Essentials of Neurocritical Care for the Neurosurgical Patient

Lori A. Shutter, MD
lori.shutter@uc.edu
Director, NSICU/Neurocritical Program
Assoc. Professor, Clinical Neurosurgery & Neurology
University of Cincinnati Medical Center
Disclosures

- Grants / Research
  - NIH, DoD
  - UCB Pharma
Topics

- What is a Neurointensitivist?
- Respiratory: Breathe Deep
- Infections: What bugs are in your home?
- Cardiac: Under Pressure; Keep the Beat
- Blood / Electrolytes: Spice of Life
- Seizures: No Shaking Necessary
- General: A Pound of Prevention
- Outcomes: Nihilism or Hopefulness
Modern Intensive Care

- “Intensive-care medicine has become the art of managing extreme complexity—and a test of whether such complexity can, in fact, be humanly mastered.”

  Atul Gawande, The New Yorker, 1/6/08

- Bundles; Check lists; Time Outs
- Protocols; Guidelines; Evidence-based Care
- Multidisciplinary; Collaborative
- JACHO; CMS
What is a Neuro-intensivist?

- A physician devoted to comprehensive multisystem care of the critically ill neurological patient.
  - Assumes a primary care role for patients in the ICU, coordinating both **neurological & medical** management.
  - Has a unique concern with the interface between brain and other organ systems in the setting of critical illness.
  - Takes on responsibility for various elements of ICU care that might otherwise be provided by multiple subspecialists (i.e. cardiology, endocrinology, infectious diseases, pulmonary medicine, and neurology).
  - Proficiency with standard ICU monitoring, as well as specialized neuro-monitoring and interventions.
Are Neurointensivists Needed?

- Disclosure: I am biased on this topic

- Advances in the treatment of neurological conditions
- Advances in critical care
- uniqueness of the neurological patient
- Increased patient / family awareness
- Collaboration for professional & academic growth
- Multi-disciplinary team care
Neurocritical Care

- NCC recognized as ABPN subspecialty in 11/05
  - Neurointensivists added to Leapfrog’s ICU physician staffing definition of intensivists in 2008
- Dedicated Neuro-ICUs with fellowship trained neuro-intensivists in the US = 57*
  - 27 states; 45 cities & DC
- NCC Program Models
  - Division of Neurology vs Neurosurgery vs Anesthesiology
  - Department of Critical Care – Multidisciplinary
- Neuro-ICU models
  - Closed vs ‘Semi-closed’ vs Open
  - Primary providers vs Co-attendings vs Consultants
U.S. Cities with Neurocritical Care Units Staffed by Board-Certified/Eligible Neurointensivists, 2010

Not to scale, and cities with more than one unit have the number denoted in parentheses.
Neurocritical Care Training

- Fellowship Training Programs
  - 39 in the US (in 18 states)
  - 2 year training curriculum developed based on UCNS / ACGME guidelines
  - Program accreditation through UCNS starting in 2007. Currently, there are 25 accredited NCC Fellowship Training programs.
  - Training programs participate in the SF Match system

- Specialties eligible for training in NCC
  - Neurology, Neurosurgery, Emergency Medicine, Anesthesia, Internal Medicine, Pediatrics
  - Must learn to speak each others languages
NCC Training Requirements

- **Duration of training**
  - 12 months of ICU experience
  - > 50% focusing on primarily neurological & neurosurgical conditions
  - Recommend 18 – 24 months to provide adequate elective & off-service time*
    - Discussions underway with UCNS regarding a 1 year option for certain specialties / background training

- **Additional qualifications**
  - Provider / instructor in ACLS, ATLS, PALS, FCCS

- **Faculty**
  - Provide direct supervision in ICU
  - Demonstrate adequate training / experience in NCC
  - Minimum of 25% of time dedicated to NCC
Neurocritical Care Certification

- First UCNS certification exam was in 12/07
  - Eligibility through either fellowship or practice tracts
    - Fellowship tract: documentation of training in an accredited NCC fellowship program
    - Practice tract available til 2012
  - Current diplomates in NCC in US = 215

- Exam components
  - Neurological – 48%
  - General medical critical care – 47%
  - Procedural – 5%
Neurological Conditions

- Cerebrovascular
- Neurotrauma
- Seizures
- Neuromuscular diseases
- Neuro-oncology
- Infections
- Toxic-metabolic
- Inflammation / demyelination
- Encephalopathies
- Movement disorders
- Neuroendocrine
- Clinical syndromes
- Peri-operative neurosurgical care
- Neurorehabilitation
- Pharmacotherapeutics
General Medical Conditions

- **Cardiovascular**
  - Shock / resuscitation; Ischemia; Neurogenic Cardiac Abnormalities; Cardiac Arrhythmias; Hypertensive Crisis; Advanced cardiovascular monitoring & derived parameters

- **Pulmonary**
  - Respiratory failure; Pneumonitis / pneumonia; ARDS/ALI; Pulmonary edema; Pulmonary embolism Upper airway obstruction; COPD / asthma; Mechanical ventilation: modes, weaning, monitoring

- **Renal**
  - Fluids/electrolytes; Acute Renal Failure; Acid-base disorders; Rhabdomyolysis; UTI / Urosepsis

- **GI**
  - Bleed/perforation; Ileus; Obstruction; Liver failure; Pancreatitis
General Medical Conditions

- **Metabolic/Endocrine**
  - Nutrition; Thyroid function; Adrenal crisis; Diabetes; SIRS; Fever/thermoregulation

- **Infectious**
  - Sepsis; Antibiotics/Drug resistance; Hospital acquired infections; AIDS; Central fever

- **Hematologic**
  - Hemostasis defects; Blood component rx; Hemolytic disorders; Hypercoagulable states; DVT prophylaxis; Anticoagulation; Transfusion reactions

- **Miscellaneous**
  - Immunology; Transplantation; General Trauma; Burn management; Agitation; Monitoring; Prognostication
Procedural Competencies

- Central lines: arterial, venous, PA
- Airway Management: non-intubated; direct laryngoscopy; intubation; mechanical/CPAP/BiPAP ventilation
- Management of vasoactive medications; IV, IA & intraventricular thrombolysis; moderate hypothermia; conscious sedation & barbiturate anesthesia; plasmapheresis/IVIG
- Interpretation of neuroimaging studies; bedside pulmonary function tests
- Lumbar puncture; Shunt / ventricular drain tap
- Neuro-monitoring: ICP; CPP; PbtO2; SjvO2; management of EVDs; TCDs; EEGs
- CPR/ACLS (with certification)
Breathe Deep
Effectiev Airway Management

- Confirm airways early to prevent hypoxemia
  - Intubate patients with GCS ≤ 8 to avoid aspiration
  - Single dose of antibiotic within 12 hours

- Neuromuscular issues (SCI)
  - Follow NIF & FVC

- Modes of ventilation
  - Non-invasive modes to bridge: CPAP; BiPAP
  - Invasive modes: SIMV; PC; AC; APRV
  - Role of NO, ECMO, proning to improve oxygenation

- Tracheostomy early when indicated
  - Facilitates secretion removal, airway management, and transfer to rehabilitation
  - Requirements: PEEP < 8, FiO² < 50%, and able to lie HOB flat x 30 minutes
Mechanical Ventilation Goals

- Optimize cerebral oxygenation
  - Brain consumes 15% of body’s cardiac output and 20% of available O² to meet energy demands.
  - Low PbtO² has been associated with poor outcome*
  - Balance of brain versus pulmonary issues

- Hyperventilation
  - May treat ICP elevations at the cost of CBF

- Hypoventilation
  - Shifts the Hgb-O² saturation curve, thus facilitating O² delivery and improving PbtO²
  - Is there a role for permissive hypercarbia?

- Extubation requirements
  - Can they oxygenate, ventilate, & protect their airway?
  - A patient does not have to be following commands
ALI / ARDS

- Incidence is 20 – 25% in isolated TBI, ? in others
  - Associated with a 3x greater risk of death or VS
- Acute Lung Injury (ALI)
  - PaO₂/FiO₂ < 300; Mortality = 39%
- Adult Respiratory Distress Syndrome (ARDS)
  - PaO₂/FiO₂ < 200; Mortality = 40 – 50%
- Etiology
  - Sepsis/SIRS - Inhalation injury
  - Pulmonary Trauma - Drug toxicity
  - Aspiration - Pancreatitis
  - *Transfusions (TRALI)
- Contributing factors: vasopressors, high Vt
Transfusion Related ALI (TRALI)

- **Definition (2003)**
  - New occurrence of acute onset ALI (hypoxemia, CXR w/ bilateral infiltrates, no evidence of left atrial hypertension) emerging during or within 6 hours of end of transfusion
  - No alternative ALI risk factors

- Incidence rates per RBC unit = 1:5,000

- The number of TRALI-related fatalities reported has steadily risen from 1995
  - Now the most frequently reported cause of transfusion-related death

05/07/09 @ 14:35

Patient transfused with 1 U PRBC @ 2400
TRALI

Developed sudden increased $O^2$ requirements
Transfusion Related Infections (TRIM)

- Prospective, observational, cohort study.
  - N = 2,085 patients, 428 received transfusions.
- 2 groups: transfusion, & non-transfusion
  - Adjusted for probability of survival
- Infection Rate
  - Transfusion = 14%
  - Non-transfused = 6% (p < .0001)
- Mortality and LOS (ICU & hospital) also significantly higher in transfused pts

Transfusions

- The concept that maintaining a HCT > 30% has little empirical supportive evidence.
- There is clear evidence that blood transfusions have an adverse impact on outcome.

Therefore present recommendation should be:

- **Do not** transfuse if Hgb ≥ 9 g/dL
- **Do** transfuse if Hgb ≤ 7 g/dL
- For Hgb between 7 – 9 g/dL transfusion triggers should be based on physiological parameters
  - Volume status, hemodynamic state, EKG, cardiovascular disease, PbtO²
Pneumonia Risk

- Loss of consciousness & alcohol use increase risk of aspiration
- 109 patients with early onset pneumonia
  - Risk factors for pneumonia – nasal carriage of *Staph aureus*, aspiration prior to intubation, barbiturate use
  - Lower PaO²/FiO² ratio, more febrile days, more frequent hypotension, increased ICPs
    *(Bronchard R et al. Anes 2004;100:234-9)*

- Goals of care
  - Eliminate risk factors – ‘vent bundles’, oral care, hygiene
  - Early diagnosis
  - Early and appropriate antibiotic therapy
Antibiotics for Pneumonia

- Establish triggers for initiation of empiric antibiotics (usually a combination of 3):
  - Leukocytosis
  - Fever
  - Increasing O² requirements
  - Increasing secretions
  - Radiographic findings
  - Laboratory findings

- Bronchoscopy (BAL) vs PAL for cultures
  - Aspiration pneumonitis can mimic a pneumonia

- Use empiric agents that match ICU biogram

- Narrow antibiotics based on culture results.
  - Do not treat a colony count < 10k, hesitate on 10 – 50k.
What bugs are in your home?
Rational Antibiotic Therapy

- Every ICU has its own biogram
  - Ask unit director or ID!
- Give a single dose of antibiotics within 1 hour prior to any surgical procedure.
  - There is no clinical evidence to support the use of any other empiric antibiotics.
- If clinical indications of infection, culture then start broad spectrum antibiotics based on ICU biogram.
- Length of antibiotic therapy generally 7 – 10 days
  - Exception: ventriculitis, osteomyelitis
Empiric Antibiotics

- **Triggers (usually a combination of 3):**
  - Leukocytosis
  - Fever
  - Abnormal culture / radiographic findings
  - Clinical findings (hemodynamic instability suggestive of sepsis, hypoxia, secretions, wound drainage, etc.)

- **Culture results**
  - If negative at 72 hrs, stop antibx
  - If positive, narrow antibiotics based on results. Do not treat a colony count < 10k, hesitate on 10 – 50k.
  - Positive urine cx: change foley 24 hrs after antibx started
## ID Issues: All sites / All pathogens

<table>
<thead>
<tr>
<th></th>
<th>2007</th>
<th>N=1057</th>
<th>2008</th>
<th>N=1168</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Organism</strong></td>
<td><strong># / %</strong></td>
<td><strong>Organism</strong></td>
<td><strong># / %</strong></td>
<td></td>
</tr>
<tr>
<td>Staph aureus</td>
<td>120 / 11%</td>
<td>Staph aureus</td>
<td>206 / 18%</td>
<td></td>
</tr>
<tr>
<td>Coag neg staph</td>
<td>118 / 11%</td>
<td>Coag neg staph</td>
<td>128 / 11%</td>
<td></td>
</tr>
<tr>
<td>E. Coli</td>
<td>87 / 8%</td>
<td>E. Coli</td>
<td>53 / 8%</td>
<td></td>
</tr>
<tr>
<td>Enterococcus</td>
<td>60 / 6%</td>
<td>MRSA</td>
<td>68 / 6%</td>
<td></td>
</tr>
<tr>
<td>H. flu</td>
<td>41 / 4%</td>
<td>E. faecalis</td>
<td>53 / 5%</td>
<td></td>
</tr>
<tr>
<td>Candida albicans</td>
<td>32 / 3%</td>
<td>Klebsiella</td>
<td>37 / 3%</td>
<td></td>
</tr>
<tr>
<td>Klebsiella</td>
<td>30 / 3%</td>
<td>H. flu</td>
<td>36 / 3%</td>
<td></td>
</tr>
<tr>
<td>MRSA</td>
<td>30 / 3%</td>
<td>Proteus</td>
<td>34 / 3%</td>
<td></td>
</tr>
<tr>
<td>Pseudomonas</td>
<td>30 / 3%</td>
<td>Candida albicans</td>
<td>30 / 3%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pseudomonas</td>
<td>30 / 3%</td>
<td></td>
</tr>
</tbody>
</table>
Develop Unit Based Empiric Regimens

<table>
<thead>
<tr>
<th>Site</th>
<th>Antibiotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>VAP</td>
<td>Vancomycin + cefepime</td>
</tr>
<tr>
<td>Meningitis</td>
<td>Vancomycin +/- ceftriaxone</td>
</tr>
<tr>
<td>Ventriculitis</td>
<td></td>
</tr>
<tr>
<td>UTI</td>
<td>Nitrofurantoin# or Bactrim or ciprofloxacin</td>
</tr>
<tr>
<td>Bacteremia</td>
<td>Vancomycin + cefepime</td>
</tr>
</tbody>
</table>

# Contraindicated in CrCL < 60ml/min; use care in elderly

- Increasing incidence of MDR bacteria
- Rational antibiotic use
  - Narrow coverage whenever possible
  - Set duration of therapy
Under Pressure

“Give me your wallet. And the name of your antiperspirant.”
Vasopressors in the ICU

- What are you treating?
  - CPP, Septic shock, Vasospasm, Neurogenic heart

- What are your options
  - Phenylephrine (Neosynephrine) – $\alpha$ effects
  - Norepinephrine (Levophed) – mixed $\alpha$ & $\beta$ effects
  - Dobutamine – inotrope
  - Vasopressin dose = 0.04 u/min (do not titrate)

- Consider adrenal insufficiency.
  - Stress dose steroids: hydrocortisone 50 mg q 8 hrs

- Lactic acid level are elevated in sepsis
Why Not Dopamine?

- Dopamine was considered an essential drug in ICUs
  - Cardiovascular effects and protective effects on renal function & mucosal perfusion (supposedly)

- Recent data:
  - Ineffective in prevention/treatment of ARF or gut protection

- Adverse effects:
  - Induces renal failure in normo- and hypovolemic patients
  - Impairs mucosal blood flow
  - Aggravates reduced gastric motility
  - Suppresses secretion & function of anterior pituitary hormones, thus aggravates catabolism and cellular immune dysfunction and induces central hypothyroidism.
  - Blunts ventilatory drive, thus ↑ risk of respiratory failure
Septic Shock

- **Goals**
  - MAP of 65
  - SV 0.7-1 ml/kg
  - CVP 8 – 12
  - UOP > 0.5 ml/kg

- **Initial treatment: isotonic crystalloids**
  - Should see a response in 30 min

- **Norepinephrine (Levophed)**
  - Peripheral vasoconstrictor (α1/2) & potent inotrope (β1>2)
  - Cardiac effect may vary
  - If norepinephrine > 10 mcg/min, then

- **Vasopressin**
  - If remains hyperdynamic w/ impaired heart function, then

- **Inotrope**
  - Dobutamine (1st); Epinephrine
  - Combining therapies may maintain CO & MAP
CPP Driven Therapy

- CPP Goals: Management of Severe TBI guidelines
  - CPP goal = 50 – 70 mm Hg
  - Review medications, stop / ↓ those that lower BP or affect heart function

- Goal related fluid resuscitation may result in very high volume infusions. Monitor cardiac & respiratory effects
  - Addition of bicarbonate to fluids has no proven benefit.

- Remember vasopressors may contribute to increased pulmonary injury and ARDS

- Vasopressor must be used cautiously with HTS
SAH Related Issues

- Vasospasm Triple H therapy
  - Phenylephrine for hypertension
  - Dobutamine for hyperdynamic state
  - Norepinephrine for both (2 for 1)
  - Vigileo monitor / FloTrac sensor
    - Option for non-invasive monitoring of CCO, SV, SVV, & SVR through an existing arterial line
    - Vasopressors may contribute to increased pulmonary injury and ARDS

- Neurogenic Stress Cardiomyopathy
Keep the Beat

Atrial Fibrillation with rapid ventricular response

Irregularly irregular. No p-waves
Rapid ventricular rate = 177

These beats are abarely conducted

There is some ST depression V4 V5 V6
Cardiac Issues: Incidence Data

Presence of cardiac abnormalities

- **SAH**
  - 76% (95% CI 73-90) of patients
  - Irrespective of preexisting heart disease

- **AIS / ICH**
  - 90% of all patients
  - Lower when exclude pre-existing cardiac disease

Neurogenic Stress Cardiomyopathy

- AKA “neurogenic stunned myocardium”
- Develops within hours of SAH, etc.
  - Sudden death in 12% of SAH
  - Post-menopausal females
  - May see in AIS and other neurological conditions

- Spectrum of severity

- Clinical features
  - Substernal chest pain; dyspnea; cardiogenic shock
  - CXR with pulmonary edema
  - Elevated cardiac markers
    - Troponin I peaks on day of rupture
    - BNP
Neurogenic Stress Cardiomyopathy

- **Clinical features**
  - **EKG changes**
    - 25-75% of patients with SAH
    - Sinus brady or tachy, ST abnormalities, T wave inversions, QTc prolongation
    - Arrhythmias: A-fib, A-flutter, SVT, PVCs, junctional rhythms, ventricular rhythms
  - **Echo**
    - Regional wall motion abnormalities beyond single vascular territory
    - Apical ballooning akinesis or dyskinesis
    - Reduced LVEF
  - Normal coronary angiogram
Neurogenic Stress Cardiomyopathy: Pathogenesis

- Coronary artery spasm
  - Normal angiography
- Microvascular dysfunction
  - Normal perfusion ↑
- Catecholamine hypothesis
  - Direct myocardial toxicity
  - Microvascular myocardial contraction band necrosis
    - ↑ norepinephrine levels

Lee et al. Neurocrit Care 2006
Neurogenic pulmonary edema

- Lung edema of noncardiogenic origin
  - Normal PCWP
- Cause
  - Increased vascular permeability?
- Overlap
  - SAH patients with ‘neurogenic pulmonary edema’ have evidence of concomitant acute myocardial injury
    - Reduced LV function, initially normal PCWP that may worsen 19–60 hours after onset
Neurogenic Stress Cardiomyopathy

- **Management**
  - Supportive
    - Diuretics; low dose beta-blockers
    - Pump dysfunction: inotropes; IABP
  - Limit exogenous catecholamines
  - Be wary of vasospasm

- **Prognosis**
  - Increased in-hospital mortality
  - Increased risk of vasospasm
  - Potential for complete recovery of LV dysfunction
# Atrial Fibrillation

- Most common arrhythmia in general population
- **Causes**
  - Structural heart disease, CAD, HTN, pulmonary disease, thyrotoxicosis, post cardiac surgery
- **Management**
  - Rate Control $\leq 100$ bpm
  - If unstable & duration $< 48$ hrs: Cardioversion

---

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diltiazem</td>
<td>0.25 mg/kg over 2 min; then infuse at 5 – 15 mg/hr x 24 hrs</td>
</tr>
<tr>
<td>Esmolol</td>
<td>500 mcg/kg over 1 min; then 50 mcg/kg/min</td>
</tr>
<tr>
<td>Metoprolol</td>
<td>2.5 – 5.0 mg IV</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>300 mg over 15 min; then 45 mg/hr for 24 hours</td>
</tr>
</tbody>
</table>
Spice of Life

UNIMPRESSIONED
If you want to thrill me, bring me an empty paper sack.
Electrolytes

- **Glucose**
- **Sodium**
  - Determination of volume status is critical
- **Potassium**
  - May transiently increase with traumatic tissue injury or underperfusion
  - Increased filtered/excreted $K^+$ with elevated aldosterone may cause overall $K^+$ depletion
- **Magnesium**
  - Potential neuroprotectant but the Phase III study showed no benefit
Hyperglycemia

- Associated with increased mortality & morbidity

- Effects in injured brain:
  - Increased acidosis, release of excitatory amino acids, increases edema formation, disrupts blood-brain barrier, increased risk of hemorrhage

- Systemical effects:
  - increased risk of infection, impaired wound healing

- Early, tight glucose control has been shown to improve clinical outcomes after MI & surgery.
Glucose Control: Good?

- **Trauma: 516 patients**\(^1\)
  - Early hyperglycemia = BG elevation in first 48 hours
  - Glucose > 200 mg/dL associated with higher infection and mortality rates independent of injury characteristics

- **Severe TBI: 63 patients**\(^2\)
  - Conventional vs intensive glucose control
  - Intensive: significant ↓ mean/max ICP; fewer seizures

- **Stroke: 25 patients**\(^3\)
  - Measures: MRI infarct volume & clinical outcome
  - ↑ BG associated w/ worse outcomes & ↑ infarct volume

- **ICH: 764 patients**\(^4\)
  - Hyperglycemia = BG ≥ 130
  - DM & hyperglycemia: independent predictors of outcome, ↑ risk of infection & CNS complications

---

Glucose Control: Bad?

- Severe TBI; loose vs tight glucose control
  - Non-randomized, consecutive design (n=47)
  - Microdialysis measures of cerebral glucose
  - Tight control decreased cerebral glucose by 70% vs 33%.
  - Other signs of cellular distress:
    - ↑ glutamate
    - ↑ L:P ratio
    - ↑ global O² extraction

Glucose Control: Bad?

- 228 TBI patients (GCS 3 – 15)
  - No demographic differences
  - Different goal glucose ranges during 2 time periods:
    - 5 – 8 mmol/l (90-144 mg/dl)
    - 3.5 – 6.5 mmol/l (63-117 mg/dl)
- Lower glucose range showed
  - ↑ ICP in 1st wk (14 vs 12 mmHg; \( P < 0.001 \))
  - ↑ mortality in 1st 2 wks (25% vs 19%; NS)

Take Home: Goal glucose = 80 – 140 mg/dl

No Shaking Necessary
Seizure Incidence in the ICU

- Retrospective review of 570 patients undergoing continuous EEG in the Neuro-ICU
- All were on prophylactic anticonvulsants
- Indication for monitoring:
  - Unexplained decrease in LOC
  - Detection of subclinical seizures
- Time to 1st seizure:
  - 88% within 24 hrs; 93% within 48 hrs
- Seizure frequency
  - Seizures occurred in 110 patients (19%)
  - 101 of these 110 patients (92%) had only NCSE

## Seizure Incidence in the ICU

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>N</th>
<th>Any Sz (%)</th>
<th>NCS (%)</th>
<th>NCSE (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epilepsy</td>
<td>51</td>
<td>17 (33)</td>
<td>16 (31)</td>
<td>10 (20)</td>
</tr>
<tr>
<td>CNS Infection</td>
<td>35</td>
<td>10 (29)</td>
<td>9 (26)</td>
<td>6 (17)</td>
</tr>
<tr>
<td>Brain Tumor</td>
<td>43</td>
<td>10 (23)</td>
<td>10 (23)</td>
<td>5 (12)</td>
</tr>
<tr>
<td>SAH</td>
<td>108</td>
<td>20 (19)</td>
<td>19 (18)</td>
<td>14 (13)</td>
</tr>
<tr>
<td>TBI</td>
<td>51</td>
<td>9 (18)</td>
<td>9 (18)</td>
<td>4 (8)</td>
</tr>
<tr>
<td>↓ LOC (NOE)</td>
<td>105</td>
<td>17 (17)</td>
<td>16 (15)</td>
<td>5 (5)</td>
</tr>
<tr>
<td>ICH</td>
<td>45</td>
<td>6 (13)</td>
<td>6 (13)</td>
<td>4 (9)</td>
</tr>
<tr>
<td>CVA</td>
<td>56</td>
<td>6 (11)</td>
<td>5 (9)</td>
<td>4 (7)</td>
</tr>
</tbody>
</table>

cEEG at TUH

- NCC team member must request
- Indications
  - Not waking up after sz or SE
  - Transfer for refractory SE or to r/o NCSE
  - ICU: recurring activity suspicious for sz
  - ICU: AMS without clear explanation
  - Assess spells in comatose pts
- Duration:
  - 24 hrs if awake
  - 72 hrs for all others
Treatment of Seizures in the ICU

- What are you treating?
  - Prophylaxis
  - Seizures – convulsive or non-convulsive
  - Status – convulsive or non-convulsive

- Status is a neurological emergency
  - Seizures should be controlled within 60 minutes.
  - If not – treatment urgency needs to increase, aim for burst suppression within next 1 – 2 hours
  - Do NOT hesitate to go to pentobarbital

- IV formulations
  - Benzodiazepines: midazolam, lorazepam
  - Phenytoin, Levetiracetam, Phenobarbital, Valproate
Seizure Prophylaxis: TBI

- **Severe TBI (GCS < / = 8):**
  - No witnessed seizures, or immediate seizures in 1st 24 hours after injury: 7 days of therapy then stop.
  - Witnessed seizures, or seizure activity on EEG, occurring 1 - 7 days after injury and easily controlled: continue AED x1 mo, f/u EEG & refer to epileptologist
  - Refractory seizures, or seizure activity on EEG, occurring 1 – 7 days after injury: continue the AED(s) and refer the patient to the epilepsy clinic for follow-up.
  - Witnessed seizures, or seizure activity on EEG monitoring, developing beyond 7 days after injury = post-traumatic epilepsy. Continue AED(s) for a minimum of 3 months & refer to an epileptologist
Seizure Prophylaxis: TBI

- **Moderate TBI (GCS 9 – 12)**
  - There are no recommendations for AED use, and empiric use not indicated. If there is a lot of blood in the head, or the patient had a seizure, you can follow the guidelines for severe TBI listed above.

- **Mild TBI (GCS 13 – 15)**
  - Empiric use of AEDs is not recommended. If a patient has a seizure, then a consult should be obtained from either the NCC team or one of the epileptologists for advice as the data on seizures after TBI is different than general neurology patients.
Seizure Prophylaxis

- **SAH**
  - No witnessed seizures, or immediate seizures in 1st 24 hours: 3 – 7 days of therapy then stop.
  - Witnessed seizures, or seizures on EEG, occurring 1 - 14 days after injury: continue AED & refer to epileptologist

- **Brain Tumors**
  - Pre-op start on LEV
  - Postoperative
    - No seizures & no adjuvant rx – stop AED post-op d7
    - No seizures & plans for adjuvant rx – continue AED
    - Known seizures/high-risk patients – continue AED + Ativan 1 mg IV Q6 for 24-48 hours
TUH NSICU: General Patient Data

- Retrospective review
  - All NSICU admissions 9/03 to 9/04 (n = 552); NO cEEG
  - 379 patients were treated with AEDs
    - 358 (94%) were included in the study
    - 125 patients received LEV as adjunct therapy

- Breakthrough seizure occurrence
  - 2 (1.6%) patients on LEV
  - 8 (2.2%) patients on PTN, VPA or PB

- Complication data
  - 268 (75%) had complications; ≥ 2 complications in 28%
  - LEV alone vs other AEDs = 33 vs 73% (p = 0.001)
  - Encephalopathy: LEV vs others: 0 vs 7 – 34% (p = 0.009)

Szafarz J, et al. NCC 2007;7:140-147
# Prophylactic AEDs

<table>
<thead>
<tr>
<th>Patient Characteristic</th>
<th>LEV dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age: &lt; 65 years Normal renal function</td>
<td>LEV 1000 mg po BID (N/V with above dose, ↓ to 500 mg po BID)</td>
</tr>
<tr>
<td>Age: &gt; 65 years Normal renal function</td>
<td>LEV 500 mg po BID (N/V with above dose, ↓ to 250 mg po BID)</td>
</tr>
<tr>
<td>Renal dysfunction</td>
<td>If creatinine &gt; 1.5 then LEV 500 mg po BID</td>
</tr>
<tr>
<td></td>
<td>If creatinine &gt; 2.5 then LEV 500 mg po daily</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>LEV 500 – 1000 mg po daily. Dose after dialysis</td>
</tr>
<tr>
<td>Heavy ETOH use, psych disorders or anxiety</td>
<td>LEV 500 mg po BID; or consider a different medication like PTN, CBZ, OXC or VPA for mood effects</td>
</tr>
</tbody>
</table>
Status Epilepticus

- **Definition:**
  - Traditional: Any type of seizure lasting > 30 minutes, or 2 or more sequential seizures without full recovery of consciousness between them *(JAMA 1993)*
  - *Modern: any seizure lasting > 10 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
Status Management

- **Continuous infusions**
  - Midazolam. If slow to respond, go to pentobarbital
  - Pentobarbital
  - Propofol. Distant third choice as seizure control is hard to maintain

- **EEG recommendation:**
  - Infusions may be started without EEG running, but a cEEG must be made available ASAP
  - EEG burst general rule: 1 – 2 seconds of ‘burst’ separated by 3 – 8 seconds of suppression (no data to support this).

- **Epileptologist consultation**
  - Any patient not responding to initial 24 hrs of treatment

- **Supplemental seizure control**
  - Supplement initial AED, many options but prefer IV
Pound of Prevention

What, can't handle a little head trauma?

SUZUKI

dribbleglass.com
Reversal of Anticoagulation

- Discontinue warfarin; Target INR < 1.5
  - It may be difficult to achieve with FFP & vit K
  - FFP 15 – 20 mL / kg
  - Vitamin K, 10 mg IV. May repeat Q 8 – 12 hours for 1-2 days based on INR
  - Prothrombin Complex Concentrate (if available)
  - Recombinant Factor VIIa (selected patients?)

- If PTT > 50
  - Protamine 50 mg IV

- Platelet dysfunction
  - Thrombelastography testing
Is Fever Good?

- Natural response to inflammation and infection
  - Kills bacteria
  - Increases immunity
  - Improves survival.
  - Treating fever can increase mortality
  - Inflammation is necessary for regeneration and repair
  - Glial scars may contain a lesion
Is Fever Bad?

- Injured brain cells have reduced tolerance to heat
  - Hyperthermia accelerates ischemic injury
  - Glial scar limits axonal sprouting

- Meta-Analysis
  - Pooled analyses of 39 studies involving 14,431 patients
  - Fever / ↑ temperature associated with worse outcomes

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>No. of Articles/ Hypotheses*</th>
<th>Total N</th>
<th>Zc†</th>
<th>Effect Size‡</th>
<th>RR</th>
<th>Fever/Higer Body Temperature Associated Significantly With</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>24/24</td>
<td>10,460</td>
<td>6.31</td>
<td>0.46</td>
<td>1.5</td>
<td>Death</td>
</tr>
<tr>
<td>GOS</td>
<td>9/11</td>
<td>1625</td>
<td>3.66</td>
<td>0.26</td>
<td>1.3</td>
<td>Neurological deficit/death</td>
</tr>
<tr>
<td>BI</td>
<td>8/10</td>
<td>2841</td>
<td>4.85</td>
<td>0.65</td>
<td>1.9</td>
<td>More dependence</td>
</tr>
<tr>
<td>mRS</td>
<td>5/5</td>
<td>1423</td>
<td>−27.6</td>
<td>0.89</td>
<td>2.2</td>
<td>Lower functioning</td>
</tr>
<tr>
<td>CSS</td>
<td>5/8</td>
<td>910</td>
<td>6.09</td>
<td>0.35</td>
<td>1.4</td>
<td>Greater severity</td>
</tr>
<tr>
<td>ICU LOS</td>
<td>6/6</td>
<td>5418</td>
<td>48.48</td>
<td>1.66</td>
<td>2.8</td>
<td>Longer ICU stay</td>
</tr>
<tr>
<td>Hospital LOS</td>
<td>3/3</td>
<td>4468</td>
<td>39.55</td>
<td>1.53</td>
<td>3.2</td>
<td>Longer hospital stay</td>
</tr>
</tbody>
</table>

Therapeutic Hypothermia

Known Benefit
- Cardiac Arrest***

Uncertain Benefit
- Traumatic Brain Injury
- Acute Ischemic Stroke
- Acute Spinal Cord Injury
Methods for Cooling

Alsius

Artic Sun
Fever Summary

- Fever is a natural response
- Fever has poor prognostic implications in neurological patients
- No prospective randomized trials show a benefit to fever control

So what to do?
- Induced normothermia
- Develop trials
NSICU DVT Prophylaxis

- **Timing**
  - Start 24 hr after admission or neurosurgical procedure
  - Exclusions:
    - Follow-up CT shows hemorrhagic changes. In this situation, start prophylaxis once CT is stable.
    - Known unsecured AVM
    - Planned surgical intervention within 24 hours
    - Uncorrected coagulopathy
    - Spinal surgery (wait until 72 hrs post-op)
  - Hold for 4 hrs prior to removal of ICP or Licox monitor, lumbar drain
NSICU DVT Prophylaxis

- **Method:**
  - Mechanical prophylaxis on everyone
  - SQ heparin for cranial patients
  - LMWH for spinal and trauma patients
  - Empiric IVC filters in: hypercoagulable states or bleeding disorders that limit use of heparin or LMWH

- **Surveillance:**
  - Duplex study of lower extremities on 3rd day after admission, then weekly
  - D-dimers
  - Anytime if clinical symptoms or suspicion are present

- **Duration:**
  - May be discontinued once ambulating >/= 150’.
DVT / PE Treatment

- **Below knee DVT**
  - ↑ surveillance to every 3 days to monitor propagation. If stable on 2 repeats, return to weekly

- **Above knee / propagating DVT or PE**
  - Therapeutic anticoagulation vs IVC filter: this *always* warrants a discussion with attending(s).
  - Non-surgical patient with stable head CT: anticoagulation
  - Surgical patient: IVC filter if < 14 days post-op
  - Hemorrhagic conversion of AIS: ??
  - Endovascular patient: possible anticoagulation
GI Bleeding

- Low incidence
- Prophylactic Antacids or H2 blockers
  - Decreased gastric acidity may reduce gastric erosions and aspiration acidic injury
  - Changes in gastric acidity may remove a barrier to nosocomial infection
  - Some older studies report that antacids are equal to H2 blockers in prevention
  - Sucralfate may be beneficial, but reduces absorption of medications

- New Protocol for NSICU*
  - Use is based on 1 major or 2 minor indications
Stress Ulcer Prophylaxis

- **All** other patients **DO NOT** require SUP.
  - Who does? Those with 1 ‘Major’ or 2 ‘Minor’ indications

**Major Indications**
- Mechanically ventilated (predict > 48 hours)
- Coagulopathy:
  - Plts < 50k/mm³; INR > 1.5; PTT > 2 x control

**Minor Indications**:
- Severe TBI; Acute SCI; Septic shock or pressors > 8 hrs; occult bleeding x 6d; MOF (>3); hx of GIB in last year; high dose steroids; major surgery; acute hepatic failure; acute renal insufficiency
Stress Ulcer Prophylaxis

- **Treatment:**
  - Histamine-2 receptor antagonist (H2RA) (i.e. famotidine)
  - Proton pump inhibitor (PPI)*
    - * When to use a PPI? If it was a home medication; or there is evidence of current GI bleeding (hematemesis, coffee ground aspirates, hematochezia, or melena)

- **When to stop?**
  - When risk factors are no longer present

- **Rationale:**
  - Not always indicated (i.e. risks of ulceration not present)
  - ↓ risk of drug related adverse events (c.diff., PNA)
  - ↓ risk of drug-drug interactions (CYP 450 mediated, absorption issues)
  - Improve cost efficacy

Shaun P. Keegan, Pharm.D. 5/09
Transition to Rehabilitation

- Early consultation of rehabilitation specialties
  - PM & R involvement shortly after admission
  - Multidisciplinary rounds
  - PT, OT, Speech
  - Mobilization of patient

- Surgical interventions
  - Tracheostomy, PEG tube, IVC filter

- Facilitation of transfer to rehabilitation setting
  - Role of LTAC
Changing a Paradigm
# Current Neurological Monitoring

<table>
<thead>
<tr>
<th>CCU</th>
<th>NSICU</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP, DBP, MAP, CVP, PA, PWP, CO, SVR</td>
<td>MAP</td>
</tr>
<tr>
<td>Sat, O₂, CO₂, pH, Hg, CK-MB, troponin, EKG, ECHO, Thallium</td>
<td>ICP; CPP</td>
</tr>
<tr>
<td></td>
<td>PbtO²</td>
</tr>
<tr>
<td></td>
<td>EEG</td>
</tr>
<tr>
<td>200 drugs</td>
<td>4 drugs</td>
</tr>
</tbody>
</table>
ICP Severity

Similar Pathophysiology

- Mass lesion
- Consider repeating CT scan
- Hyperemia
- Ventricular Drainage (if available)
- Hyperventilation
- Hyperemia
- Edema
- Mannitol
- ICP > 20 mmHg
- Seizures
- Infection
- Systemic issues
New Directions: Intensive Care Unit

Similar Pathophysiology

Different Pathophysiology

Linear vs Targeted Therapy

Courtesy of Geoff Manley, MD; UCSF
Research Activities

- Search [www.ClinicalTrials.gov](http://www.ClinicalTrials.gov) to learn about ongoing studies
- Neuroprotection / Outcome
  - Hypothermia, medications, assessment tools
- Pathophysiology
  - ECog, cEEG, Imaging, CBF
- Technology
  - Devices for Monitoring; Stimulation; Patient Safety
- Interventions
  - Decompression, Minimally Invasive Surgery
- Hot topics
  - Aquaporins, Progesterone, Vasospasm, mild TBI
Questions?