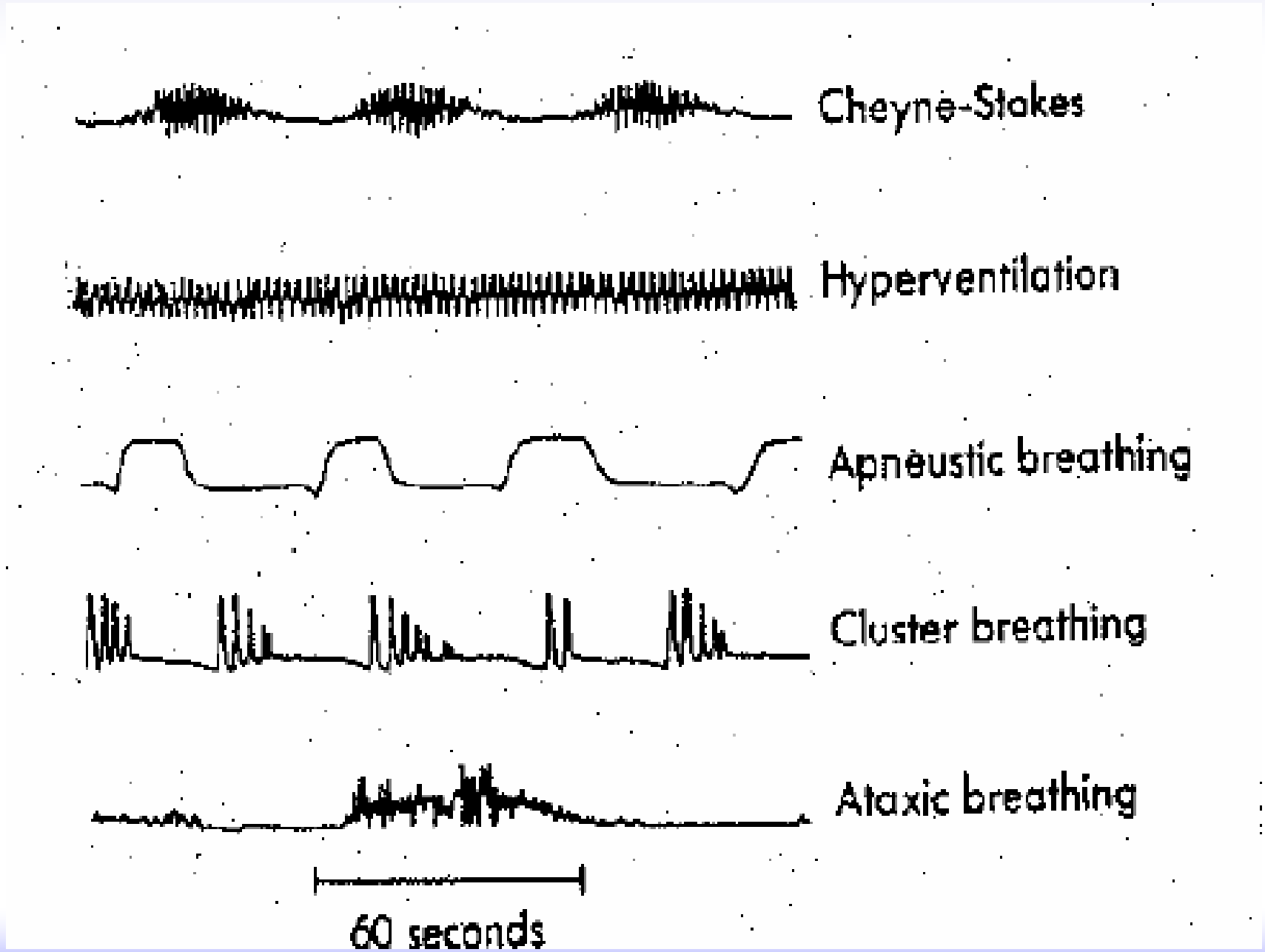
# Motor Testing

- Tone / resistance
- Central vs peripheral stimulation
- Response to noxious stimulation
  - Symmetrical or asymmetrical
  - Localization of reflexive movements
    - Flexor (decorticate)
    - Extensor (decerebrate)
- DTRs

# Respiratory Patterns

| Respiration | Localization | Consider |
|---|---|---|
| Cheyne – Stokes | Bilateral dysfunction of descending pathways<br>Diencephalon<br>Forebrain to upper pons | Metabolic abnormalities<br>Transtentorial herniation<br>Hydrocephalus |
| Hyperventilation | Rostral brainstem tegmentum<br>Lower midbrain to mid-pons | Metabolic abnormalities<br>Early ICP elevations |
| Apneustic | Mid to lower pons | Brainstem lesion |
| Hypoventilation | Medulla or upper cervical spine | Drug overdose<br>ICP elevation<br>SCI injury |
| Ataxic | Dorsomedial medulla | Pre-terminal |

# Respiratory Patterns



# Diagnostic studies

- Basic labs: CBC, Renal, LFTs
- CT
- MRI
- LP
- EEG
- Angiography

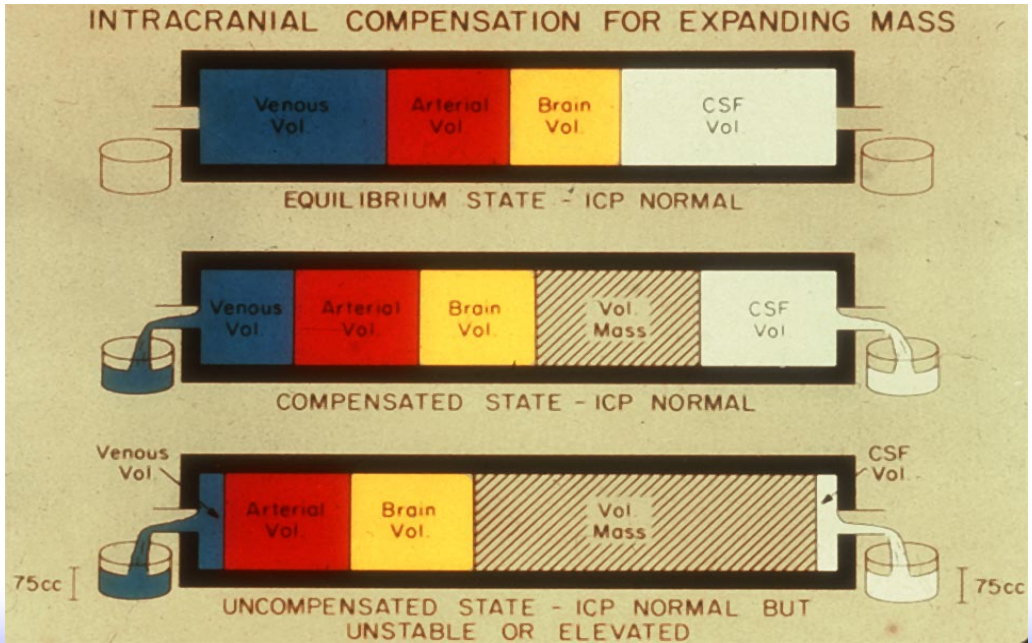
# Empiric treatment: Reversible causes

- Thiamine 100 mg (adult)
- Dextrose 50 mls 50% (adults)
- Naloxone 0.4 mg (adults)
- Stop Seizures
- Treat Metabolic Disturbances
- Lower Intracranial Pressure
- Treat Infection

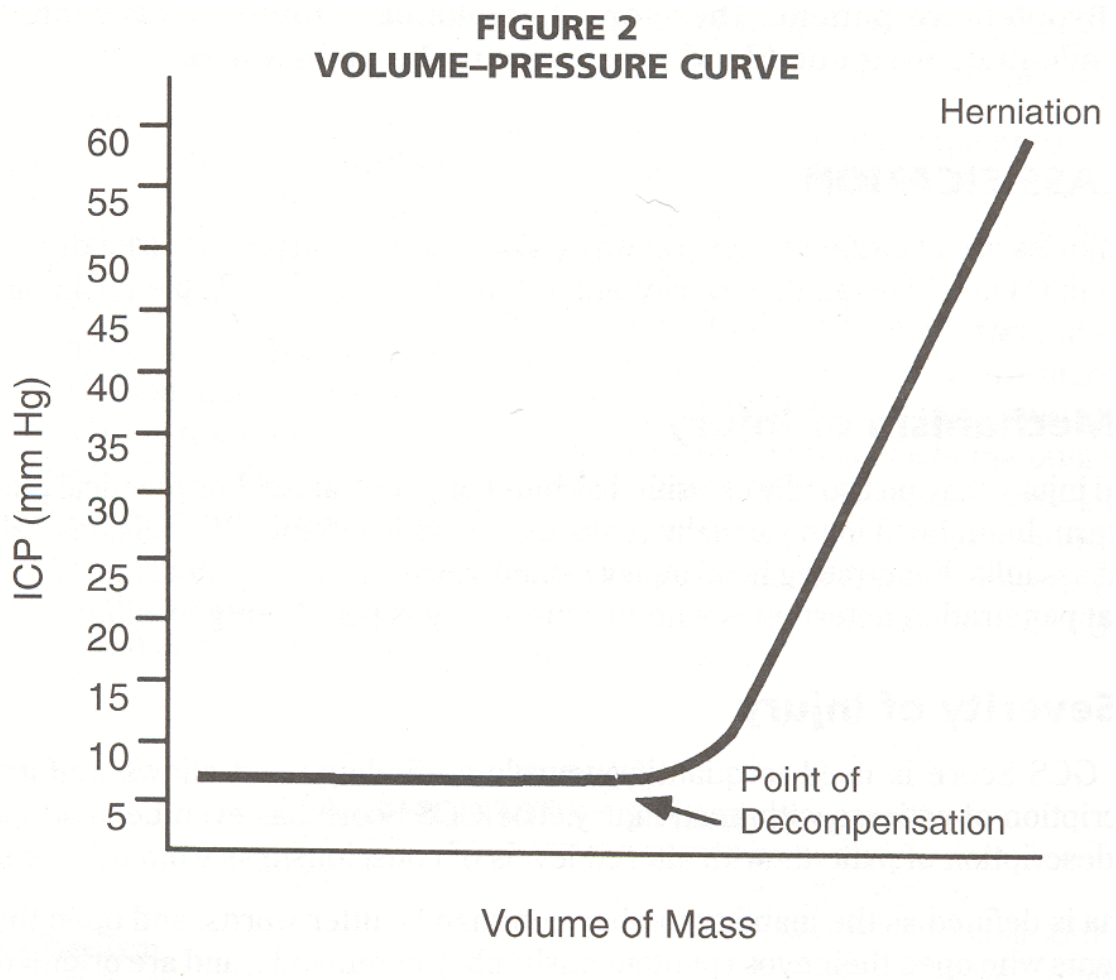
# Cerebral Edema / ICP Elevations

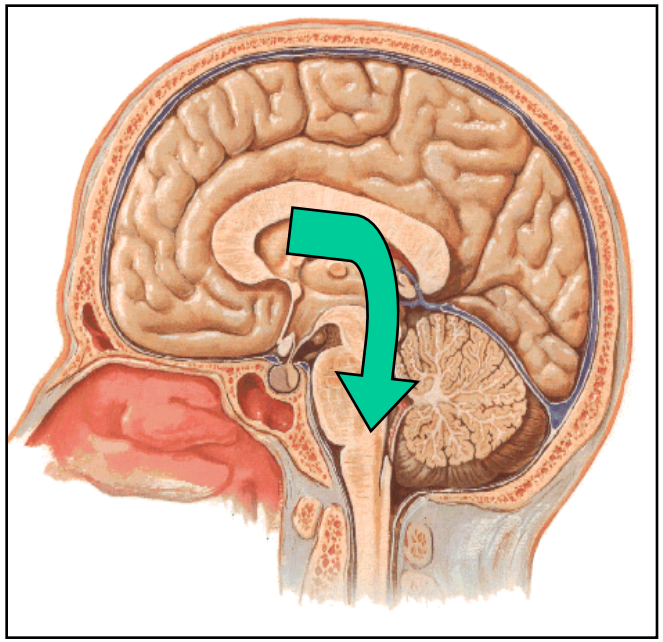
# Monro - Kellie Doctrine

- Intracranial contents are encased in a rigid skull, thus volume is constant
  - Avg adult male ~ 1450mL (1300 brain, 65 CSF, 110 blood)
- If pathology is introduced, something (blood/CSF) must be squeezed out.
- When can not compensate further, ICP rises rapidly



# Volume-Pressure Curve



# Intracranial Components

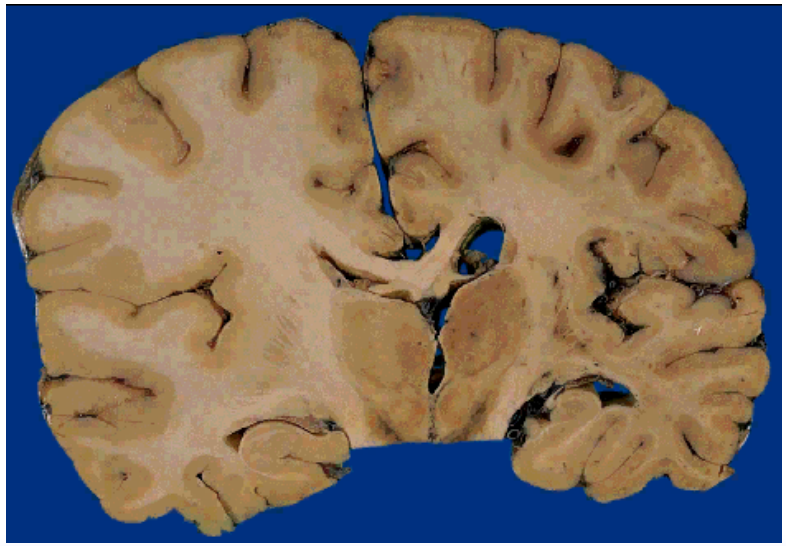
- Brain: viscoelastic solid
  - Minimally compressible, minimally displaceable
  - Slowing expanding masses are better tolerated than rapid growth with pressure gradients of up to 20 mm Hg across 2 cm of WM reported
  - ICP is not always uniform
- CSF: fluid
  - 500 cc produced & resorbed every day
  - Resorption rate tightly linked to ICP
  - Readily compressible & displaceable
- Blood: fluid
  - Arterial & venous aspects
  - Effects of cerebral blood flow can worsen ICP issues
  - Displacing or compressing is achievable, but costly

# Autoregulation

- At constant gas pressures, CBV stays constant through a wide range of MAP (50 – 150)
  - Over 150 results in arterial regulatory systems being overwhelmed & CBV is ‘forcibly’ increased
  - Less than 50 results in cerebral ischemia
- Autoregulation may fail in neurological conditions
  - Trauma, stroke, status epilepticus
  - In these cases, departure from normotension can impact on brain perfusion & CBV
- Concept of cerebral perfusion pressure
  - Pathology decreases compliance & threatens CPP
  - Arterial dilatation occurs to preserve CPP, which increases CBV and decreases compliance further

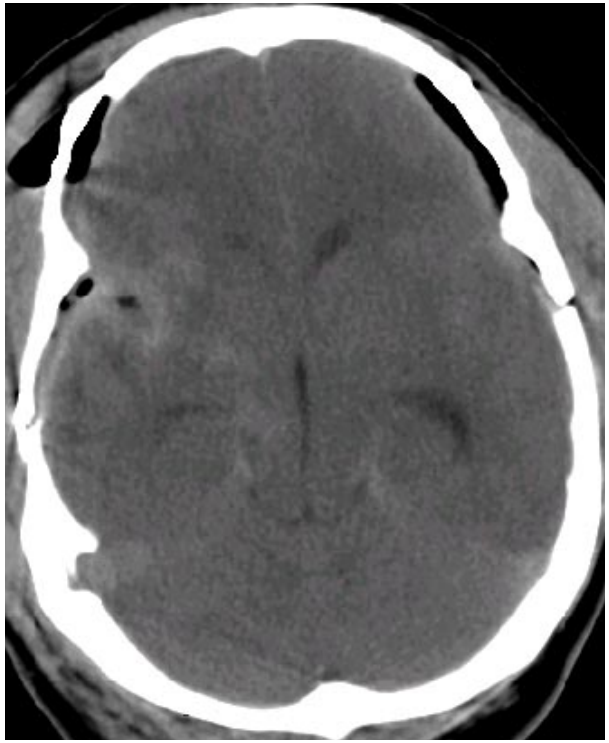
# Intracranial Pressure

- Normal ICP = 0 – 10 mm Hg
- Intracranial hypertension is an ICP of ≥ 20* mmHg at rest
  - Treatment should be initiated above 20 – 25 mm Hg
  - Interpretation and treatment decisions should also consider the clinical exam & CPP data
- Cerebral Perfusion Pressure (CPP) = MAP - ICP
- ICP can be raised by:
  - Agitation
  - Outflow obstruction
  - Hypercarbia*
  - Hypoxia
  - Edema



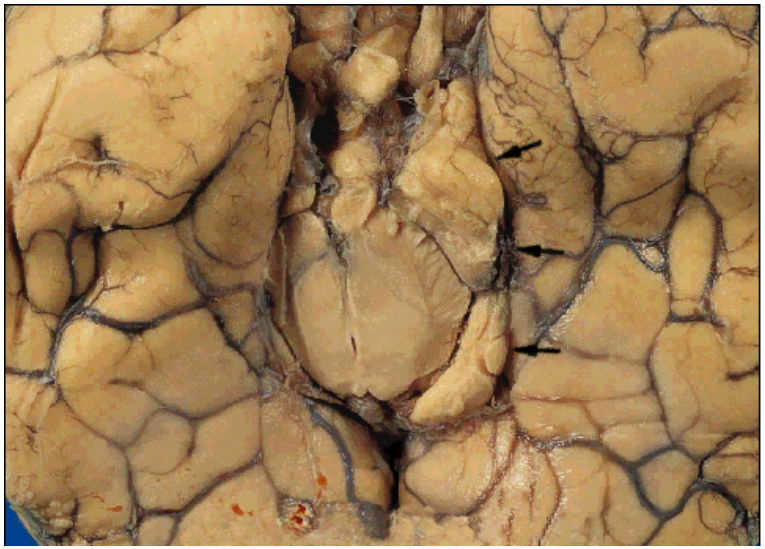
# Intracranial Hypertension: Clinical Conditions

- Neurosurgical
  - TBI, SAH, IVH, SDH/EDH, HCP, mass lesions
- Neurologic
  - Stroke, seizures (transient), CNS infections
- Medical
  - Hepatic encephalopathy, hypercarbia, anoxia/hypoxia, eclampsia, H20 or lead intoxication, HACE
- Edema types
  - Vasogenic, cytotoxic, hydrocephalic



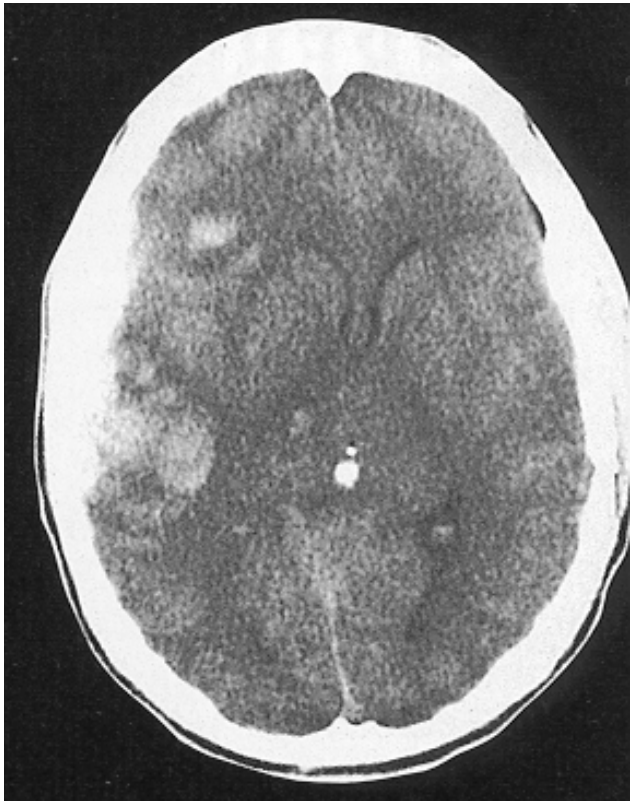
# Intracranial Hypertension

- Final Common Pathway of Injury
- Incidence:
  - Occurs in 40% of severe TBI patients
    - (10 – 15% develop intractable ICP elevations, with a mortality = 84 – 100%)
  - Occurs 50-70% of patients w/ hematomas
  - Numbers in CVA & other disorders less well known



# Intracranial Pressure

- Normal ICP = 0 – 10 mm Hg
- Elevated ICP = ≥ 20 mmHg at rest
  - = Intracranial hypertension
- ICP can be raised by:
  - Worsening mass lesion
  - Edema / inflammation
  - Agitation / pain
  - Outflow obstruction
  - Hypercarbia* / Hypoxia
  - Seizures
  - Fever

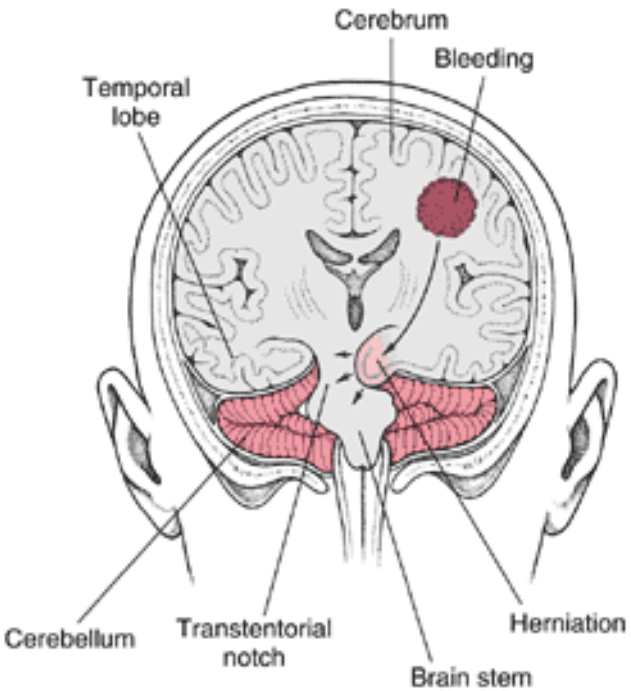


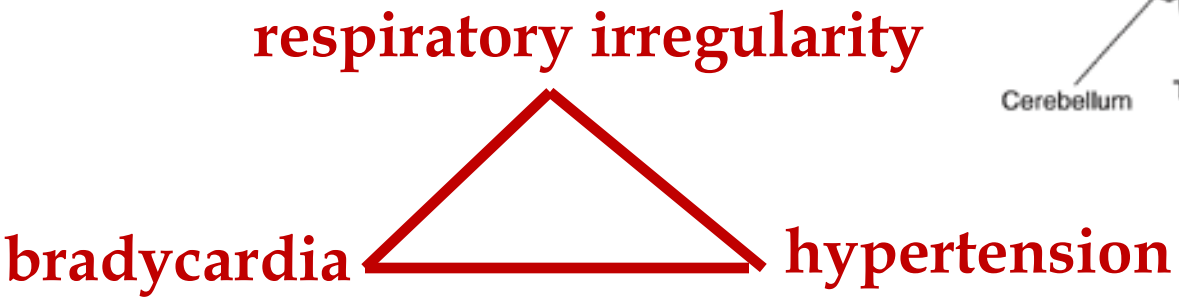
# Intracranial Hypertension

- Clinical symptoms
  - Headache
  - Nausea / vomiting
  - Blurred vision
  - Altered level of consciousness
  - Coma
  - =/- focal deficit

# Signs of Herniation

- Deteriorating level of consciousness (GCS)
- Pupillary asymmetry
- Motor asymmetry
- Cushing's triad



# Herniation Syndromes

- Subfalcine (Cingulate, supracallosal)
  - Cingulate gyrus moves under falx cerebri
  - Personality change, contralateral leg weakness, ACA infarct
- Uncal (lateral transtentorial)
  - Medial temporal lobe past edge of tentorium
  - 3rd nerve effects, contralateral cerebral peduncle (Kernohan's notch)
- Tonsillar (foraminal impaction)
  - Pontomedullary junction moves into the foramen magnum
  - Dysregulation then collapse of respiratory & cardiovascular systems

# Acute Herniation Treatment

- Secure Airway
- Hyperventilation
- Hyperosmotic bolus therapy
  - Mannitol 1gm/kg
  - 3% HTS 250 ml OR 23.4% NaCl 30 ml
- Consider acute treatment of:
  - Pain, anxiety, seizures, fever, outflow obstruction

# ICP Monitoring

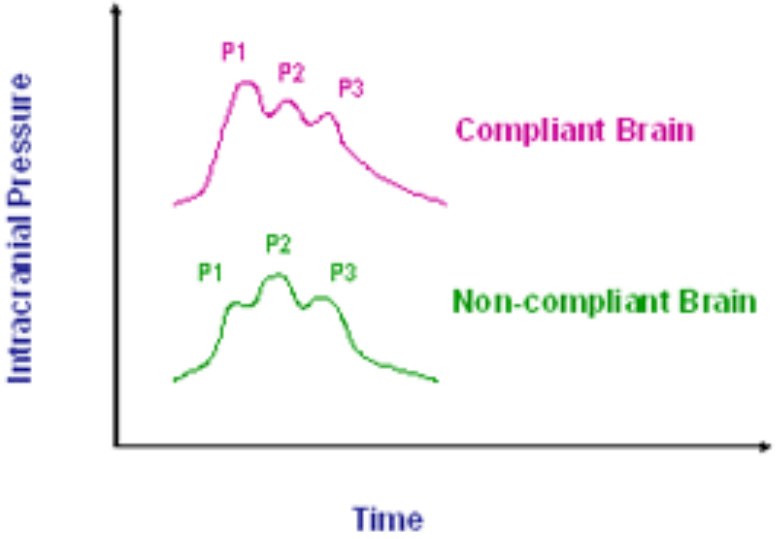
- TBI Indications:
  - GCS ≤ 8 & abnormal CT
  - GCS ≤ 8 & normal CT with 2 or more of the following:
    - Age > 40
    - Motor posturing
    - Hypotension (SBP < 90)
  - Risk of increased ICP > 50 – 60% with above risk factors
- Stroke
  - ICP monitoring is controversial
  - Remember this is a compartment syndrome
  - Follow AANS guidelines and monitor for GCS ≤ 8
- Hepatic encephalopathy – coagulation issues contribute to additional risk of monitoring

# Risks of ICP Monitoring

- Overall Complication rate: 6 -10%
- Infection rate
  - 3 – 6%, mostly represents colonization
  - ± prophylactic antibiotics
- Bleeding
  - 1 – 3% with normal coagulation profile
  - One study reported rates with abnormal coagulation profiles. 1 of 10 with patients with borderline INRs (1.2 – 1.6) and 1 of 12 with elevated INRs (>1.7) had clinically insignificant hemorrhages
- No evidence that these complications worsen outcome

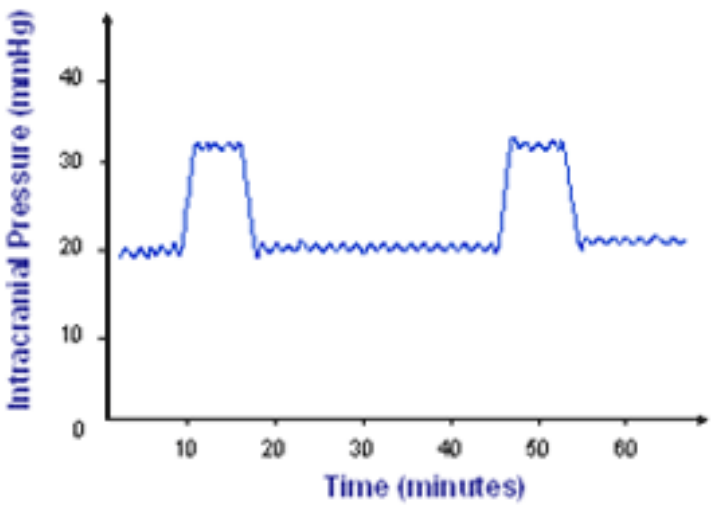
# ICP Waveforms

- Modified arterial pressure trace with characteristic waveforms
  - 1st peak (P1): the "percussive" wave, results from arterial pressure transmitted from choroid plexus
  - 2nd peak (P2): the "tidal" wave, its amplitude varies inversely with brain compliance
    - If P2 > P1, then the brain has lost compliance
  - 3rd peak (P3): the dicrotic notch, caused by closure of aortic valve

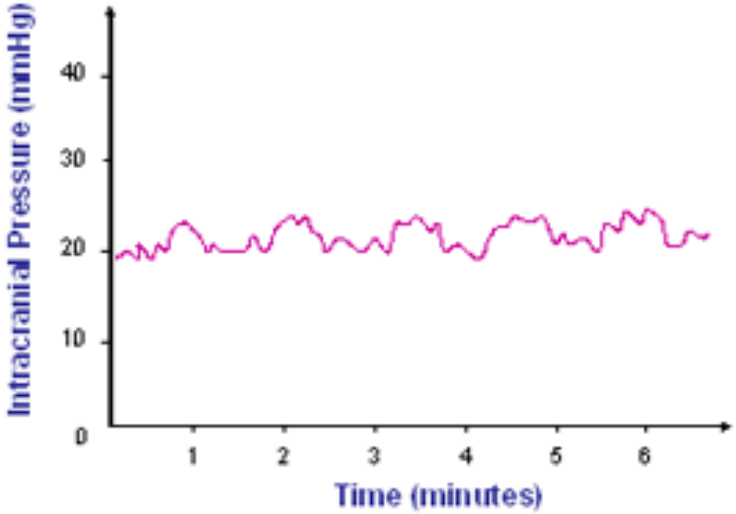


# ICP Waveforms

- Lundberg A waves
  - "Plateau waves"
  - Steep increases in ICP lasting for 5 to 10 minutes
  - Always pathological, represent ↑ ICP & early herniation




- Lundberg B waves
  - ICP oscillations at a frequency of 0.5 to 2 waves/min
  - Associated with an unstable ICP
  - May be the result of cerebral vasospasm

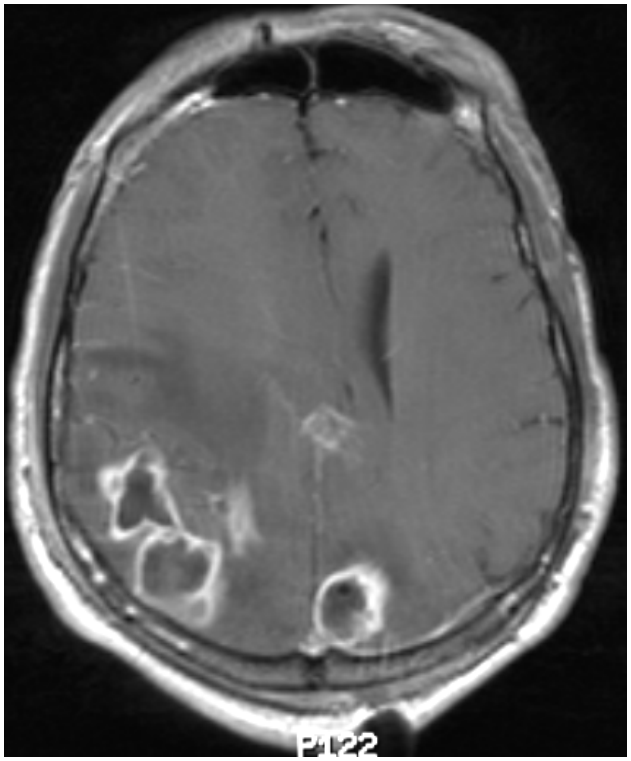


# ICP Treatment: General Medical Issues

- Hemodynamics
  - Avoid systemic hypotension (SBP < 90 mm Hg)
  - If HTN is contributing to ICP issues (ie, HTN encephalopathy), lower MAP carefully based on CPP
  - Avoid vasodilating BP medications (NTG, nitroprusside, hydralazine). Labetolol is drug of choice.
  - Isotonic or hypertonic fluids only
- Glucose
  - Hyperglycemia is an independent predictor of poor outcome after TBI, CVA, SAH, & meningitis.
- Nutrition – avoid free water

# ICP Treatment: Specific

- *Intubation
- *Head position (30°, midline)
- *Sedation/Analgesia (+/- Paralytics)
- CSF drainage
- Hyperosmotic therapy**
- Hyperventilation**
  - Mild (pCO2 = 30 – 35)
  - Moderate (pCO2 = 25 – 30)
- Barbiturates, Decompression, Hypothermia



# ICP Treatments

Empiric treatments that don't work:

- Hyperventilation
- Barbiturates
- Paralysis
- Hypothermia
- Mannitol

# Initial Therapy

- Mechanical issues: head, collar
- IV Narcotics
  - morphine, fentanyl
- Sedatives
  - diazepam, midazolam, propofol
- Short-acting paralytic agents
  - vecuronium, cistacuronium
  - use sparingly, document time given
  - Train of 4
- CSF drainage

# Mannitol for ICP

Effects:

- Plasma expander - ↓ hematocrit, ↑ blood flow, ↑ cerebral oxygen delivery
- Osmotic effect delayed for 15 to 30 minutes while gradients established between plasma and cells
  - "opening of BBB" → mannitol accumulation → reversed osmotic shift → ↑ brain osmolality → exacerbates ICP by ↑ brain edema = REBOUND ICP
- Never subjected to randomized, placebo-controlled trial in TBI
- Causes harm in stroke

# 3% Saline: Mechanism of Action

- Establishes osmotic gradient
- Systemic volume expander w/ minimal renal effects, thus maintains MAP
- Tendency to cross BBB less than mannitol, thus less rebound cerebral edema
- Vascular endothelial effects may reverse vasospasm & related hypoperfusion
- Modulation of inflammatory response
  - ↓ WBC adherence, migration & prostaglandin production
- NMDA receptor effects
- May have a role in TBI, CVA, ICH

*Neurocrit Care*
https://doi.org/10.1007/s12028-020-00959-7

NEUROCRITICAL CARE SOCIETY

SPECIAL ARTICLE

# Guidelines for the Acute Treatment of Cerebral Edema in Neurocritical Care Patients

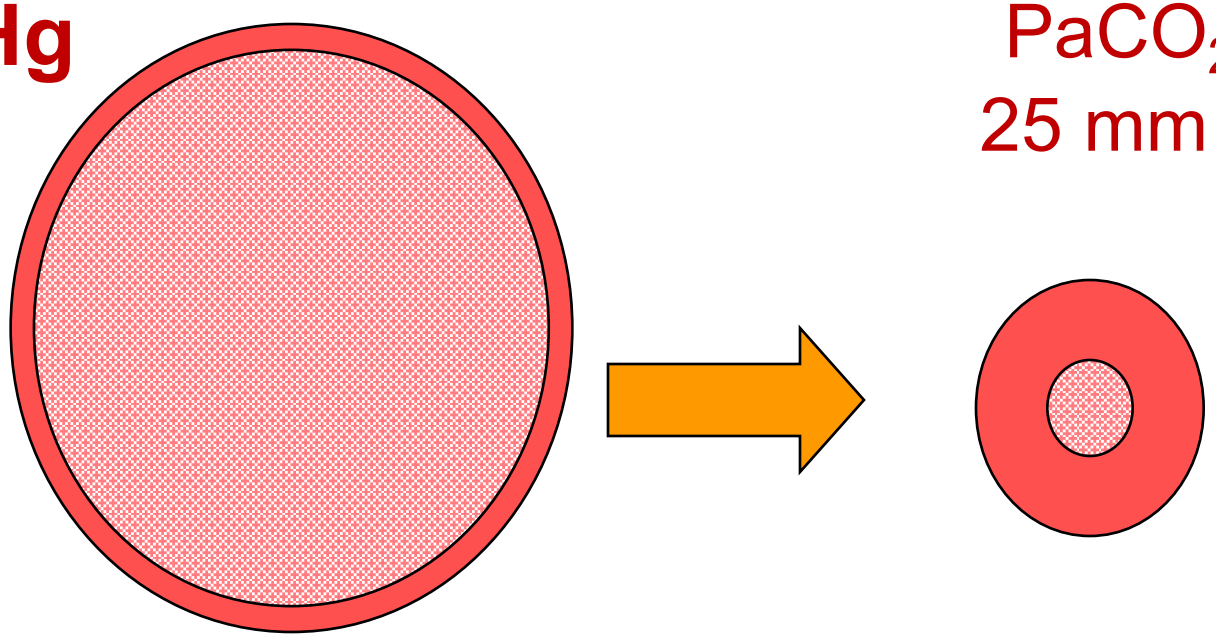
Aaron M. Cook[1*], G. Morgan Jones[2], Gregory W. J. Hawryluk[3], Patrick Mailloux[4], Diane McLaughlin[5], Alexander Papangelou[6], Sophie Samuel[7], Sheri Tokumaru[8], Chitra Venkatasubramanian[9], Christopher Zacko[10], Lara L. Zimmermann[11], Karen Hirsch[9] and Lori Shutter[12]

- SAH: symptom based HTS bolus dosing
- TBI & ICH: HTS over mannitol for elevated ICP; no steroids
- AIS & Hepatic Encephalopathy: HTS or mannitol for elevated ICP
- Meningitis: Bacterial – Decadron helps, give early; TB – steroids decrease mortality. No benefit from osmotic agents.
- Assessing risk of renal injury:
  - Mannitol – use osmolar gap over serum osmolarity
  - HTS – monitor closely and keep serum Na $\leq$ 160, Cl $\leq$ 115
- HTS administration method: can not recommend a specific method (bolus versus continuous infusion); avoid hyponatremia
- Non-pharmacological methods: recommendations to treat ICP elevations include HOB at 30º, brief HV for herniation, CSF diversion;

# Hyperventilation

Can be life saving in setting of acute herniation
Long-term use is harmful!

**PaCO2 =**
**40 mm Hg**



$PaCO_2$ =
25 mm Hg

# Hyperventilation

- Start out w/ normocapnia (pCO2 35 – 40).
  - Hypocapnia induces vasoconstriction, thus ↓ CBF
  - CBF already compromised (esp in 1st 24º after injury), thus can worsen ischemia early
- Therapeutic hyperventilation (pCO2 30 – 35 mm Hg) may be beneficial for acute ICP elevations
  - Use with CBF monitoring (SjO2, PbtO2)
  - After 10 – 20 hours, arterioles re-dilate causing a rebound increased CBF/CBV & ICP
- There is no indication for prophylactic hyperventilation ***(Muizelaar JP, et al. J Neurosurg 1991;75:731-739)***

# Steroids

NO BENEFIT
(except in vasogenic edema)


- May actually be harmful
  - CRASH trial (10k pts) showed increased mortality
    (Lancet 2004; 364:1321-28)
- Detrimental systemic effects
  - Hyperglycemia, ↑ infections, other complications

# Brain Death

# Brain Death Exam Prerequisites

- UPMC policy: HS-PS0502 *
  - Determination of Death in Adults; December 30, 2019
- Known neurologic process
- No metabolic or electrolyte abnormalities
  - Na >110 < 160; pH > 7.2; osmolarity < 350; Ca < 12; Glu 70 - 300
- No CNS depressants
- Systolic BP $\geq$ 100 mm Hg
- Core temperature >36° C

# Anoxic-ischemic brain injury

- NO therapeutic hyperthermia
  - 24 hour period of observation with the patient at a normal body temperature following the onset of the brain injury is required
- Therapeutic hypothermia
  - Defined as TTM to < 36º C for 24 or more hours
  - A minimum of 24 hours observation at ≥ 36ºC is necessary prior to brain death testing, unless a confirmatory test demonstrating absent cerebral blood flow is performed in addition to the neurological examination.

***UPMC policy: HS-PS0502* Determination of Death in Adults; December 30, 2019***

# Brain Death Examination

- Perform one neurologic examination (sufficient to pronounce brain death in most US states).
  - Some US state statutes require two examinations
- Sufficient time period has passed since onset of the brain insult to exclude possibility of recovery
  - “usually several hours”
- All physicians are allowed to determine brain death in most US states.
  - It is reasonable that physicians determining brain death should demonstrate competency in this examination. Neurologists, neurosurgeons, and intensivists may have specialized expertise. Requirements of their involvement are based on state and hospital regulations.

***AAN Practice Parameter 2010***

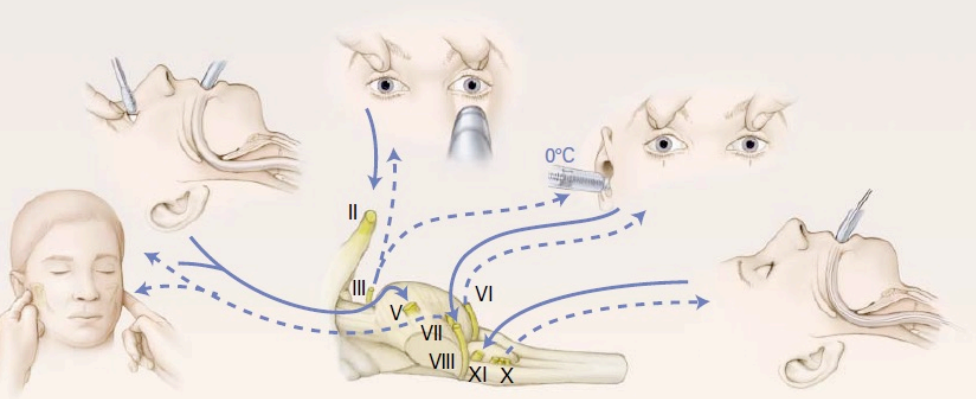
# Brain Death Examination

- Bilateral pupil response
- Oculocephalic reflex (Doll's Eyes)
- Corneal reflex
- Vestibulo-ocular reflex
- Cough / Gag reflex
- Cerebral motor response to central pain
- Assess for spontaneous breathing

***AAN Practice Parameter 1995; 2010***

# Examination of Brainstem Reflexes

- Pupils
  - Mid-position
  - Size: 4 – 5 mm
  - Shape: round, oval or irregular
  - No response to light

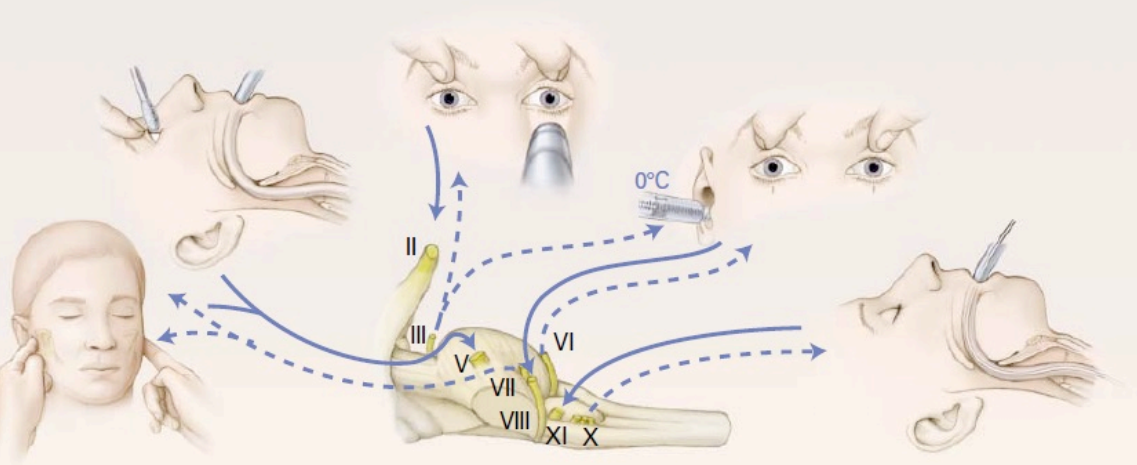



- Ocular movement
  - No oculocephalic reflex – Doll's eyes (C-spine injury?)
  - Caloric testing with >/= 50 ml ice cold water
    - HOB at 30°, exam TM to assure no obstruction
    - Observe for 1 min, wait before testing other side

***Report of the Quality Standards Subcommittee of the American Academy of Neurology, 1995***

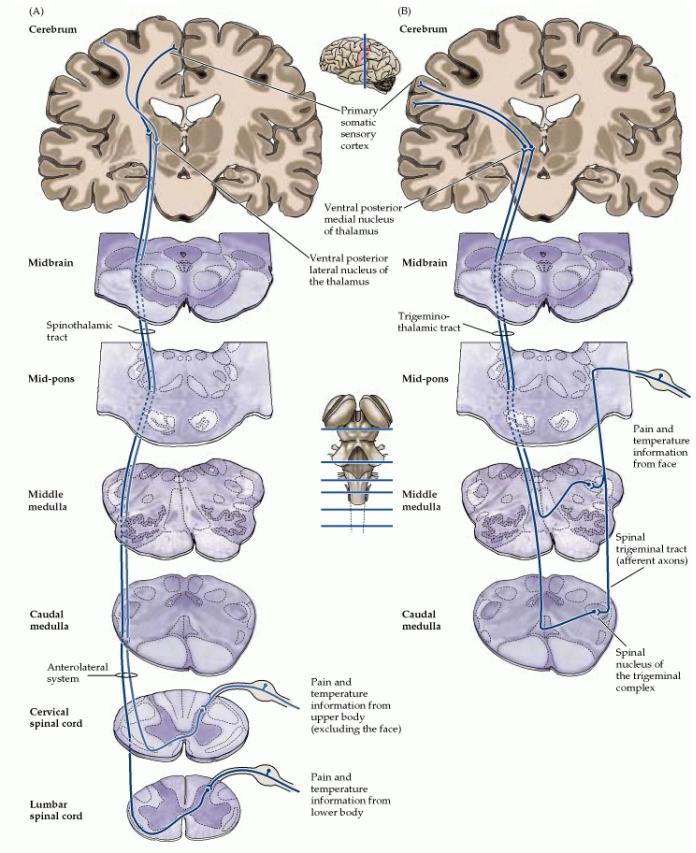
# Examination of Brainstem Reflexes

- Facial sensation and facial motor response
  - No corneal reflex
  - No grimacing to painful stimuli
- Pharyngeal and tracheal reflexes
  - No gag
  - No cough to bronchial suctioning



# Motor Testing

- No cerebral motor response in any extremity to painful stimuli
  - Supraorbital nerve
  - Trapezius squeeze
  - Sternal rub
  - TMJ pressure
  - Axillary squeeze



# Brain Death Examination

- *Atropine Test*
  - *UPMC practice, not a national practice*
- Apnea Test
  - Vitals: Core temperature > 36.5º C or 97º F and SBP > 90mm Hg.
  - Draw a baseline ABG, PCO2 must be ~ 40.
  - Pre-oxygenate with 100% FiO2.
  - Disconnect ventilator, give O2 at 8-12 lpm by tracheal cannula.
  - Observe for any respiratory movements.

***AAN Practice Parameter 1995; 2010***

# Brain Death Examination

- Apnea Test
  - Duration varies, usually 5 -10 minutes.
    - General rule: after 2 minutes off ventilator the $PCO_2$ will increase by 5, then for every additional minute the $PCO_2$ will increase by 2.
  - Draw post-test ABG and reconnect the ver
  - The patient has no CNS respiratory drive i 60mm Hg.
    - Adjust criteria for known $CO_2$ retention.
  - During test if patient becomes hemodynam unstable, stop testing, draw ABG and reco ventilator. Test is indeterminate if $PCO_2$ < ( Consider confirmatory studies.

Sample

61 – 40 = 21

21 - 5 = 16 / 2 = 8

(2 min) + (8 min)

Total = 10 min

Sample 2

61 – 46 = 15

15 – 5 = 10 / 2 = 5

(2 min) + (5 min)

Total = 7 min

***AAN Practice Parameter 1995; 2010***

# Brain Death Declaration

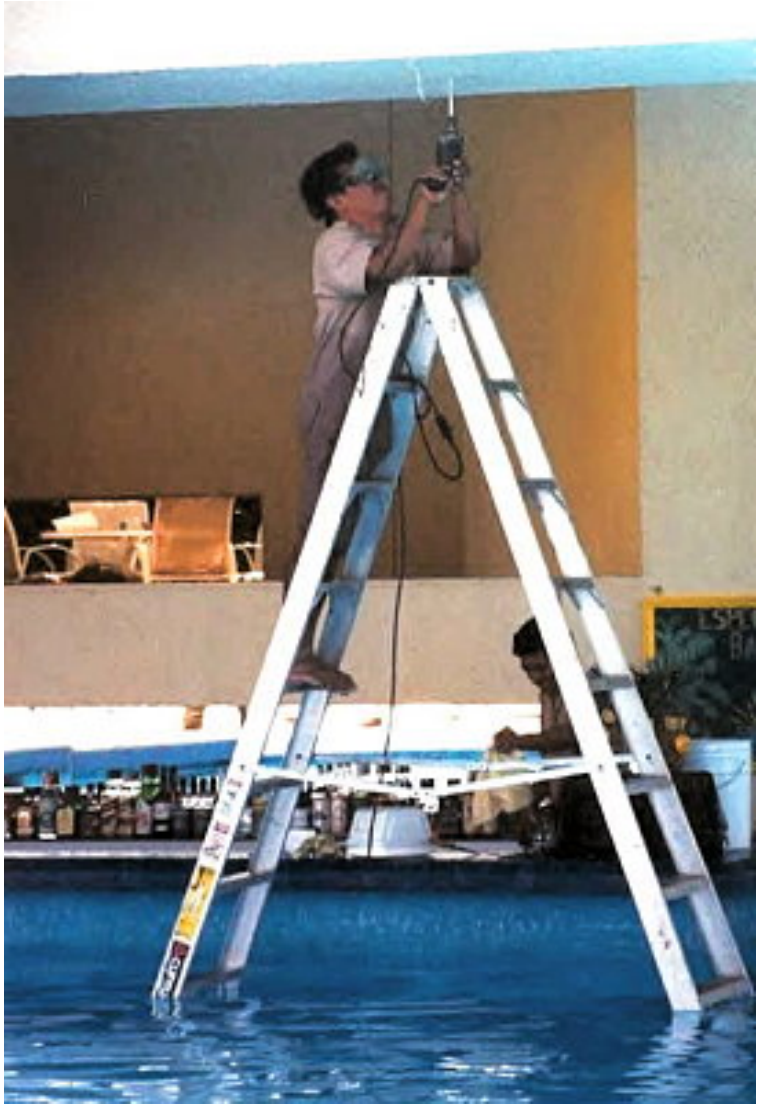
- Brain death criteria are met if there is no response to any component of the examination.

- Confirmatory tests are NOT necessary.
  - Recommended if unable to assess all cranial nerves.
  - Options are: CBF, EEG, TCD, EP, CTA, MRI/MRA
  - Barbiturate levels are required in setting of barbiturate coma.

# Documentation

- Worksheet
  - Developed to assist in exam performance.
  - Two physicians can document separately on worksheet ALL of the following:
    - Absence of each brain stem reflex tested
    - Absence of motor response to pain
    - Absence of respiration with PCO2 > 60 mm Hg
    - Date, time of death*, and signature.
      - Time of death = time arterial PCO2 reached target value.
- Brain Death Note Template in Power Chart
  - Developed to improve documentation

# Seizures



# Status Epilepticus

- Definition:
  - Traditional: Any type of seizure lasting > 30* minutes, or <u>2 or more sequential seizures without full recovery of consciousness between them</u> *(JAMA 1993)*
  - *Modern: any seizure lasting > 5 minutes
  - Practical: any patient who is still seizing
- Neurological emergency
  - Lorazepam 2 mg q 2 min seizing, max dose = 0.1 mg/kg
  - Fosphenytoin 20 PE mg/kg IV, max rate = 150 mg/min. Monitor for hypotension & arrhythmias
  - If seizures persist, start a continuous IV medication. Intubation, arterial and central access will be necessary

# Prognosis

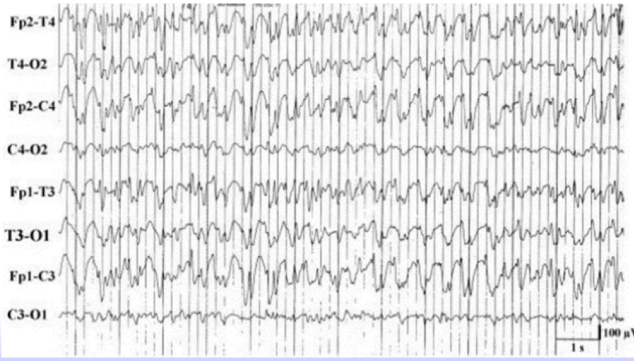
- Mortality: 17-23%[1, 2]
- New disabling neurological deficits: ~10%[3]
- Some functional deterioration in ~23%
- Predictors of worse outcome
  - Age (higher mortality in elder pts)
  - Etiology (acute symptomatic worst)
  - Long SE duration, continuous szs
  - Nonconvulsive szs; +/-periodic discharges


***1. DeLorenzo et al. Neurology, 1996: 46***
***2. Hesdorffer et al. Neurology, 1998:50.***
***3. Hirsch and Claassen, Current Neurology and Neuroscience Reports, 2002.***

# Refractory SE: Prognosis

- Some studies have reported 50% mortality [1]
- Poor prognosticators: same as for SE
- For RSE, most important predictor of outcome is duration of SE.
  - Mortality = 32% (SE > 60 mins) vs. 2.7% (SE 30-59 mins)
- Conflicting evidence for prognosis of NCSE.
  - Mortality rates range from 18-52% (depending on duration, etiology, delayed dx) [2]


1. ***Hirsch and Claassen, Current Neurology and Neuroscience Reports, 2002.***
2. ***Abou Khaled et al. Crit Care Clin, 2006.***

# Critical Care Treatment

| Intervention | Timing |
|---|---|
| Non-invasive airway protection | Immediate (0–2 min) |
| Intubation (if airway/gas exchange compromised or elevated ICP suspected) | Immediate (0–10 min) |
| Vital signs: O2 saturation, BP, HR | Immediate (0–2 min) |
| Vasopressor support of BP if SBP <90 mmHg; MAP <70 | Immediate (5–15 min) |
| Finger stick blood glucose | Immediate (0–2 min) |
| Peripheral IV access<br>1. **Emergent initial AED therapy (i.e. benzodiazepine)**<br>2. Fluid resuscitation<br>3. Nutrient resuscitation (thiamine then dextrose) | **Immediate (0–5 min)** |
| **Urgent SE control therapy with AED** | **Immediate after initial AED given (5–10 min)** |

***Brophy et al. Neurocrit Care 2012; 17:3-23***

# Treatment: General

| | Strong Recommendations |
|---|---|
| **High or Moderate Quality Evidence** | • Treatment should occur rapidly and continue sequentially until clinical seizures are halted<br>• Critical care treatment and monitoring should be started simultaneously with emergent initial therapy and continued until further therapy is consider successful or futile |

***Brophy et al. Neurocrit Care 2012; 17:3-23***

# Treatment: Emergent Initial Therapy

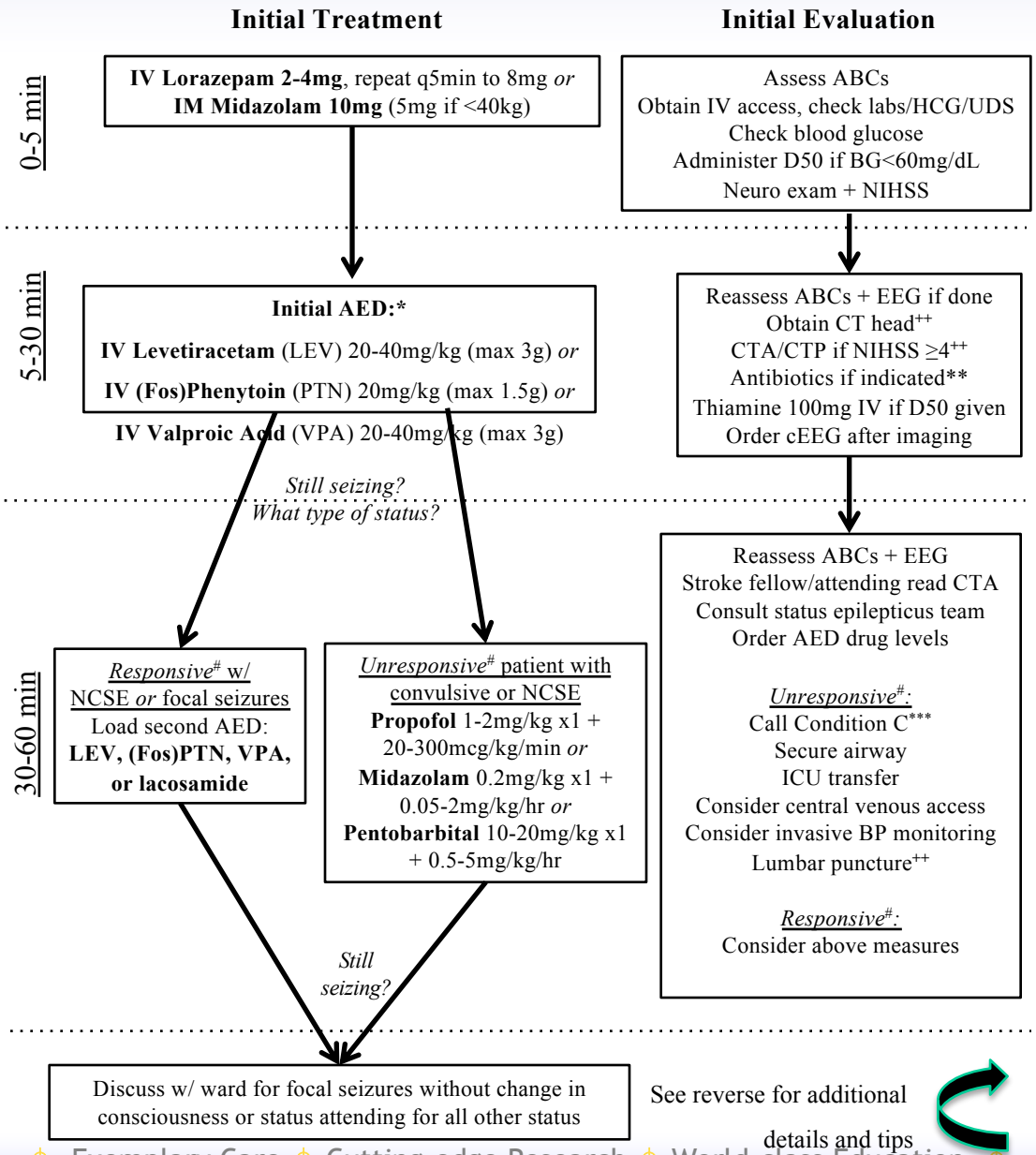
| | Strong Recommendations |
|---|---|
| **High or Moderate Quality Evidence** | ▪ Benzodiazepines are preferred emergent initial therapy<br>▪ Lorazepam is the drug of choice for IV administration<br>▪ Midazolam is the drug of choice for IM administration<br>▪ Rectal diazepam can be given when there is no IV access and IM administration of midazolam is contraindicated |

# Treatment: Urgent Control Therapy

| | Strong Recommendations |
|---|---|
| **High or Moderate Quality Evidence** | ▪ Urgent control AED therapy recommendations include use of IV fosphenytoin/phenytoin, valproate sodium, or levetiracetam |

***Brophy et al. Neurocrit Care 2012; 17:3-23***

# Initial evaluation and management: confirmed or suspected status epilepticus



# Urgent Drug Dosing

| Drug | Initial Dose | Administration Rates |
|---|---|---|
| Diazepam | 0.15 mg/kg IV up to 10 mg per dose, may repeat in 5 min | Up to 5 mg/min (IVP) |
| Lorazepam | 0.1 mg/kg IV up to 4 mg per dose, may repeat in 5–10 min | Up to 2 mg/min (IVP) |
| Midazolam | 0.2 mg/kg IM up to maximum of 10 mg | Up to 2 mg/min (IVP) |

***Brophy et al. Neurocrit Care 2012; 17:3-23***

# Urgent Drug Dosing

| Drug | Initial Dose | Administration Rates |
|---|---|---|
| Fosphenytoin | 20 mg PE/kg IV, may give additional 5 mg/kg | Up to 150 mg PE/min; may give additional dose 10 min after loading infusion |
| Phenytoin | 20 mg/kg IV, may give additional 5–10 mg/kg | Up to 50 mg/min IV; may give additional dose 10 min after loading infusion |
| Levetiracetam | 20 – 40 mg/kg, max 3 gm* | Administer over 15 minutes; dosage adjustments necessary in patients with impaired renal function. |
| Valproic Acid | 20 – 40 mg/kg, max 3 gm | Administer over 30 minutes; hepatotoxicity & pancreatitis are concerns |

***Brophy et al. Neurocrit Care 2012; 17:3-23***

# Critical Care Treatment

| Intervention | Timing |
|---|---|
| Neurologic exam | Urgent (5–10 min) |
| Triage lab test panel | Immediate (5 min) |
| Refractory SE treatment | Urgent (20–60 min after 2nd AED) |
| Urinary catheter | Urgent (0–60 min) |
| Continuous EEG | Urgent (15–60 min) |
| Diagnostic testing (selection depends on clinical presentation)<br>CT; LP; MRI | Urgent (0–60 min) |
| Intracranial pressure monitoring (depending on clinical presentation) | Urgent (0–60 min of imaging diagnosis) |

***Brophy et al. Neurocrit Care 2012; 17:3-23***

# Refractory Status Epilepticus

| | Strong Recommendations | Weak Recommendations |
|---|---|---|
| **Low, Very Low or Poor Quality Evidence** | ▪ Refractory SE therapy recommendations should consist of continuous infusion AEDs, but vary by the patient's underlying condition<br>▪ Dosing of continuous infusion AEDs for RSE should be titrated to cessation of electrographic seizures or burst suppression | ▪ A period of 24–48 h of electrographic control is recommended prior to slow withdrawal of continuous infusion AEDs for RSE |

***Brophy et al. Neurocrit Care 2012; 17:3-23***

# RSE Dosing Recommendations

| Drug | Initial Dose | Continuous Infusion |
|---|---|---|
| Midazolam | 0.2 mg/kg; administer at a rate of 2 mg/min | 0.05–2 mg/kg/hr CI<br>Breakthrough SE: 0.1–0.2 mg/kg bolus, ↑ CI rate by 0.05–0.1 mg/kg/hr every 3–4 h |
| Pentobarbital | 5–15 mg/kg, may give additional 5–10 mg/kg; administer at a rate ≤ 50 mg/min | 0.5–5 mg/kg/h CI<br>Breakthrough SE: 5 mg/kg bolus, ↑ CI rate by 0.5–1 mg/kg/h every 12 h |
| Propofol | Start at 20 mcg/kg/min, with 1–2 mg/kg loading dose | 30–200 mcg/kg/min CI. Use caution when administering high doses (>80 μ/kg/min) for extended periods of time<br>Breakthrough SE: ↑ CI rate by 5–10 μ/kg/min every 5 min or 1 mg/kg bolus plus CI titration |
| Thiopental | 2–7 mg/kg, administer at a rate ≤ 50 mg/min | 0.5–5 mg/kg/h CI<br>Breakthrough SE: 1–2 mg/kg bolus, ↑ CI rate by 0.5–1 mg/kg/h every 12 h |

***Brophy et al. Neurocrit Care 2012; 17:3-23***

## Additional considerations

This protocol is not intended for the management of simple partial status

*** Initial AED selection:**

**Prefer home AED** if epilepsy with noncompliance
**LEV 1st choice** if: stocked on floor (i.e. immediately available); liver disease; pregnancy
**VPA 1st choice** if: renal disease, myoclonic status, absence status
**FosPTN** preferred to **PTN** if available (less infusion-associated hypotension)
**Prefer to avoid** combination VPA + PTN

# **Unresponsive** = Not mentating/responding to questions and/or not localizing to pain

****Empiric antibiotics:**

**Vancomycin** 25mg/kg x1 (max 2.5g)
**Ceftriaxone** 2g x1
**Acyclovir** 10mg/kg x1
**Ampicillin** 2g x1 if >50y/o or immunocompromised
**Penicillin allergy:** Bactrim 2.5mg/kg IV + aztreonam 2g IV x1

++ CTA/CTP results are to be reviewed with stroke fellow/attending. If patient has a contrast allergy, discuss vascular imaging options with stroke fellow/attending
++ Defer brain imaging until convulsive activity controlled
++ Defer lumbar puncture (LP) if CT has mass effect

***** Call Condition C** if patient on the floor and still seizing with alteration in consciousness (i.e. anything other than simple partial status) → allows for intubation and transfer to ICU

**Other pointers**

- A history, past medical history, medication list, physical examination and review of basic labs should be obtained before calling the status attending
- If possible, discuss cases with senior resident, however, care should not be delayed
- If continuous EEG (cEEG) is ordered, inform the EEG techs know if the patient is actively seizing (864-3791 or -3792)
- Draw at least 10mL of CSF on LP. Consider sending cells, protein, glucose, bacterial culture, fungal culture, viral PCRs (HSV 1/2, VZV, EBV, CMV), and in certain cases autoimmune panel (Send out to Mayo or ARUP)
- Some types of post-anoxic myoclonus (myoclonic status epilepticus) do not benefit from treatment with this protocol → discuss with status attending or PCAS team

**Common acute adverse drug effects**

Phenytoin: hypotension, cardiac arrhythmias, somnolence. Slower infusion rate is better tolerated.
Valproic Acid: hyperammonemia, hepatotoxicity, thrombocytopenia
Lacosamide: AV block, hypotension

# Approach: Diagnostic Work-up

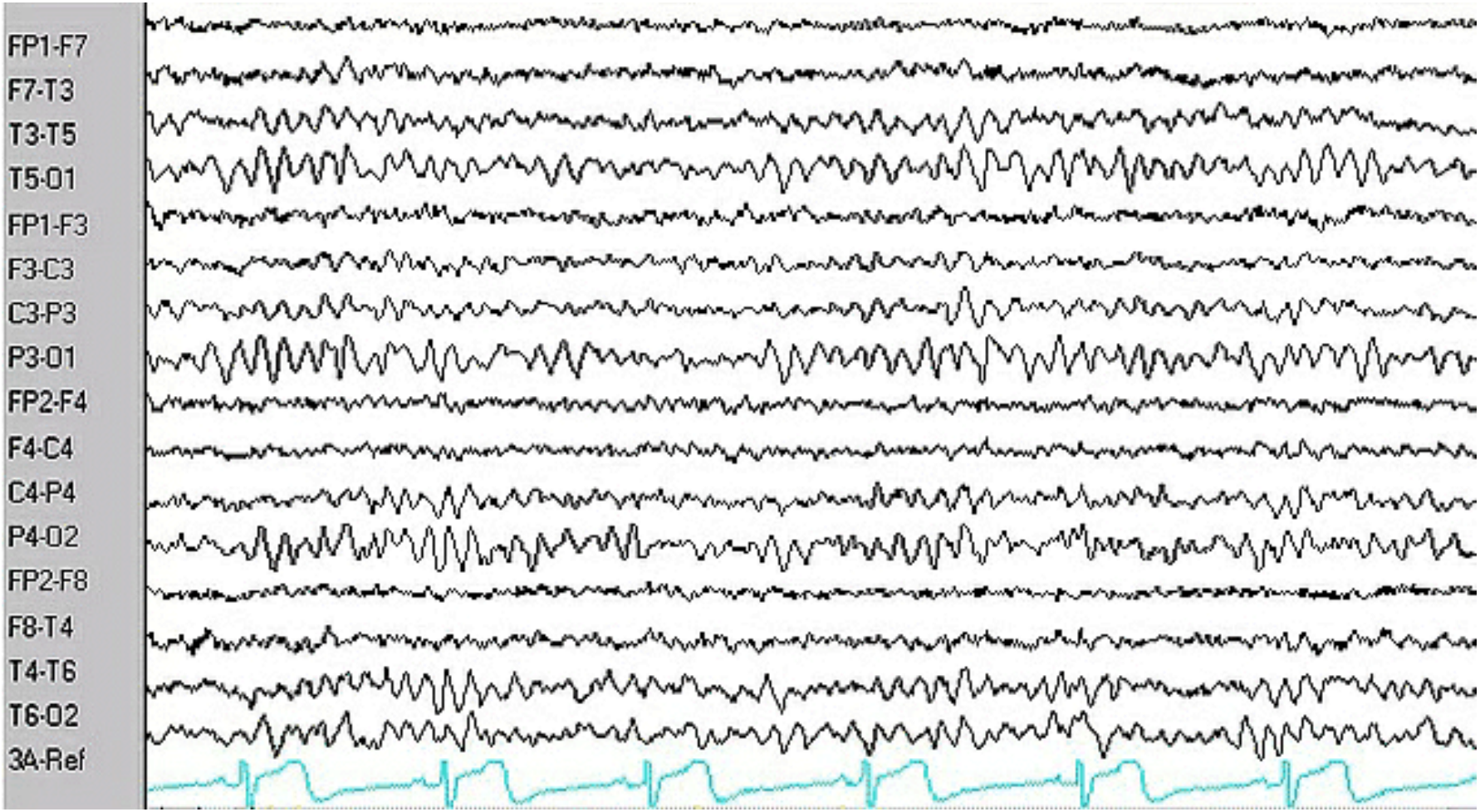
| All patients |
| --- |
| ▪ FS glucose |
| ▪ Monitor vital signs |
| ▪ Head CT (appropriate for most cases) |
| ▪ Labs: blood glucose, CBC, BMP, Ca, Mg |
| ▪ cEEG monitoring |
| **▪Consider based on clinical presentation** |
| ▪ Brain MRI |
| ▪ Lumbar Puncture |
| ▪ Toxicology panel (ie, isoniazid, TCA, theophylline, cocaine, sympathomimetics, alcohol, organophosphates, cyclosporin |
| ▪ Other labs: LFT, troponin, T&H, coags, ABG, AED levels, tox screen (urine, blood), inborn errors of metabolism |

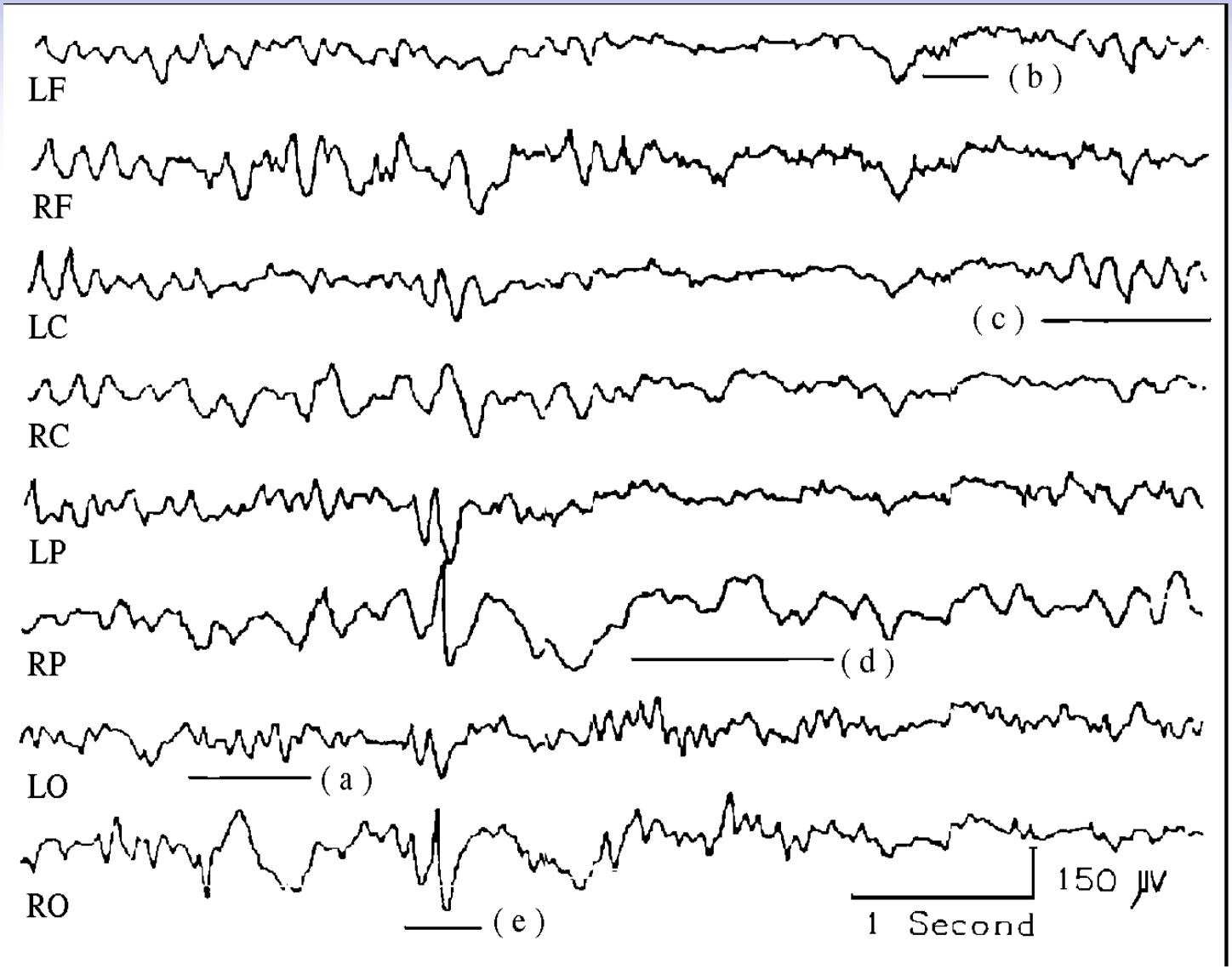
***Brophy et al. Neurocrit Care 2012; 17:3-23***

# EEG Basics

- Page usually = 10 seconds
- Activity Descriptors
  - Alpha = normal background, 8 – 11 Hz
  - Beta = fast activity; ≥ 12 Hz
    - Often see with medications
  - Theta = slowing; 5 – 7 Hz
  - Delta = Very slow; 2 – 4 Hz
- Stimulations
  - Pain
  - Photic
- Processed EEG

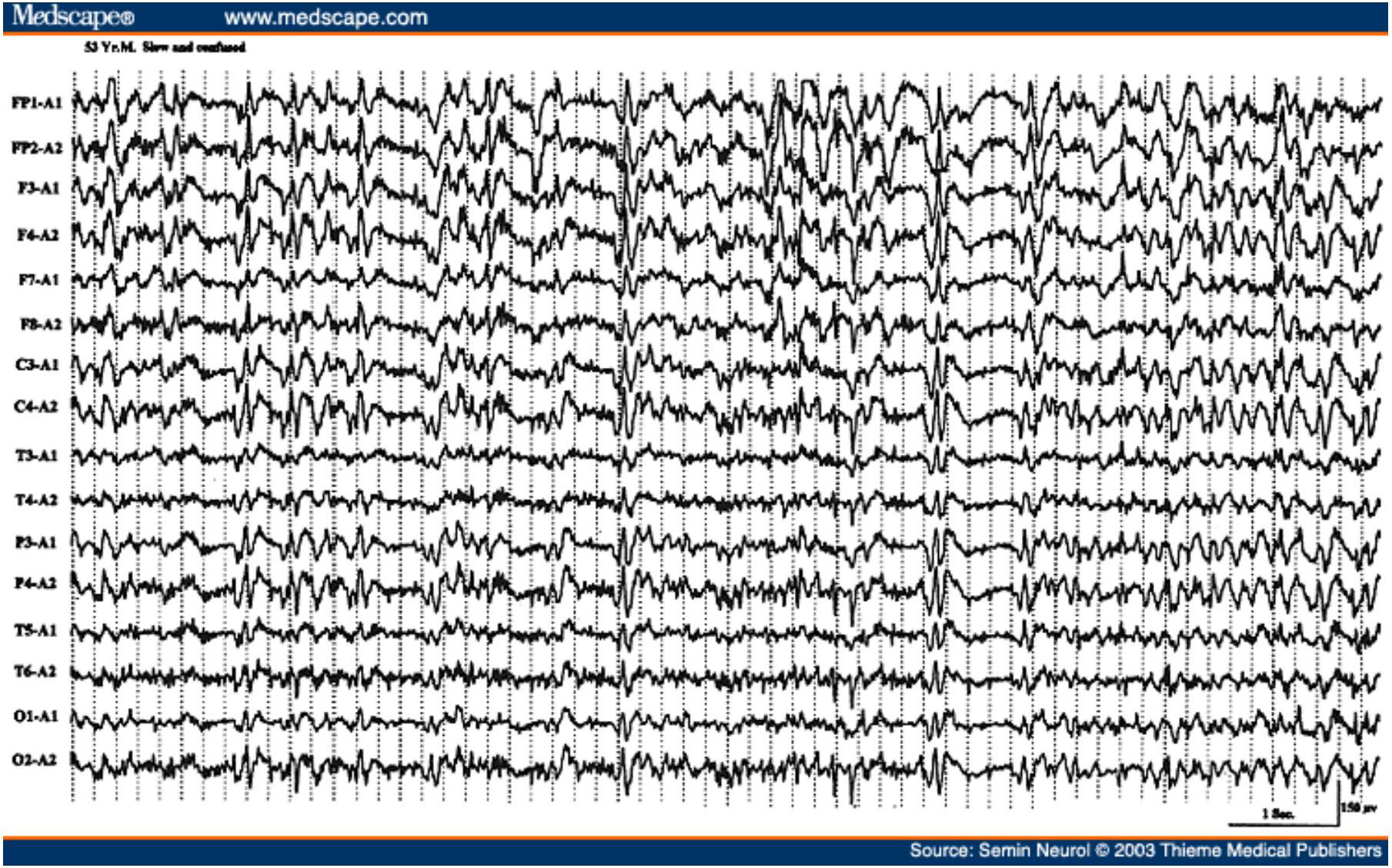
# Normal EEG


FP1-F7
F7-T3
T3-T5
T5-O1
FP1-F3
F3-C3
C3-P3
P3-O1
FP2-F4
F4-C4
C4-P4
P4-O2
FP2-F8
F8-T4
T4-T6
T6-O2
3A-Ref

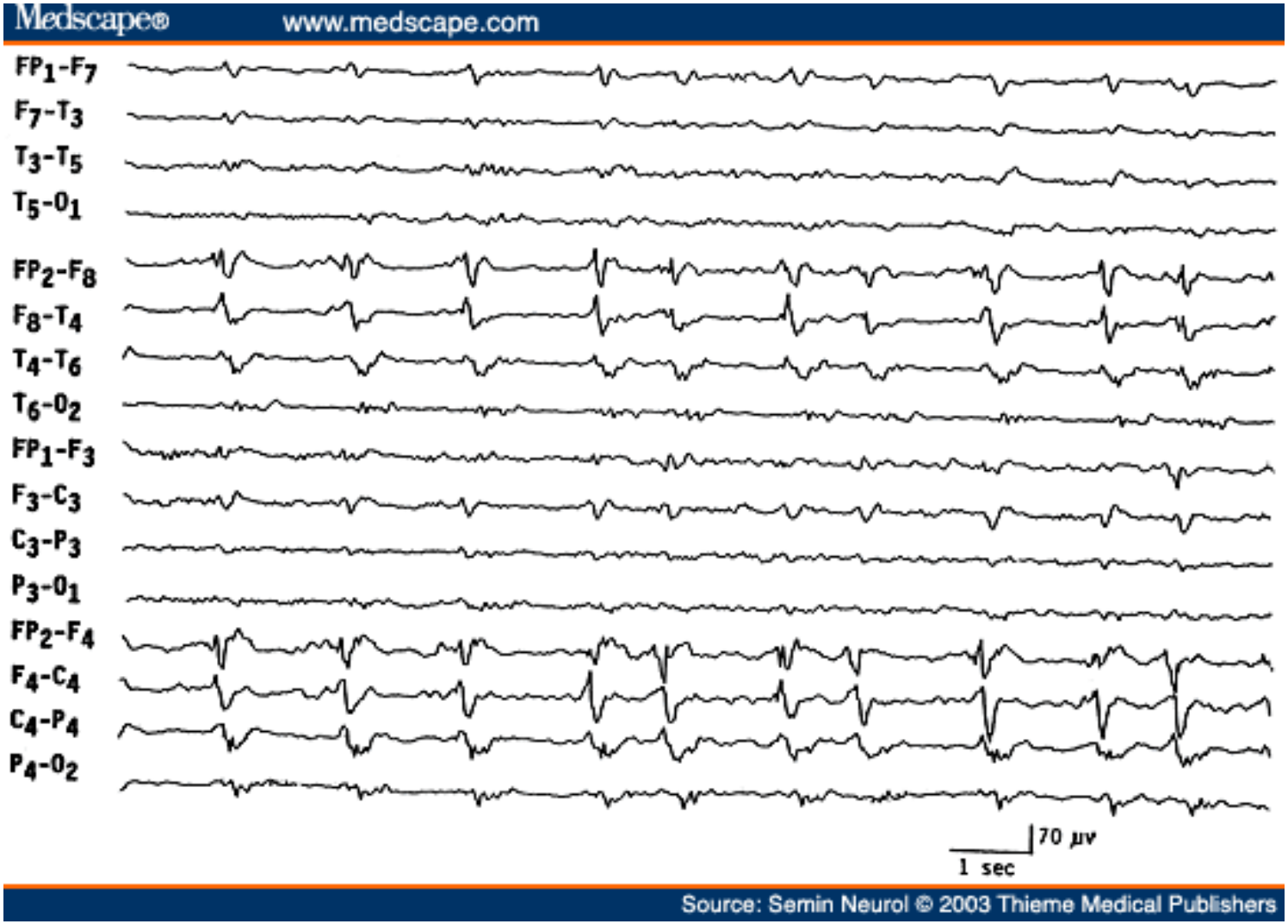



A. Alpha - L occipital B. Beta – L frontal C. Theta – L central
D. Delta – R parietal E. Spike wave – R occipital

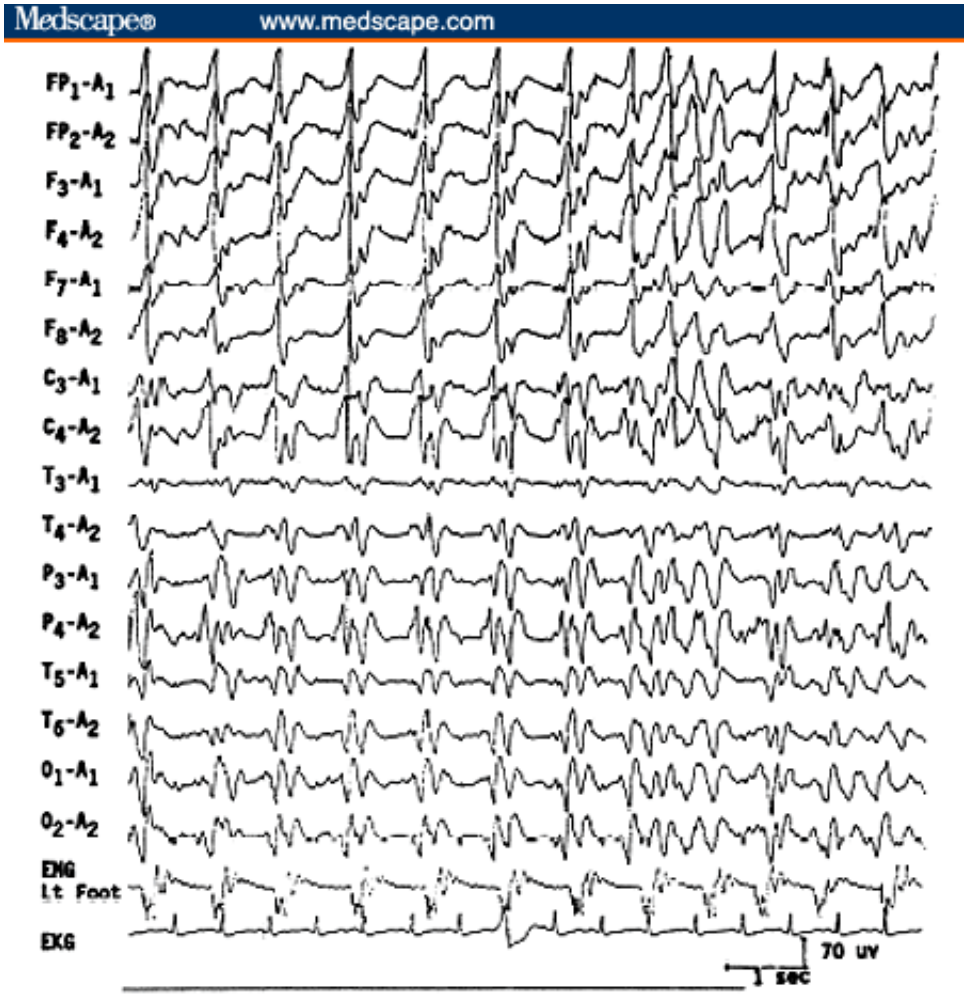
# Generalized Seizure



# PLEDs
# (R Temporal d/t HSV)



# Bisynchronous PEDS (post Anoxia)




49 yr. M. Comatose Anoxic Encephalopathy, Jerks of Lower Extremities (Lt > Rt)

Source: Semin Neurol © 2003 Thieme Medical Publishers

# Neuromuscular Conditions & Respiration

# Neuromuscular System & Respiration

- Conditions
  - Guillain-Barre (AIDP); Myasthenia Gravis
  - Spinal Cord Injury
- General Respiratory Issues
  - ABGs are not helpful
  - Use clinical exam and bedside PFTs (NIF & FVC)
  - Do NOT extubate too early
    - Usual parameters are not helpful
  - Assisted cough; Percussion & Postural Drainage (P & PD)
  - Anticholinergics for secretions

# Guillain-Barre Syndrome

- Acute inflammatory demyelinating PN (AIDP)
- Preceding trigger (60-70%)
  - Infection: Campylobacter jejuni; Viruses
  - Vaccinations
  - Surgical procedures
- Presentation (within 2 weeks of trigger)
  - Limb paresthesias followed by progressive weakness of legs before arms, proximal > distal
    - Difficulty with stairs, standing up, brushing hair and teeth
  - Cranial muscle weakness (>50%)
  - Diaphragmatic weakness/respiratory failure
  - Autonomic disturbances (arrhythmias, BP lability)

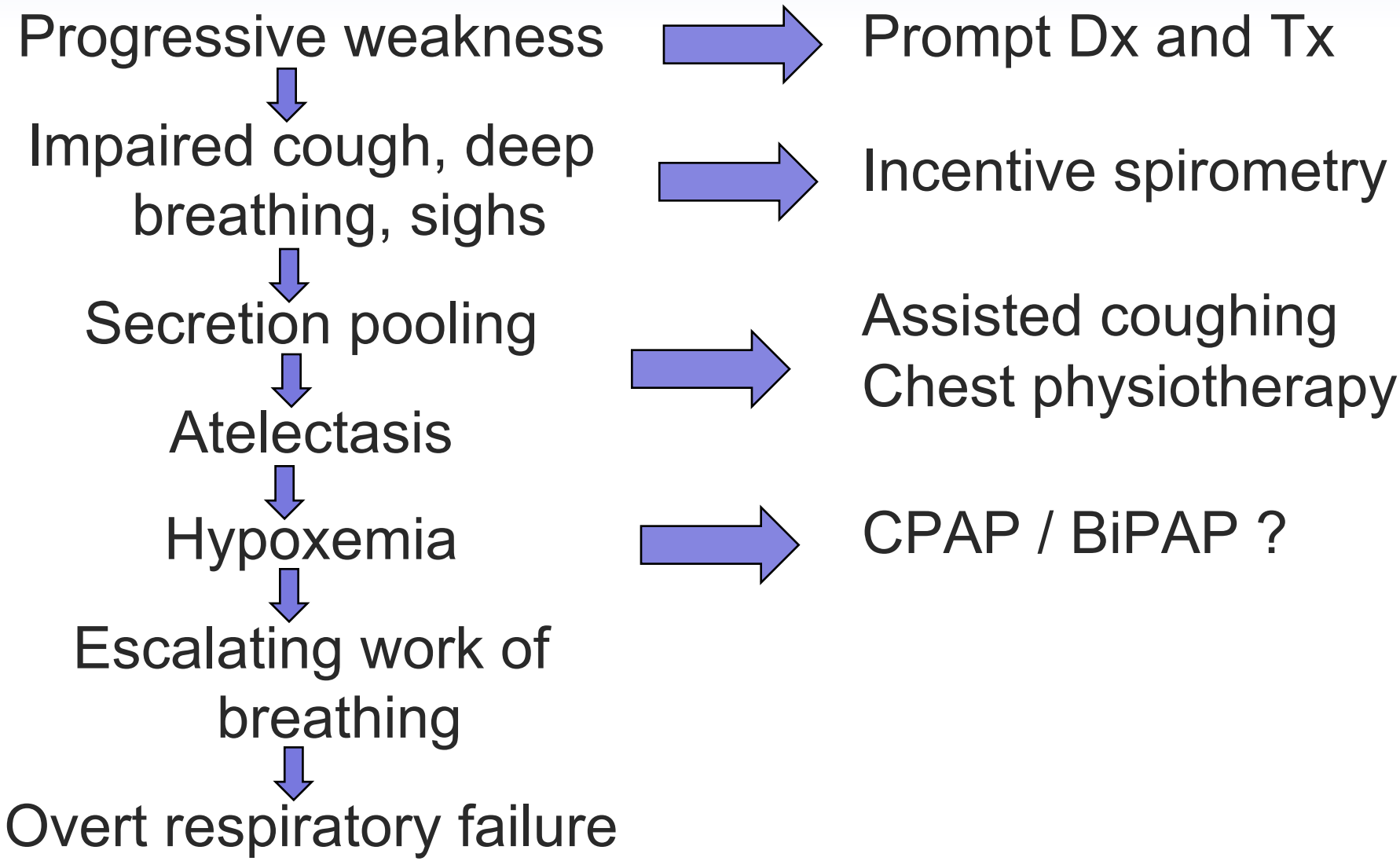
# Myasthenic Crisis

- Severe exacerbation of myasthenic symptoms with life-threatening bulbar symptoms
  - Respiration & swallowing difficulties result in ICU stay
  - Aspiration and dysphagia: NPO or modified diet
- Provocation?
  - Infection, systemic illness, surgery, labor / delivery, etc.
  - Drugs: antibiotics, cardiovascular, psychiatric, OCP, steroids (high dose, withdrawal),
- D/C Acetylcholinesterase inhibitors
    - Is it cholinergic crisis vs myasthenic crisis?
- Treatment: Plasmapheresis or IVIG
  - IVIG Adverse side effects: Anaphylaxis, rash, hyponatremia, aseptic meningitis, HA, DVT / PE, Pulmonary edema

# Signs of NM Respiratory Failure

- Agitation
- Interrupted speech patterns
- Tachypnea
- Tachycardia
- Hypertension
- Brow sweating
- Accessory respiratory muscle use
  - Paradoxical breathing pattern
  - Respiratory alternans

# Sequence of Respiratory Decline



# Neuromuscular: Pulmonary Care

- Why NOT use ABG?
  - pO2 does not change until imminent failure
  - pCO2 does not change until VC at 25% of normal
- Clinical examination triggers
  - Dyspnea/tachypnea; Somnolence; Paradoxical breathing; Use of accessory muscles; Bedside PFTs
  - FVC and NIF every 2 – 8 hours (bedside)
    - 15-20 cc/kg: ICU
    - 10-15 cc/kg: Voluntary Intubation
    - <10 cc/kg: Intubation
    - NIF: - 20 mm Hg
  - Bedside counting test
    - Normal > 70; Impaired < 40

# Ventilator Weaning

- Tracheostomy sometimes required
- Weaning approach
  - Avoid phenomenological empiricism
  - Anticipate improvement as neck and arm strength improves
  - Changes should be slow and gradual
  - End tidal CO2 monitoring can be helpful
  - Account for:
    - Patient anxiety
    - “Shift” mentality

# SCI Pulmonary Management

- Retrospective; cervical SCI, ASIA A, n=156
  - Tracheostomy performed in 107 (69%)
  - Factors associated with tracheostomy
    - Age (> 45), Co-morbidities, Prior lung disease, PNA
    - Higher cervical level:

| C2 or 3 | C4 | C5 | C6 | C7 |
|---|---|---|---|---|
| 100% | 81% | 64% | 45% | 3% |

*Harrop JS, et al. J Nsurg (Spine 1) 2004;100:20-23*

- Retrospective; cervical SCI, n=119
  - Tracheostomy required in 32/45 complete (71%) & 26/74 incomplete (35%)
  - Injury level

| | Definitive airway | Tracheostomy |
|---|---|---|
| C1 – C5 | 100% | 100% |
| C6 – C8 | 79% | 50% |
| Incomplete | 35% | 7% |

*Como JJ, et al. J Trauma 2005;59:912-916.*

# SCI: Management of Respiratory Dysfunction

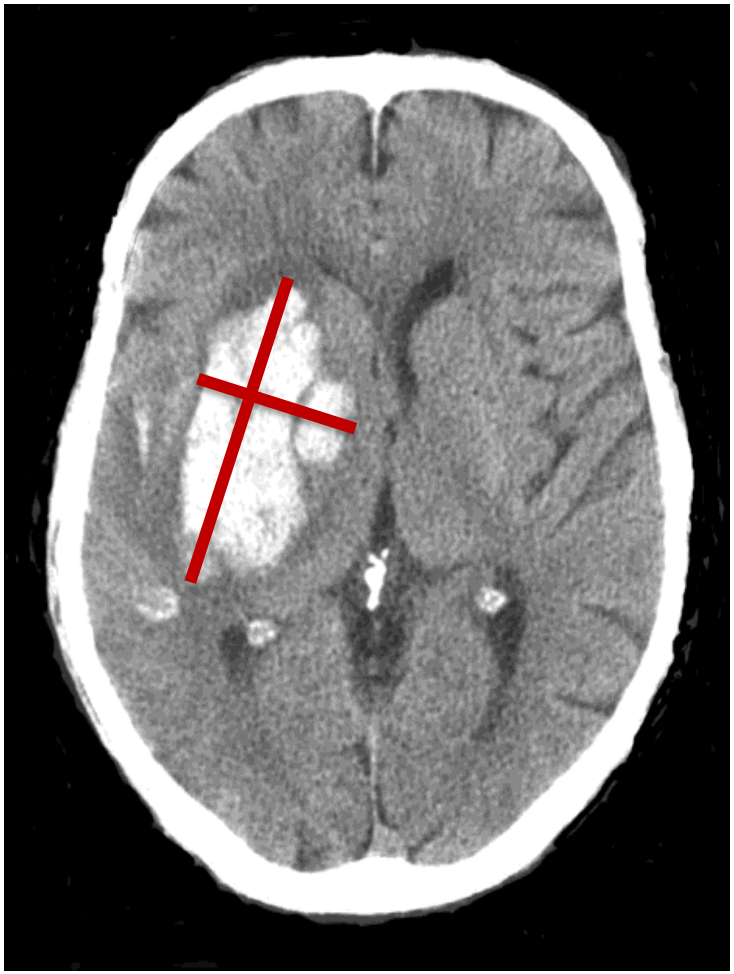
- Dyspnea / breathlessness occurs with cervical or thoracic level lesions
  - May be related to level of fitness
- Interventions
  - Respiratory muscle training / pacing
  - Abdominal binder
  - Ventilator assisted speech
  - Assisted Cough
  - In-exsufflator
  - Bronchoscopy

# Pearls

# Blood in Head

- Primary goals
  - Stop bleeding: reversal, BP control
  - Prevent secondary injury: seizure, glucose, fever control
  - Prepare for surgical intervention
- Cerebellar ICH
  - If more than 30ml, consider a neurosurgical emergency
- Reversal
  - FFP; Vitamin K
  - PCC; Factor VII
- BP control
  - IV agents.  Goal will vary.

# Measuring an ICH



- A = length
- B = width
- C = height
  - How many cuts?
  - Each cut = 5mm (usually)
- Volume = (A x B x C) / 2
- Key Volumes
  - < 30 ml = small
  - 30 – 60 = moderate, where?
  - > 60 ml = not good

# Critical Illness Myopathy or Polyneuropathy

- CIP = Critical illness polyneuropathy
  - Acute axonal sensorimotor polyneuropathy
- CIM = Critical illness myopathy
  - Acute myopathy: atrophy and necrosis
- CIP and CIM often occur together (CIP>CIM)
- Present > 50% critically ill ventilated > 7 days
  - Often detected when patient can't be weaned
  - Symmetrical, flaccid quadriparesis, atrophy
  - Decrease or absence of DTR's
  - CK may be normal

# Critical Illness Myopathy or Polyneuropathy

- Risk Factors
  - Mechanical ventilation
  - SIRS / Sepsis
  - ARDS
  - Pneumonia
  - Severe asthma in conjunction with high dose steroids
  - Multi-system organ failure
  - Hyperglycemia*
  - Meds: Nondepolarizing blocking agents +/- steroids; Aminoglycosides

# *Questions?*

# UPMC Critical Care

www.ccm.pitt.edu