### NEUROLOGICAL DISEASE/BURNS

SURGICAL CRITICAL CARE BOARD REVIEW

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#### **Nothing To Disclose**



American College of Surgeons

Inspiring Quality: Highest Standards, Better Outcomes

#### Outline

- Burns Fluid Management
- CO Exposure Indications for HBO
- Cerebral edema Role of DC
- Subarachnoid hemorrhage Prevention and treatment of vasospasm
- Stroke Indications for Thrombolytics

### Burns - Fluid management – How much?

- The profound inflammatory response generated by a burn surpasses that seen in trauma or sepsis
- The resultant fluid needs can be extreme
- Resuscitation should be titrated to urine output (0.5 ml/kg/hour in adults and 1 ml/kg/hour in children) and hemodynamic parameters.



#### Burns – Fluid management

- Parkland formula 4 (3.5-4.5) mL/kg per %TBSA
- Modified Brooke formula
  2 mL/kg per %TBSA

**Parkland Formula** 





### Burns - Fluid management – How much?

- The most consistent criticism of the Parkland formula is that patients tend to receive more fluid than the formula would have predicted.
- Called "fluid creep." (1)
  - Engrav et al. 58% of patients required more fluid than predicted by the Parkland formula.
  - Confirmed by multiple researchers
- Recent data suggests that lower volume resuscitation may be beneficial in prevent complications such as ACS

Pruitt BA. Protection from excessive resuscitation: "Pushing the pendulum back. J Trauma. 2000;49:567–568
 Engrav LH, Colescott PL, Kemalyan N. et al. A Biopsy of the Use of the Baxter Formula to Resuscitate Burns or Do We Do It Like Charlie Did It? J Burn Care Rehabil. 2000;21(2):91–95.

### Burns - Fluid management – How much?

- In an effort to reduce the dependence on clinical decisionmaking, several centers have experimented with standardized algorithms derived from hourly urine output.
- Nurse-driven resuscitation protocols
  - Jenabzadeh et al. showed a significant decrease in fluid volumes during resuscitation and a dramatic decrease in the incidence of ACS.
- Computer-based resuscitation algorithms.
  - Salinas et al. resulted in less 24-hour and 48-hour crystalloid volumes and less total crystalloid volumes
  - Volumes by body weight and by burn area were also less
  - Also helped patients to more effectively meet hourly goals for urine output .

Jenabzadeh K, et al. Nurse driven resuscitation protocol in the burn unit to prevent "fluid creep. Presented at the American Burn Association Annual Meeting, San Antonio; 2009. Salinas J, et al. Computerized decision support system improves fluid resuscitation following severe burns: An original study. Crit Care Med. 2011;39:2031–2038.

- Hypertonic Fluids
  - In an attempt to prevent overresuscitation, some advocate using hypertonic saline, alone or in combination with colloid.
  - Belba et al. a prospective, randomized study of 55 patients who were resuscitated with LR according to the Parkland formula (Shriner's formula for children) vs. 55 patients who received a hypertonic saline lactate solution.
    - The hypertonic group used less fluid overall than the isotonic fluid group.
  - Using a hypertonic solution during resuscitation may also lower the risk of ACS(Oda et al)

Belba MK, et al. Comparison of hypertonic vs isotonic fluids during resuscitation of severely burned patients. Am J Emerg Med 2009, 27:1091-1096. Oda J, et al. Hypertonic lactated saline resuscitation reduces the risk of abdominal compartment syndrome in severely burned patients. J Trauma. 2006;60:64–71.

- Colloids
  - Historically, opinion had been that using colloid in the first 24 hours of resuscitation was contraindicated.
  - It was thought that colloid would pass through the "leaky" capillaries in burn shock and exert an osmotic pull, drawing even more fluid into the interstitial space and worsening burn edema.
  - However, many investigators more recently are advocating the use of colloid in burn resuscitation, even in the first 24 hours.



- Colloid
  - Lawrence et al. performed a retrospective review of 52 patients (>20% TBSA burns).
    - Patients requiring more fluid volumes than predicted by the Parkland formula changed to an arm of the algorithm in which they got 1/3<sup>rd</sup> of their hourly fluid volumes as 5% albumin, with the other 2/3<sup>rd</sup> given as LR solution.
    - After colloid infusion began, patients quickly returned to predicted fluid rates and stayed at those lower volumes for the remainder of their resuscitation.
  - Cochran et al. performed a case-control analysis of large burns (>20% TBSA) that either did or did not receive albumin during their resuscitation and found that it conferred a mortality benefit

Lawrence A, et al. Colloid administration normalizes resuscitation ratio and ameliorates "fluid creep. J Burn Care Res. 2010;31:40–47. Cochran A, et al. Burn patient characteristics and outcomes following resuscitation with albumin. Burns. 2007;33:25–30.

Comparison 1. Supplemental albumin

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 deaths	38	10842	Odds Ratio (M-H, Fixed, 95% CI)	1.05 [0.95, 1.16]
1.1 hypovolaemia	22	9880	Odds Ratio (M-H, Fixed, 95% CI)	1.02 [0.92, 1.13]
1.2 burns	4	205	Odds Ratio (M-H, Fixed, 95% CI)	2.93 [1.28, 6.72]
1.3 hypoalbuminaemia	12	757	Odds Ratio (M-H, Fixed, 95% CI)	1.26 [0.84, 1.88]

Roberts I, et al. Human albumin solution for resuscitation and volume expansion in critically ill patients. Cochrane Database Syst Rev. 2011;Nov 9;(11).

- "For patients with hypovolaemia, there is no evidence that albumin reduces mortality when compared with cheaper alternatives such as saline."
- "There is no evidence that albumin reduces mortality in critically ill patients with burns and hypoalbuminaemia."
- "The possibility that there may be highly selected populations of critically ill patients in which albumin may be indicated remains open to question."

• "There is no evidence from RCTs that resuscitation with *colloids*, instead of *crystalloids*, reduces the risk of death in patients with trauma, burns or following surgery."

Perel P, Roberts I. Colloids versus crystalloids for fluid resuscitation in critically ill patients. Cochrane Database of Systematic Reviews. 2012. Jun 13;6:CD000567.

- Crystalloid or Colloid?
  - First line therapy is crystalloid infusion.
  - Lactated Ringers is usually used
- Use of colloids in the first 24 hours is not recommended
- Use of colloids after the first 24 hours can be considered but is still a matter of some debate

- The administration of oxygen speeds the elimination of CO from the body
- Without oxygen, the elimination half-life of CO is 4 to 5 hours
- Supplementation with normobaric 100% decreases the half-life by approximately 1/2
- Hyperbaric oxygen HBO at 2.5 ATM decreases it to less than 30 minutes



Guzman JA. Carbon Monoxide Poisoning. Critical Care Clinics. 2012;28(4):537-548.

Wolf SJ, et al. Clinical policy: critical issues in the management of adult patients presenting to the emergency department with acute carbon monoxide poisoning. Ann Emerg Med 2008;51(2):138–52.

- HBO has been used for severe CO poisoning for decades, however, its indication remains controversial.
- Proposed mechanisms by which HBO reduces tissue hypoxia are
  - decreasing the elimination half-life of COHb
  - increasing the fraction of oxygen dissolved in plasma
  - preventing leukocyte-mediated inflammatory changes
  - improving mitochondrial oxidative processes
  - decreasing cerebral edema by inducing vasoconstriction

- Proponents of HBO recommend its use due to effect in reversal of neurologic injury in patients with
- neurologic or cardiovascular symptoms
- high COHb levels (>25%)
- Some randomized trials have failed to show any favorable effects, while some have.
- A recent clinical policy statement by ACEP concluded that HBO is a therapeutic option for CO-poisoned patients, however, its use could not be mandated.

Raphael JC, et al. Trial of normobaric and hyperbaric oxygen for acute carbon monoxide intoxication. Lancet 1989;2(8660):414–9. (estel CD, et al. Hyperbaric or normobaric oxygen for acute carbon monoxide poisoning: a randomized controlled

Scheinkestel CD, et al. Hyperbaric or normobaric oxygen for acute carbon monoxide poisoning: a randomized controlled clinical trial. Undersea Hyperb Med 2000;27(3):163–4.

Weaver LK, et al. Hyperbaric oxygen for acute carbon monoxide poisoning. NEJM. 2002;347:1057-1067. Annane D, et al. Hyperbaric oxygen therapy for acute domestic carbon monoxide poisoning: two randomized controlled trials. Intensive Care Med 2011;37(3):486–92.

 "Existing randomised trials do not establish whether the administration of HBO to patients with carbon monoxide poisoning reduces the incidence of adverse neurologic outcomes."

#### Fig. I. Comparison 01. Hyperbaric Oxygen (HBO) vs. Normobaric Oxygen (NBO)

01.01 Presence of symptoms or signs at time of primary analysis (4-6 weeks)

Review: Hyperbaric oxygen for carbon monoxide poisoning Comparison: 01 Hyperbaric Oxygen (HBO) vs. Normobaric Oxygen (NBO) Outcome: 01 Presence of symptoms or signs at time of primary analysis (4-6 weeks)

Study	Treatment	Control	Odds Ratio (Random)	Weight	Odds Ratio (Random)
	n/N	n/N	95% CI	(%)	95% CI
01 Presence of signs or sym	nptoms				
Mathieu 1996	69/299	73/276	-	27.9	0.83 [ 0.57, 1.22 ]
Raphael 1989	51/159	50/148		23.8	0.93 [ 0.57, 1.49 ]
Raphael 2004	33/79	29/74		17.8	1.11 [ 0.58, 2.12 ]
Scheinkestel 1999	30/48	25/40	<b>_</b>	12.4	1.00 [ 0.42, 2.38 ]
Thom 1995	0/30	7/30	·	1.5	0.05 [ 0.00, 0.95 ]
Weaver 2002	19/76	35/76		16.6	0.39 [ 0.20, 0.78 ]
Total (95% CI)	691	644	-	100.0	0.78 [ 0.54, 1.12 ]
Iotal events: 202 (Treatmer	nt), 219 (Control)				
Test for heterogeneity chi-s	quare=9.31 df=5 p=0.1	0 l² =46.3%			
Test for overall effect z=1.3	4 p=0.2				
			0.1 0.2 0.5 1 2 5 10		

Favours HBOT Favours Control

- Very little data exists, but because of the potential benefit to the mother and the fetus and the difficulty of assessing intrauterine hypoxia, HBO should be considered when treating CO-poisoned pregnant women.
- No data exist on children younger than 15 years.
- Side effects of HBO include
  - painful barotrauma (ears and sinuses)
  - oxygen toxicity
  - seizures
  - pulmonary edema
  - decompression sickness.

#### **Cerebral Edema**

- Blood
  - Hyperventilation
  - Sedation
  - Analgesia
  - Barbituates
  - Fever Management
  - Hypothermia
- CSF
  - EVD/IVC placement
- Brain
  - Hypertonic saline
  - Mannitol



- Decreases ICP by reducing volume constraints on the cranial contents
- Improves glucose and oxygen utilization
- Increases blood flow and decreases cerebral vascular resistance
- Enhances brain tissue oxygenation
- Improves cerebral compliance



- A review of 400 patients with severe TBI reported 11% having craniectomy and suggested overall outcome benefits
- In a 20-year case series of 57 craniectomy patients with refractory ICH, 19% died and 58% survived with mild or moderate disability
- In contrast, some series report no benefit from decompressive craniectomy, either in terms of ICP control or of outcome.

- ICP fell in 80% of patients
- 30 day mortality = 22.4%
- 51% had good neurologic outcome (GOS 4 or 5)



 38.5% were persistently vegetative

- DECRA Decompressive Craniectomy in Diffuse Traumatic Brain Injury
  - 155 adults with severe diffuse TBI and ICH that was "refractory to first-tier therapies" to undergo either bifrontotemporoparietal decompressive craniectomy vs. standard care.
  - Patients undergoing craniectomy had
    - worse scores on the GOSE than those receiving standard care (OR 1.84,1.05 -3.24; P=0.03)
    - a greater risk of an unfavorable outcome (OR 2.21, 1.14-4.26; P=0.02).
    - Rates of death at 6 months were similar in the craniectomy group (19%) and the standard-care group (18%).
  - Many criticisms about study design and characteristics of groups

- Prospective observational trial
- 2602 patients, 264 (10.1%) received DC.
- The RR of death when DC was compared to MT was 0.95 (0.71 to 1.27).
- Length of stay was significantly longer for DC patients.
- Concluded:
  - "DC does not appear to significantly improve mortality in patients with refractory ICH compared to MT."





- Vasospasm of the cerebral arteries after aSAH is common,
  - Occurs most frequently 7 to 10 days after aneurysm rupture
  - Resolves spontaneously after 21 days.
- DCI remains a major cause of death and disability in patients with aSAH.

- Diagnosis of vasospasm
  - Serial examinations (limited sensitivity in patients with poor clinical grade)
  - Various diagnostic tools are commonly used to identify
    - (1) arterial narrowing
    - (2) perfusion abnormalities
  - CT Perfusion imaging
  - MRI
  - Transcranial doppler

- The management/prevention of aSAH-induced vasospasm
  - Oral nimodipine
  - Maintenance of euvolemia
  - Triple-H therapy (hemodynamic augmentation therapy)
  - Endovascular therapy with vasodilators and angioplasty balloons

- Treatment of DCI
  - Initial treatment is the induction of hemodynamic augmentation
    - Traditionally, hemodynamic augmentation has consisted of "triple-H therapy" (hemodilution, hypervolemia, hypertension)
    - Shift in the focus AWAY from triple-H therapy to the maintenance of euvolemia and induced hypertension.

- Treatment of DCI
  - Endovascular intervention
    - balloon angioplasty for accessible lesions
    - vasodilator infusion for distal vessels
    - Used in patients
      - who do not improve with hemodynamic augmentation
      - with sudden focal neurological deficits and focal lesions on angiography referable to their symptoms.

Dankbaar JW, et al. Effect of different components of triple-H therapy on cerebral perfusion in patients with aneurysmal subarachnoid haemorrhage: a systematic review. *Crit Care*. 2010;14:R23.

- Therapies aimed at restoring perfusion are the mainstay of acute stroke therapy.
- The goal of early reperfusion therapy is to minimize neurologic impairment, long-term disability, and stroke-related mortality.
- Reperfusion can be achieved through administration of thrombolytic agents such as recombinant tissue plasminogen activator (r-tPA) or by mechanical removal of blood clots.
- A second focus of acute stroke therapy is to prevent early recurrence of cerebrovascular events with treatment with antiplatelet agents and anticoagulants.

- Treatment With IV r-tPA Within 3 h
  - There is high-quality evidence that thrombolytic therapy, administered within 3 h of symptom onset, increases the likelihood of a good functional outcome but has little or no effect on mortality.
- Treatment With IV r-tPA Between 3 and 4.5 h
  - There is high-quality evidence that IV r-tPA administered within the 3- to 4.5-h time window is associated with an increased chance of favorable functional outcome.

Lansberg MG, et al. Antithrombotic and Thrombolytic Therapy for Ischemic Stroke: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians. Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2)

- Treatment With IV r-tPA Beyond 4.5 h
  - A recent meta-analysis (ECASS I,ECASS II, ATLANTIS, EPITHET) provides evidence that IV r-tPA administered between 4.5 and 6 h after symptom onset is associated with an increased chance of death
  - There is also moderate quality evidence of an increased chance of favorable functional.
  - "In patients with acute ischemic stroke in whom treatment cannot be initiated within 4.5 h of symptom onset, we recommend against IV r-tPA (Grade 1B)."

Lansberg MG, et al. Antithrombotic and Thrombolytic Therapy for Ischemic Stroke: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians. Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2)

- Thrombolysis Compared With No Thrombolytic Therapy in Patients With Ischemic Stroke and Contraindication for IV r-tPA (after 4.5 hours)
  - There is moderate quality evidence that in patients with an ischemic stroke with a demonstrable cerebral artery occlusion, IA thrombolysis is associated with an increased chance of good functional outcome, with unclear effect on mortality.
  - The increased chance of good functional outcome is seen despite an increased risk of symptomatic ICH
  - "In patients with acute ischemic stroke due to proximal cerebral artery occlusions who do not meet eligibility criteria for treatment with IV r-tPA, we suggest IA r-tPA initiated within 6 h of symptom onset (Grade 2C)."

Lansberg MG, et al. Antithrombotic and Thrombolytic Therapy for Ischemic Stroke: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians. Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2)

#### Stroke – Mechanical Thrombectomy

- Mechanical thrombectomy is the removal of clots from the cerebral circulation using endovascular retrieval devices.
- The data is unclear on the effect of mechanical thrombectomy on survival and functional outcomes.
- Mechanical thrombectomy is *not recommended* for stroke patients in general.
- Selected stroke patients with contraindications to IV r-tPA or persistent severe deficits despite IV r-tPA could be considered if they have
  - A proximal arterial occlusion that is amenable to IA thrombectomy AND
  - A relatively small burden of irreversible ischemic injury.
- Poor candidates for thrombectomy are those with evidence of major infarction or hemorrhage on brain imaging.

#### Stroke – Treatment

- In patients with acute ischemic stroke or transient ischemic attack (TIA)
  - Recommend early (within 48 h) aspirin therapy at a dose of 160 to 325 mg over no aspirin therapy (Grade 1A).
  - Recommend early (within 48 h) aspirin therapy with an initial dose of 160 to 325 mg over therapeutic parenteral anticoagulation (Grade 1A).

