Traumatic Brain Injury
Multimodal Monitoring

Ioana GRINTESCU
ICU, Clinical Emergency Hospital Bucharest

Severe Traumatic Brain Injury (TBI)

1. Introduction

2. Pathophysiology and complications of cerebral edema

3. Monitoring

This discussion relates only to posttraumatic neurological problems in severe head injured patients!

Introduction

GCS	3 - 8	9 - 12	13 - 15
distribution	21%	10%	69%
mortality	44%	7%	2%

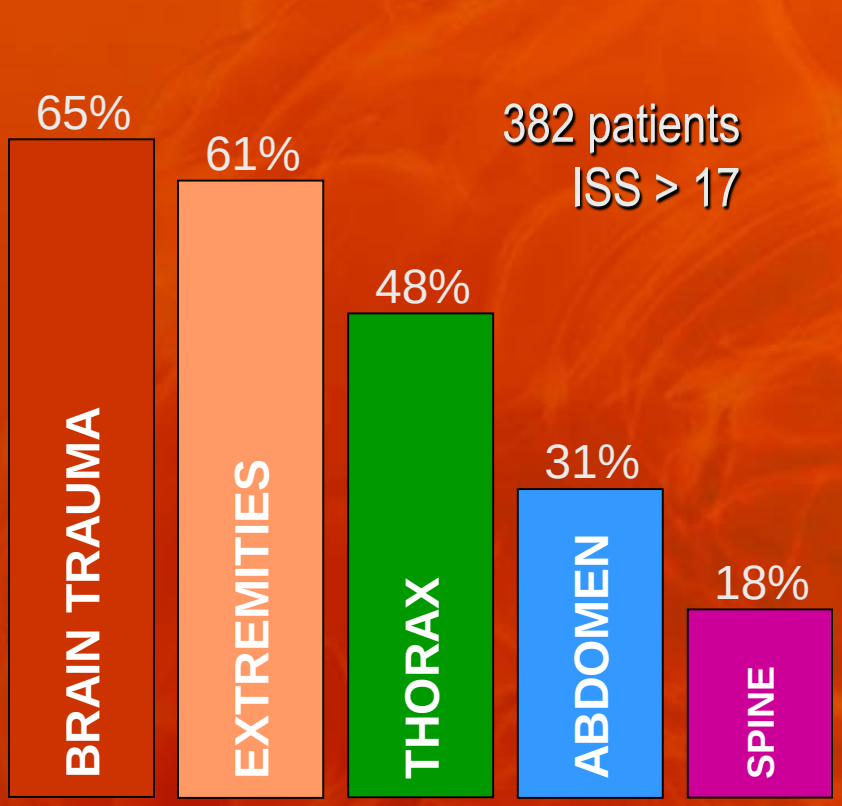
With shock

68%

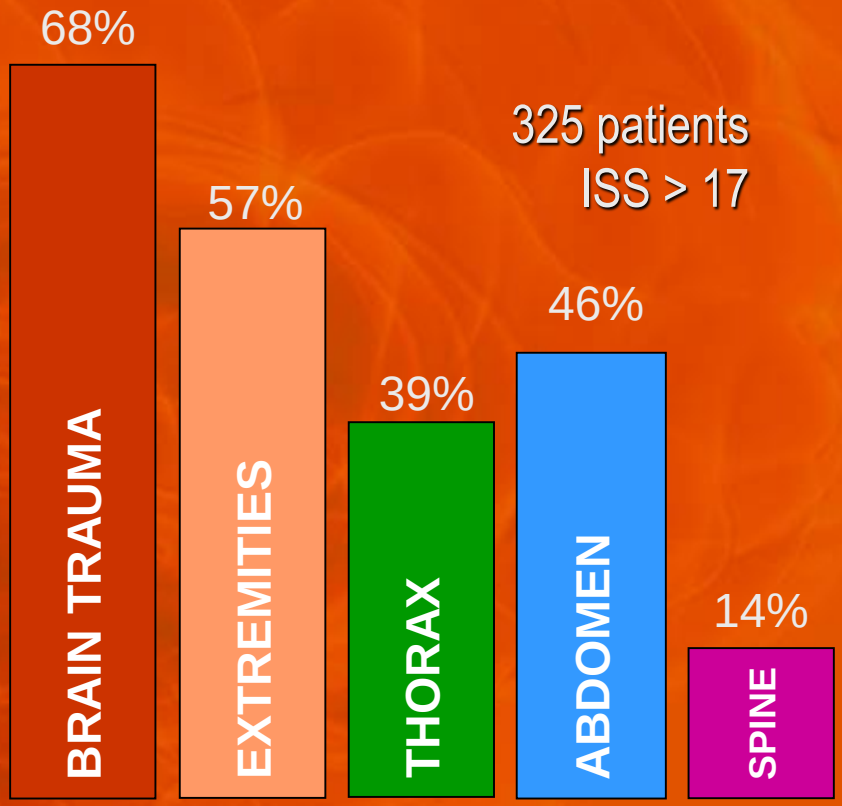
- Brain injury represents the main cause of death and disability in children and young adults
- Annual mortality due to TBI is around 1 million

- Severe TBI: GCS < 8 (respiratory support is mandatory) and ICP monitoring is recommended

Statistics



Statistics 2010, Emergency Clinical Hospital
(feb-jul) average **ISS 38**



Statistics 2016, Emergency Clinical Hospital
(feb – jul) average **ISS 45**

NICCU

The primary focus of neurocritical care for CNS problems is the prevention, identification, and treatment of secondary brain injury.

Addenbrooke's NCCU: ICP/CPP management algorithm

All patients with or at risk of intracranial hypertension *must* have invasive arterial monitoring, CVP line, ICP monitor at admission to NCCU.

- Algorithm to be used in conjunction with full protocols; stage III interventions depend on clinical picture & multimodality monitoring (to be established within six hours of admission).
- Early MRI in WBIC if no contraindications, clinical PET for selected patients.
- CPP>= 60 mmHg is acceptable in most patients.
- Autoregulation, brain chemistry to individualise targets and titrate hyperoxia as a therapy

Evacuate significant SOLs & drain CSF before escalating medical Rx.
Rx in italics and Grades IV and V only after approval by NCCU Consultant.

I

- 10-15° head up, no venous obstruction; CPP 50 to 70
- 2° targets: PRx < 0.2 (CPP> CPP_{opt}); BtpO2 > 25; LPR ≤ 25
- SpO_2 ≥ 97%; PaO_2 ≥ 11 kPa, $PaCO_2$ 4.5-5.0 kPa
- Temp ≤ 37°C; SjO_2 > 55%; blood sugar < 10 mmol/l
- Propofol 2-5 mg/kg/h; Fentanyl 1-4 µg/kg/h; atracurium 0.5 mg/kg/h (consider midazolam, remifentanil)
- Ranitidine 50mg iv 8° (or PPI), Phenytoin 15 mg/kg if indicated

yes ← ICP < 20 CPP >> 60 → no

Version 16, January 2011

II Drain CSF via EVD if possible and evacuate significant SOLs

yes ← -Recent CT? -Low risk of new SOL?

III

- 5% NaCl 2ml/kg (repeat if Na < 155 mmol/l, Posm ~320)
- (alternatively) 20% mannitol 2ml/kg X 3 or till Posm ~320
- PAC, volume ,vasoactives: trial of ↑↑CPP (>>70 mmHg)
- Temp ~ 35°C, Daily lipids, ECG and CK if still on propofol
- EEG: ? fits -> Institute or escalate antiepileptic therapy
- *↓ $PaCO_2$ to ~ 4.0 kPa. Ensure SjO_2 >> 50% /$BtpO_2$ >15*
- *Consider ↑ FIO_2 (see titration protocol) if BtpO2 < 15*

no → CT → SOL? → No / Yes - Evacuate

IV CPP < 60; ICP > 25 (Check probe, ? re-CT)

Temp 33°C ,change to midazolam (+ propofol, max 2 mg/kg/h)

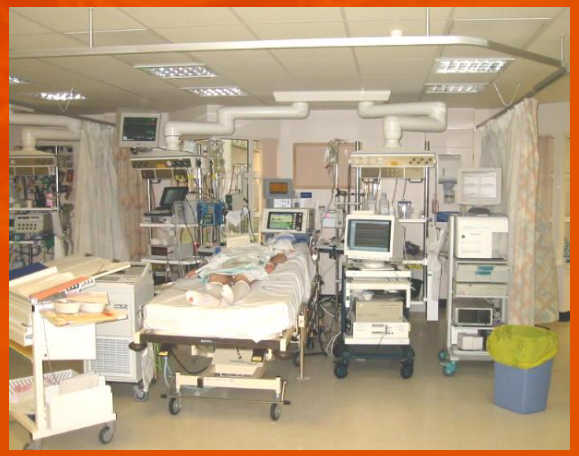
V CPP < 60; ICP > 25 (Check probe, ? re-CT)

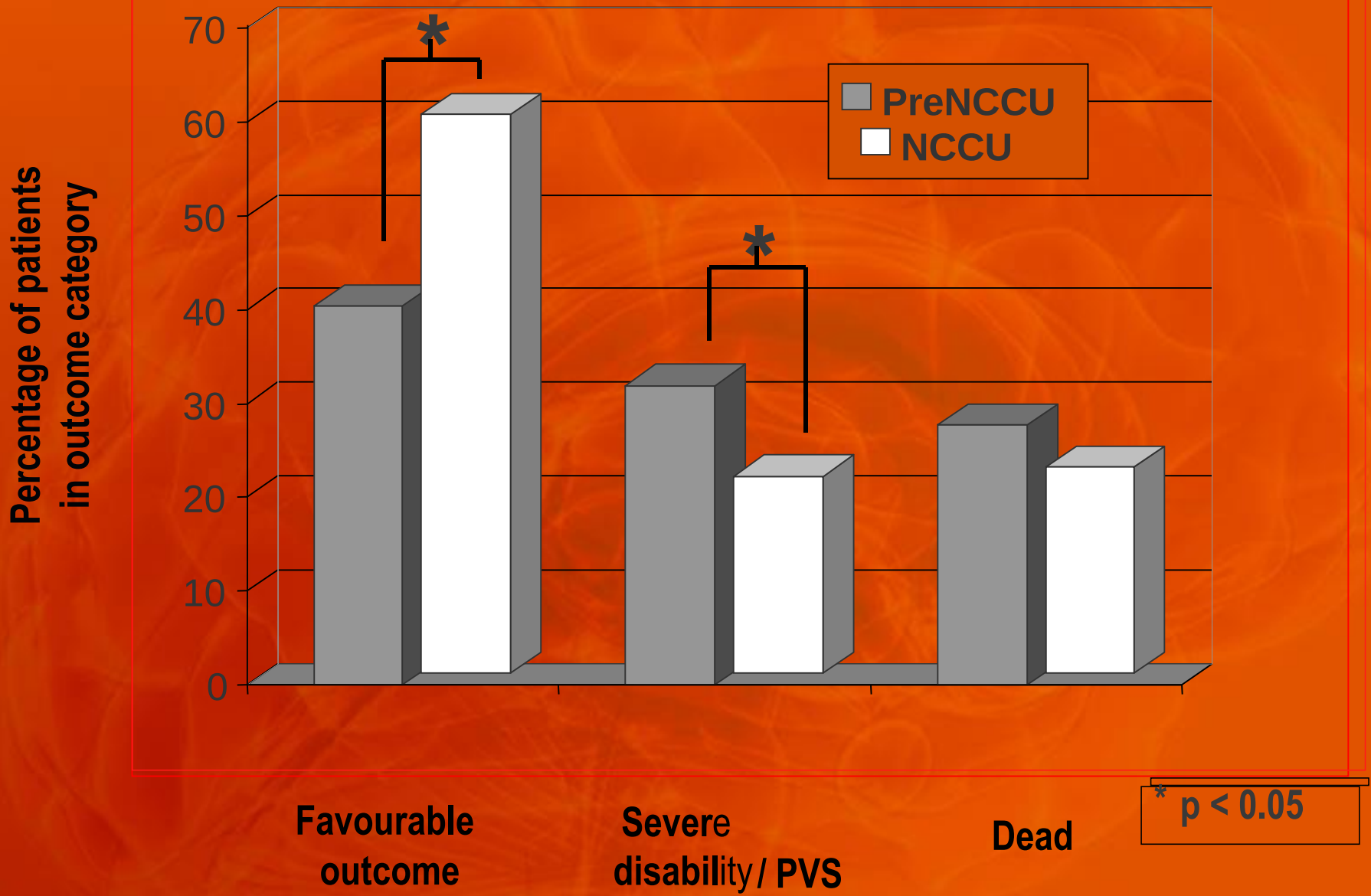
Try iv anaesthetic (eg Propofol 1mg/kg), maintain CPP (fluids & vasoactives). If ICP and CPP improve, start thio (250 mg boluses up to 3-5 g, then 3-8 mg/kg/hr to maintain burst suppression). Monitor raw EEG on BIS.

Consider decompressive craniectomy as an alternative to medical therapy for uncontrolled intracranial hypertension

Unique aspects of TBI management are driven by this:

- Brain oxygen delivery
- Cerebral perfusion
- Elevated intracranial pressure with herniation
- Exaggerated inflammatory response and risk of infection?





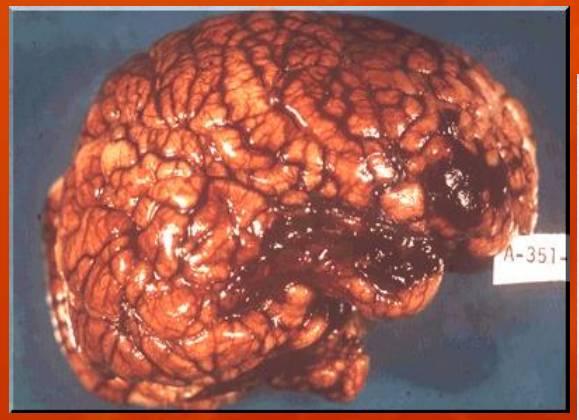
Making a marginal difference

Patel et al. Intensive Care Med 2002

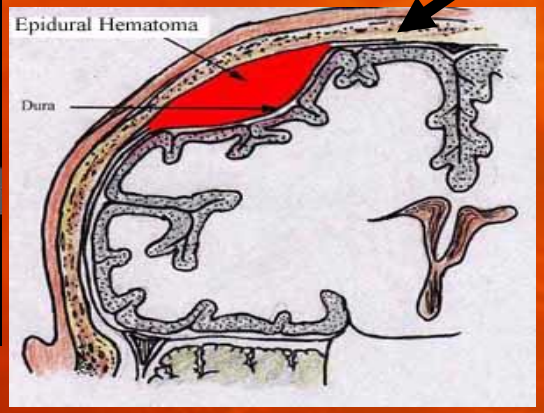
Pathopysiology in Brain Trauma

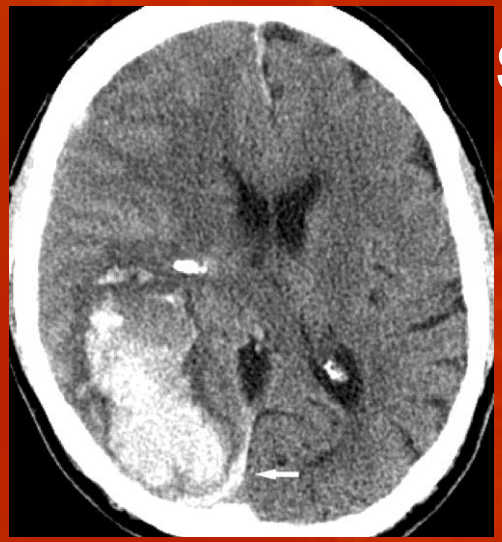
- Primary brain injury (direct impact)
- Secondary brain injury

Primary brain injury (direct impact)

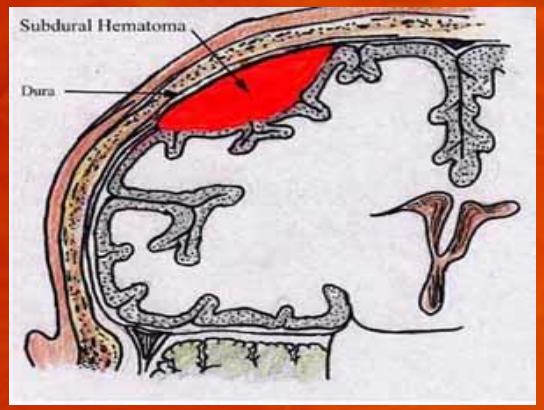


Epidural Hematoma





Subdural Hematoma



Clinical Features TBI

- Scalp Injuries
- Skull Fractures
- Depressed Skull Fractures
- Basilar Skull Fractures
- Vascular Injuries
- Penetrating Head Injury
- Intracranial Hemorrhage
  - –Epidural Hematoma
  - –Subdural Hematoma
  - –Subarachnoid Hemorrhage
  - –Intracerebral Hemorrhage

Secondary Brain Injury.

Pathophysiological events occur in minutes to days after primary injury

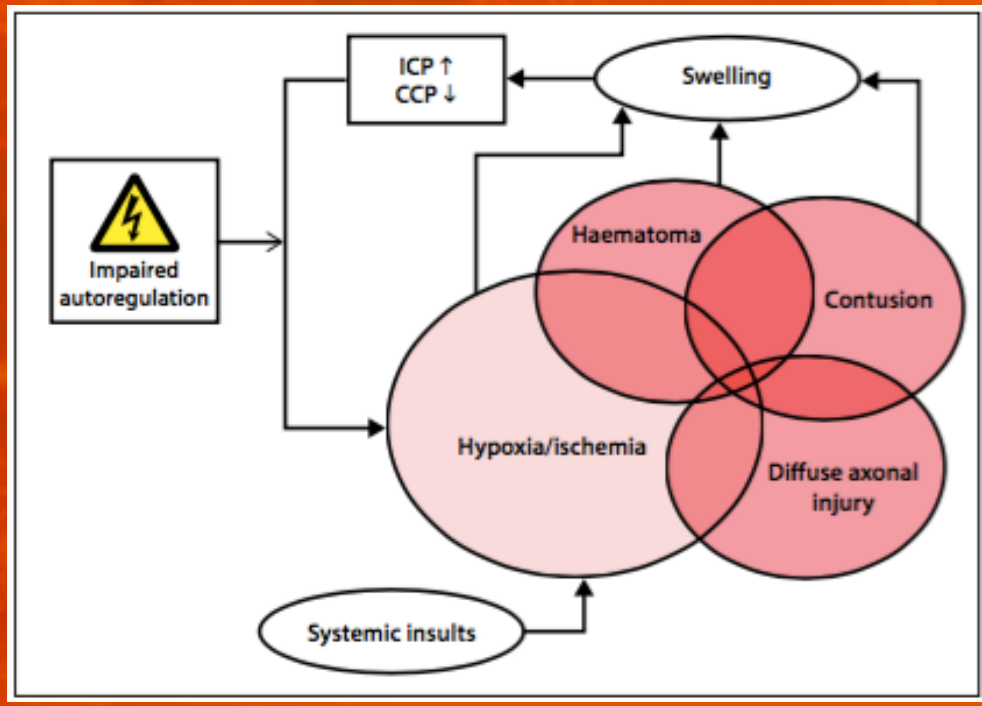
Netherlands Journal of Critical Care
Accepted October 2014

Neuromonitoring of patients with severe traumatic brain injury at the bedside

M.J.H. Aries[1,2], J. van der Naalt[3], W.B. van den Bergh[1], M. van Dijk[4], J.W.J. Elting[3], M. Czosnyka[2], J.G. Regtien[1]
Departments of [1]Critical Care, [3]Neurology and [4]Neurosurgery, University of Groningen, University Medical Center Groningen, Groningen, the Netherlands
[2]Department of Clinical Neurosciences, Division of Neurosurgery, University of Cambridge, Cambridge, United Kingdom

- ischemia / reperfusion
- cerebral edema
- intracranial haemorrhage
- intracranial hypertension

- Further distruction of brain tissue



Essential role in increasing morbidity and mortality

Secondary Brain Injury. Aggravating factors

Systemic

- **arterial hypotension**
- **hypoxia**
- hyper- / hypocapnia
- hypo- / hyperglycemia
- hyperthermia
- disturbances of water and electrolyte balance

Intracranial

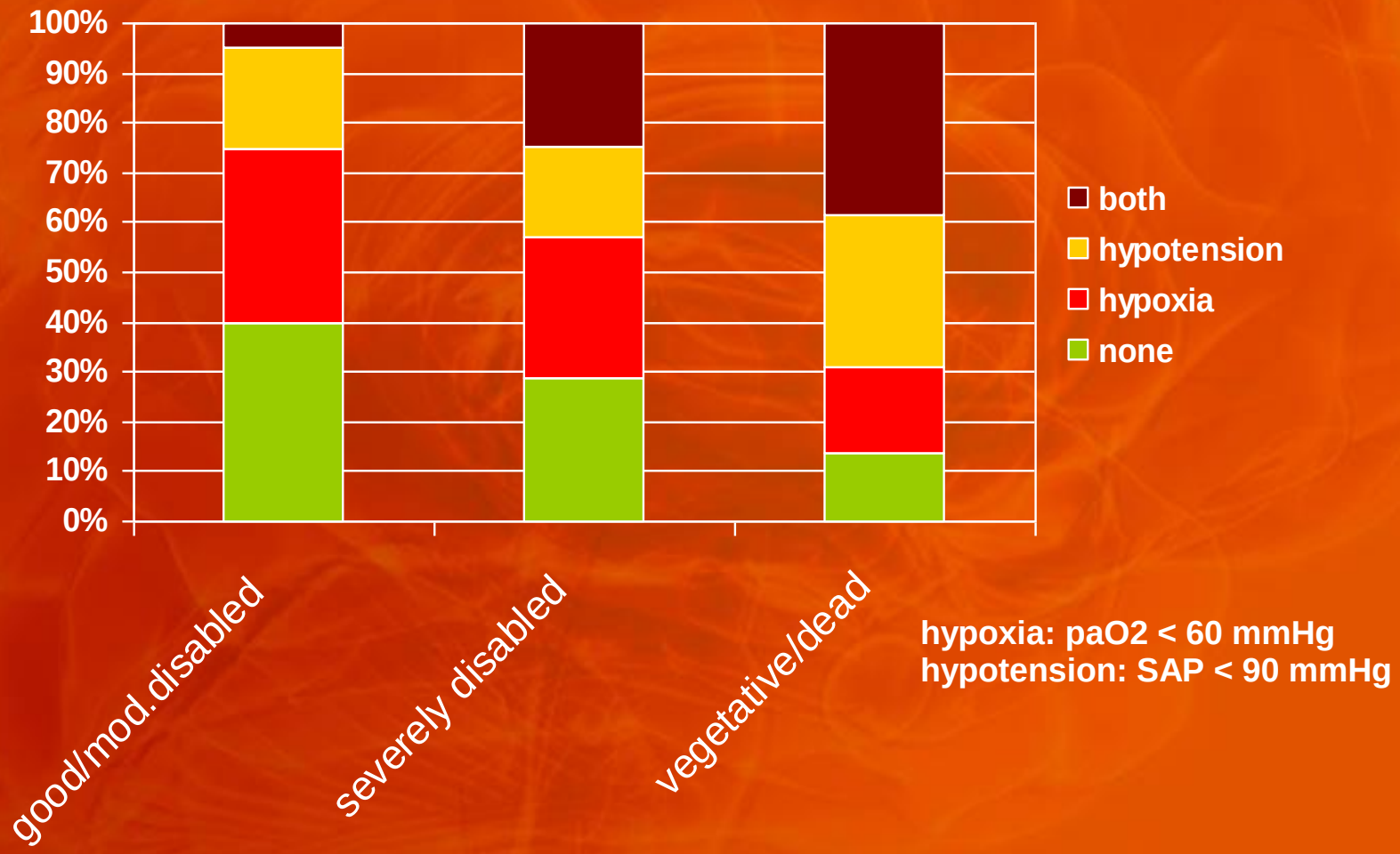
- mass lesion
- brain edema, hyperemia
- ICP ⇑, CPP ⇓
- vasospasms
- epileptic seizures
- inflammation

Secondary Brain Injury

- Early arterial hypotension increases mortality significantly
  (Chestnut 1993)
- Arterial hypotension has a negative impact on outcome
  (Fearnside 1993, Miller 1978, Pietrapoli 1992)
- Minimization and prevention of hypotension episodes improve outcome in TBI
  (Gentlemann 1992)
- Morbidity and mortality close correlate with ICP increase and hypotension

  (Marmarou, 1991)

Outcome after Secondary Insult



Chestnut RM et al. (1993). The role of secondary brain injury in determining outcome from severe head injury. J Trauma 34:216-22

Secondary Brain Injury

Effect of hypoxia (PaO2 < 60 torr) or hypotension (SBP < 90 mmHg) prior to or during resuscitation (Traumatic Coma Data Bank) - *(717 patients)*

Chesnut et al. J Trauma 34: 216-222, 1999

Secondary Insults	% of Total Patientts	Good / Mod	Severe / Vegetative	Dead
Total Cases	100	43,0	20,2	36,8
Neither	43,0	53,9	19,2	26,9
Hypoxia	22,4	50,3	21,7	28,0
Hypotension	11,4	32,9	17,1	50,0
Both	23,2	20,5	22,3	57,2

Monitoring

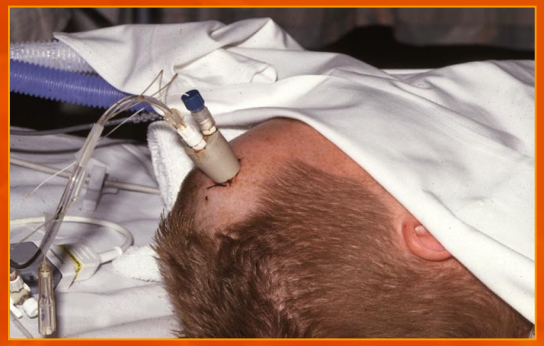
Standard Monitoring.
Systemic

- invasive arterial pressure (systemic lactate), central venous pressure (volemic status)
- cardiac rhythm (ST segment)
- ventilatory monitoring
- temperature, hourly urine output
- glycemia, plasmatic osmolarity

Systemic effects in brain trauma

- Sympathetic hyperrreactivity hyperglycemia, hydroelectrolites disturbances, protein catabolism, aldosteron secretion
- Inappropriate secretion of ADH/ inspid diabetes, ACTH, GH, cortisol
- Coagulation cascade activation by brain tissue tromboplastine DIC
- Respiratory disturbances (superior airways obstructions, bronhoplegia, apnoea)
- Cardiovascular disturbances (arrhythmia, thrombo-embolic risk, myocardial ischemia)

Multimodal monitoring



- intracranial pressure
- jugular bulb venous oxygen saturation
- brain tissue oxygen saturation
- near infrared spectroscopy
- EEG and evoked somato-sensorial potentials
- transcranial Doppler ultrasound
- microdialysis

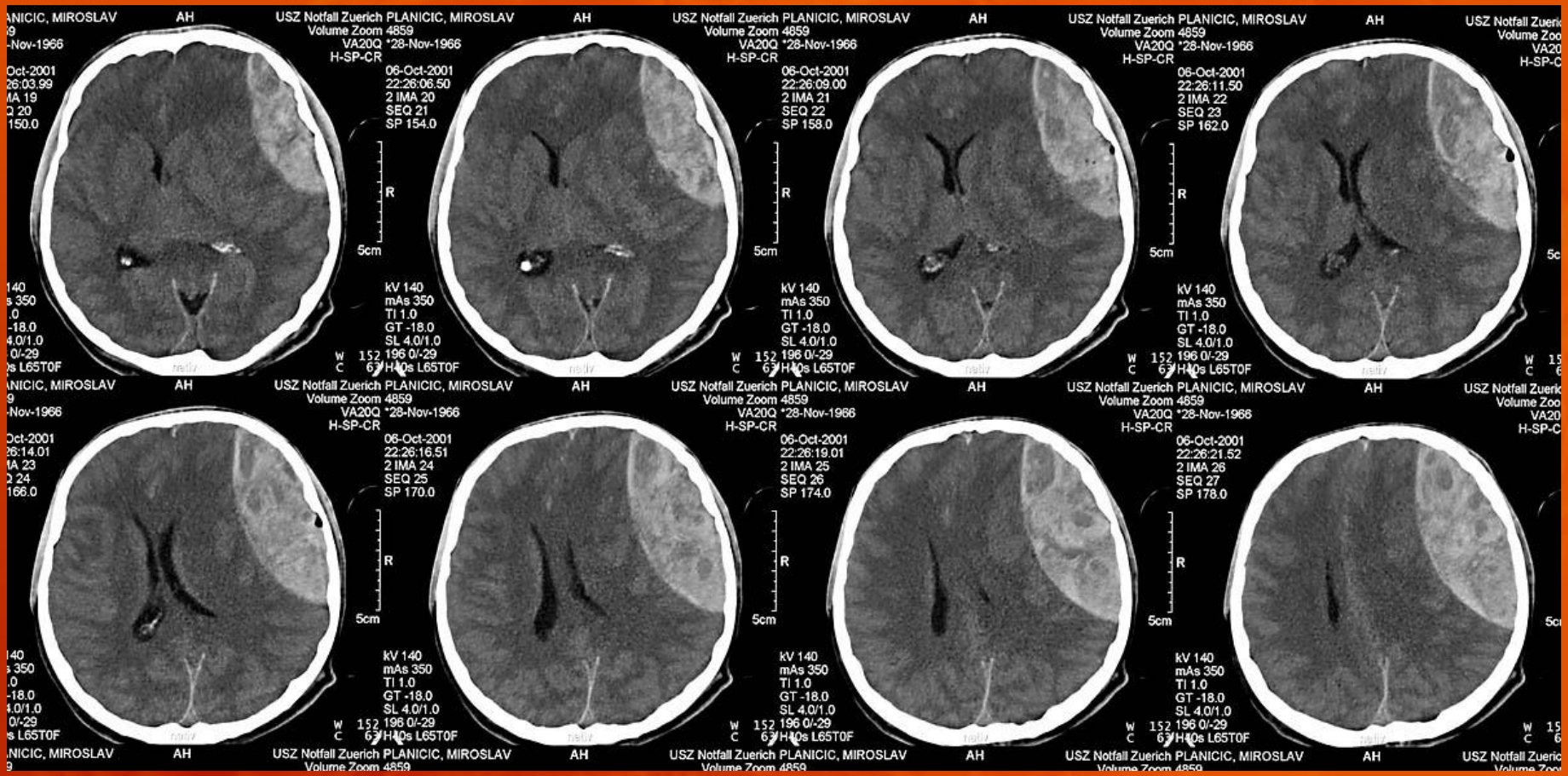
Multimodal monitoring

- Advantages:
  - continuous monitoring of more then one parameter can help overcome some of the limitations of each method alone
  - better therapy guidance
- Disadvantages:
  - increases errors occurrence
  - greater costs in equipment, personnel and time
  - increases the complexity of treatment

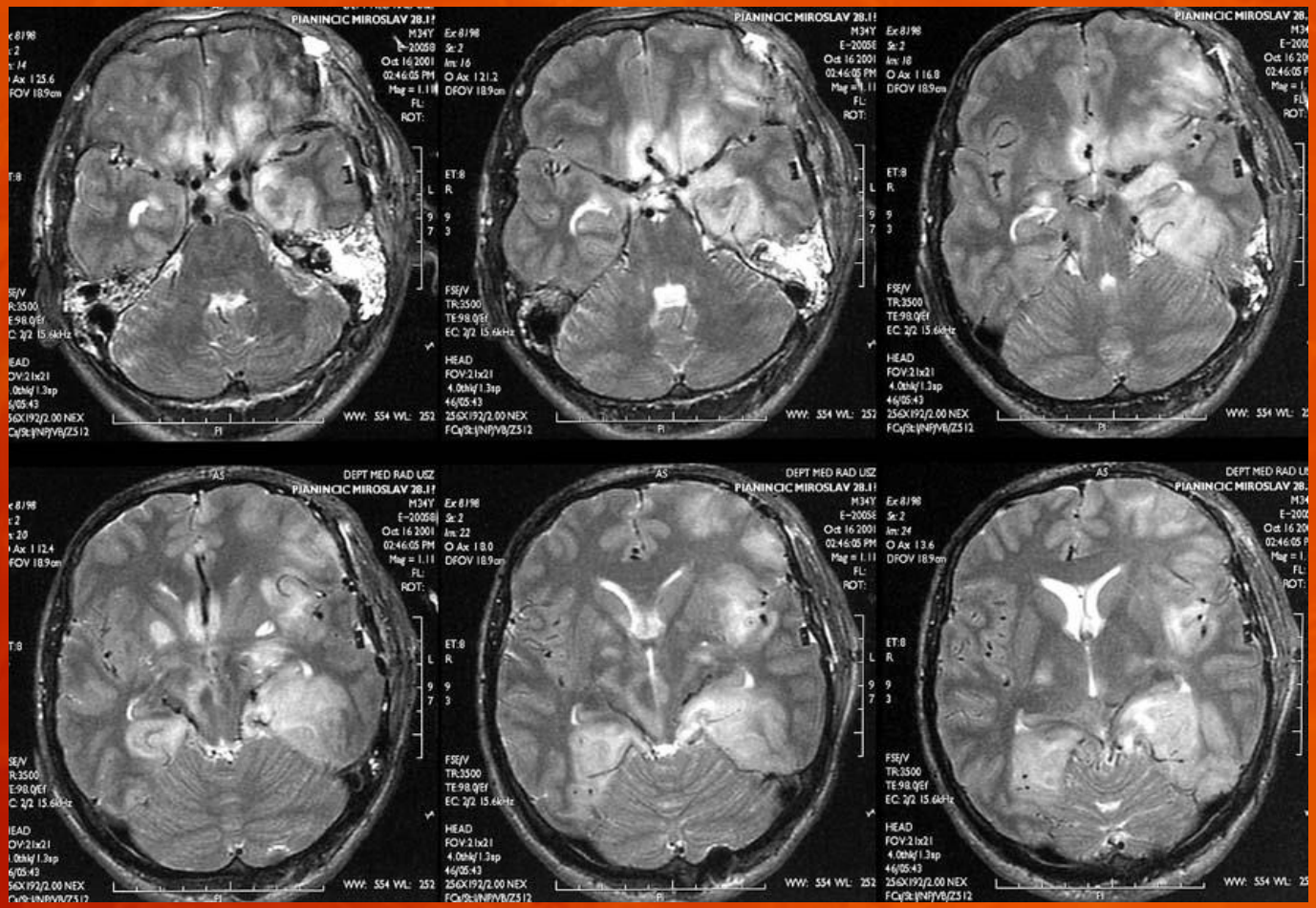
Specific Monitoring.

- CT scan
- Cerebral function assessment
  - Neurological status
  - EEG
  - evoqued potentials
- Blood flow assessment
  - ICP monitoring
  - transcranial eco Doppler
- Cerebral metabolism assessment
  - Bulbous venous jugular oxymetrie ($SvjO_2$)

CT scan

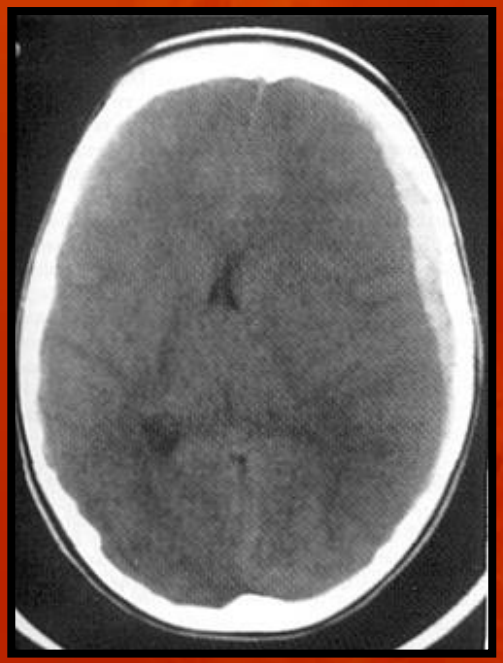


Epidural haematoma with mass effect and midline shift

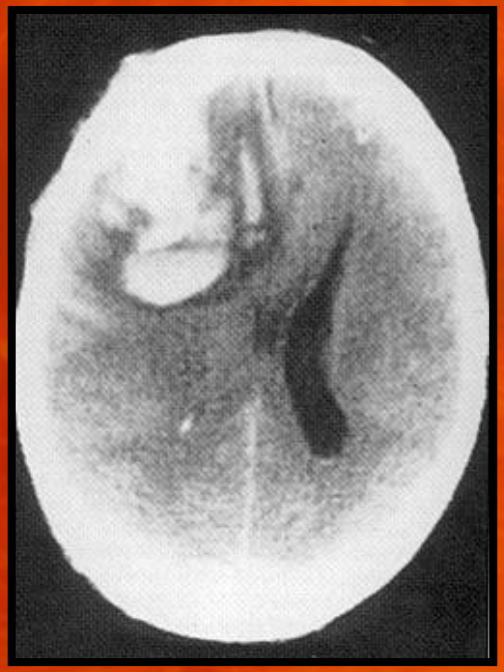


Secondary brain injury after epidural haematoma evacuation

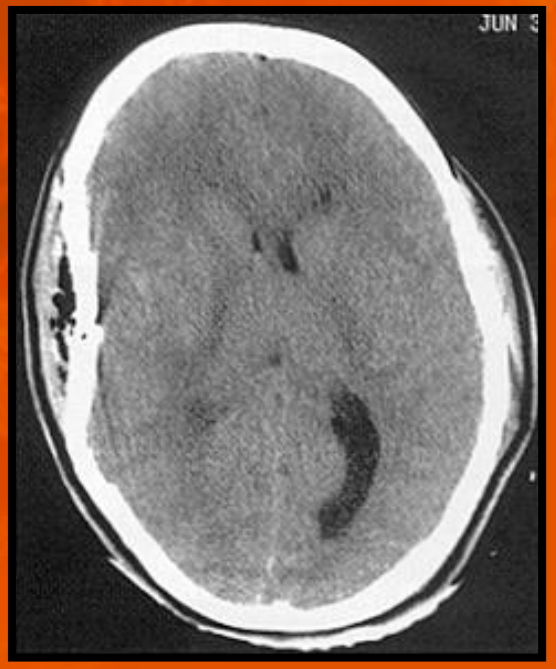
CT scan: acute left subdural haematoma with left hemispheric edema and midline shift



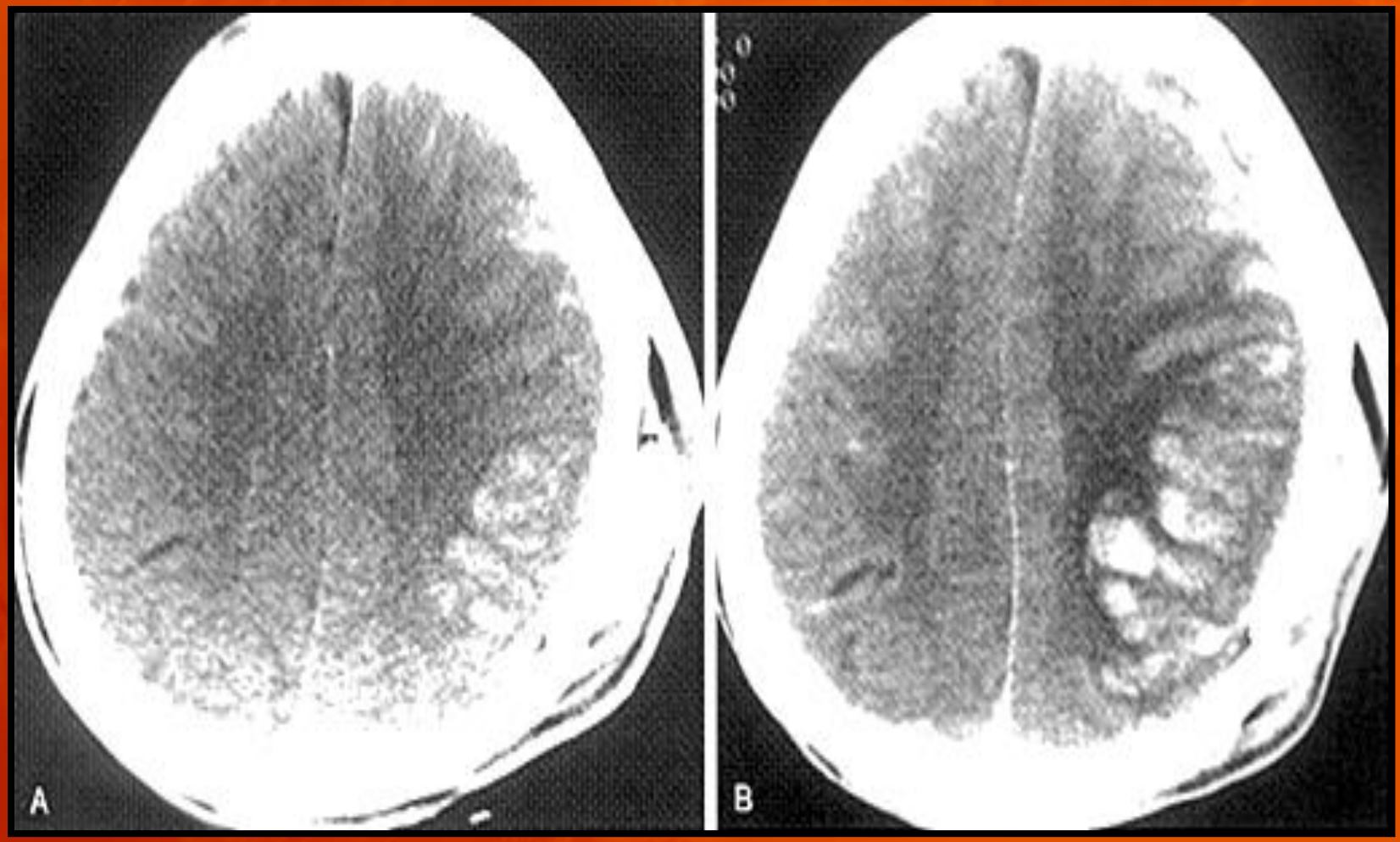
CT scan: frontal right hemorrhagic contusion and right intraparenchimal haematoma and diffuse brain edema



CT scan: right temporal fracture and right hemispheric edema with ipsilateral ventricular amputation (asymmetric cerebral edema)



CT scan: left parietal posterior hemorrhagic contusion “salt and pepper” type and intraparenchimal haematoma with perilezional edema



Cerebral function assessment

- Neurological status
  - GCS –assessment of counciousness
  - Abbreviated mental score (AMTS) & Mini mental state examination (MMSE)
  - Nerve examination – cranial & peripheral nn
- EEG
- evoqued potentials

EEG

- Early detection of seizures – first 24h (high incidence of subclinical seizures in the ICU); otherwise, best in late diagnosis
- Indicative for CBF, non-specific – continuous and regional monitor of cerebral ischemia
- Adjunctive valuable role in interpreting focal physiologic data from other MMM techniques

BUT…...

- Does not reflect activity in deep structures such as brain-stem
- Very sensitive to sedative drugs, hypothermia, metabolic abnormalities
- Artifacts from the environment (mains, ventilator, beds, intravenous pumps, personnel, endotracheal tube vibrations, neon lights)

Invasive MMM Monitoring

	ICP CPP	Brain oxygenation	CBF	Brain metabolism
Devices	Parenchymal vs ventricular	a. Parenchymal b. Jugular bulb	Thermal diffusion probe	Microdialysis
Parameter	ICP < 20 mmHg; CPP > 60 mm-Hg	a. $PbtO_2$ > 20 mmHg b. $SjvO_2$ > 55 %	>20 cm^3/100 g/min	a. LPR >25 or >40 b. Glucose 1.5–2 mM c. Glutamate <10 uM d. Glycerol <50 uM
Interpretation	Indirect surrogate for CBF	Indirect surrogate for CBF and oxygen demand a. Focal brain tissue oxygenation (perfusion and diffusion) b. Global cerebral oxygen extraction	Direct regional measurement of CBF	Brain energy crisis

Consequences of brain edema

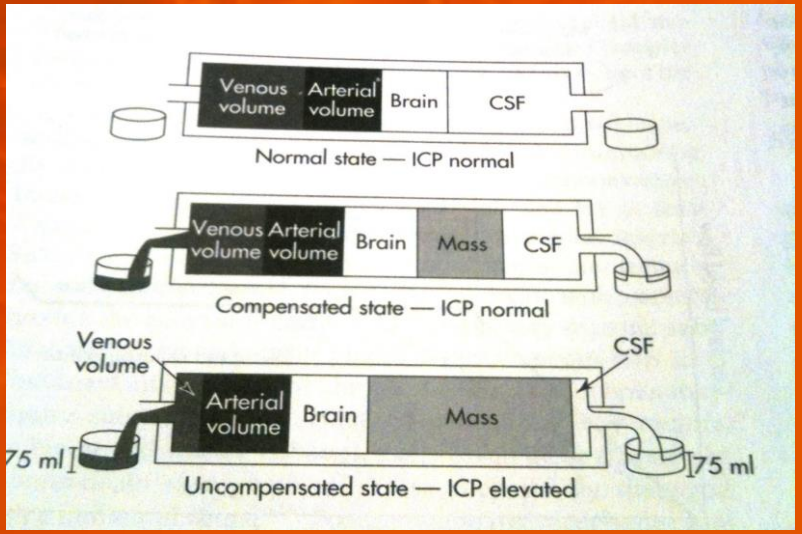
Monro-Kellie-Doctrine

$$V_{intracranial} = V_{brain} + V_{CSF} + V_{blood} + V_{mass\ lesion} = ct$$

Vol of intracranial compartment must remain constant because of inelastance of skull

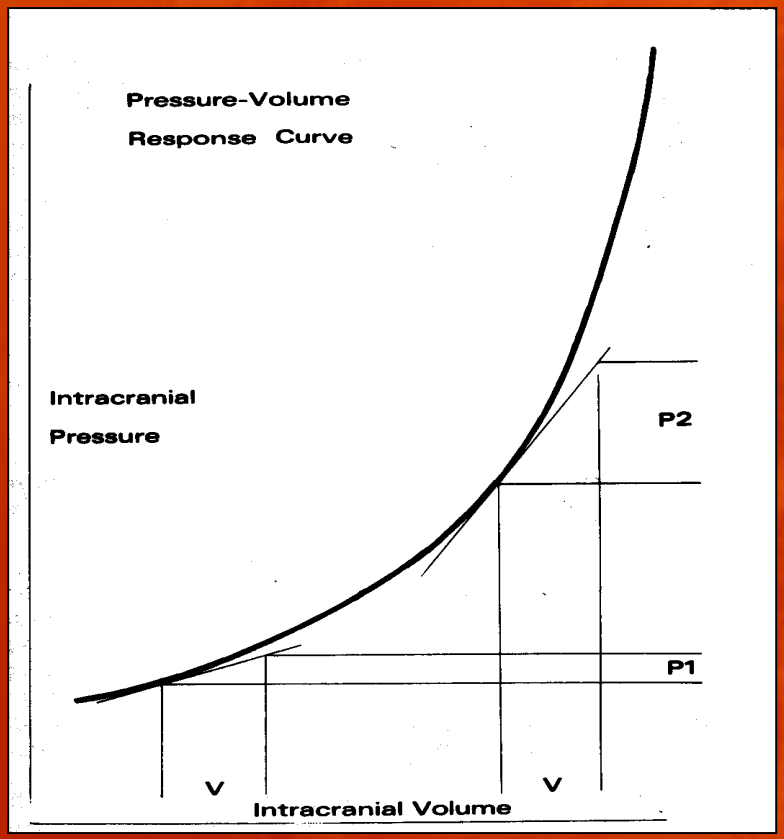
Normal State-
ICV is a balance b/n Blood, brain & CSF.

With ICSOL
ICP remains normal till compensation can occur



Volume-Pressure-Relationship

The brains compensatory reserve is called
Compliance → Pressure Volume Index (PVI) = V/ LOG P1P2

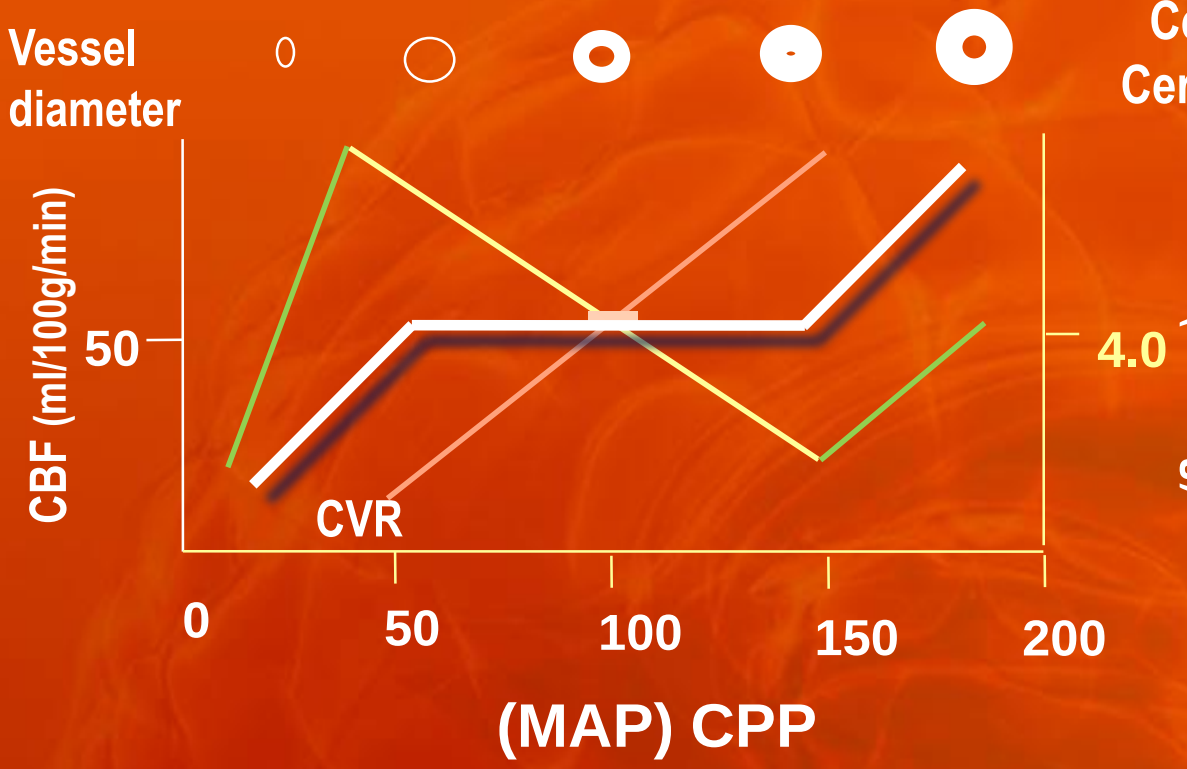


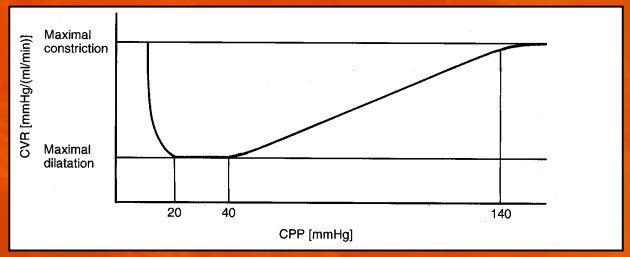
At the Point of decompensation
The ICP starts to increase.

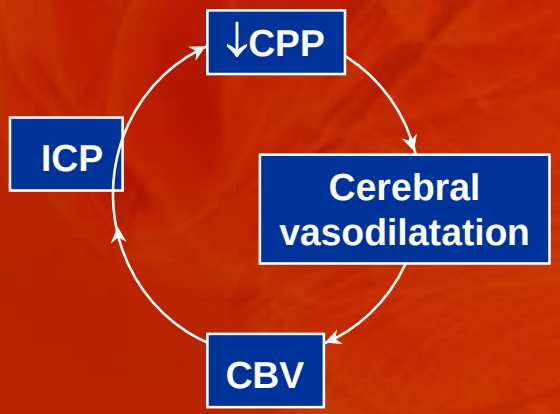
Intracranial volume-presure curve. As ICP rises, equivalent changes in volume produce increasing pressure response. (P_1<<<P_2)

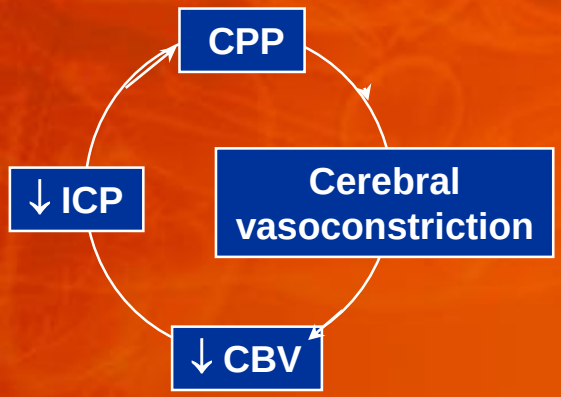
(Adapted From Jones et al)

Cerebro-vascular Resistance and Cerebral Perfusion Pressure (CPP) Intact Autoregulation

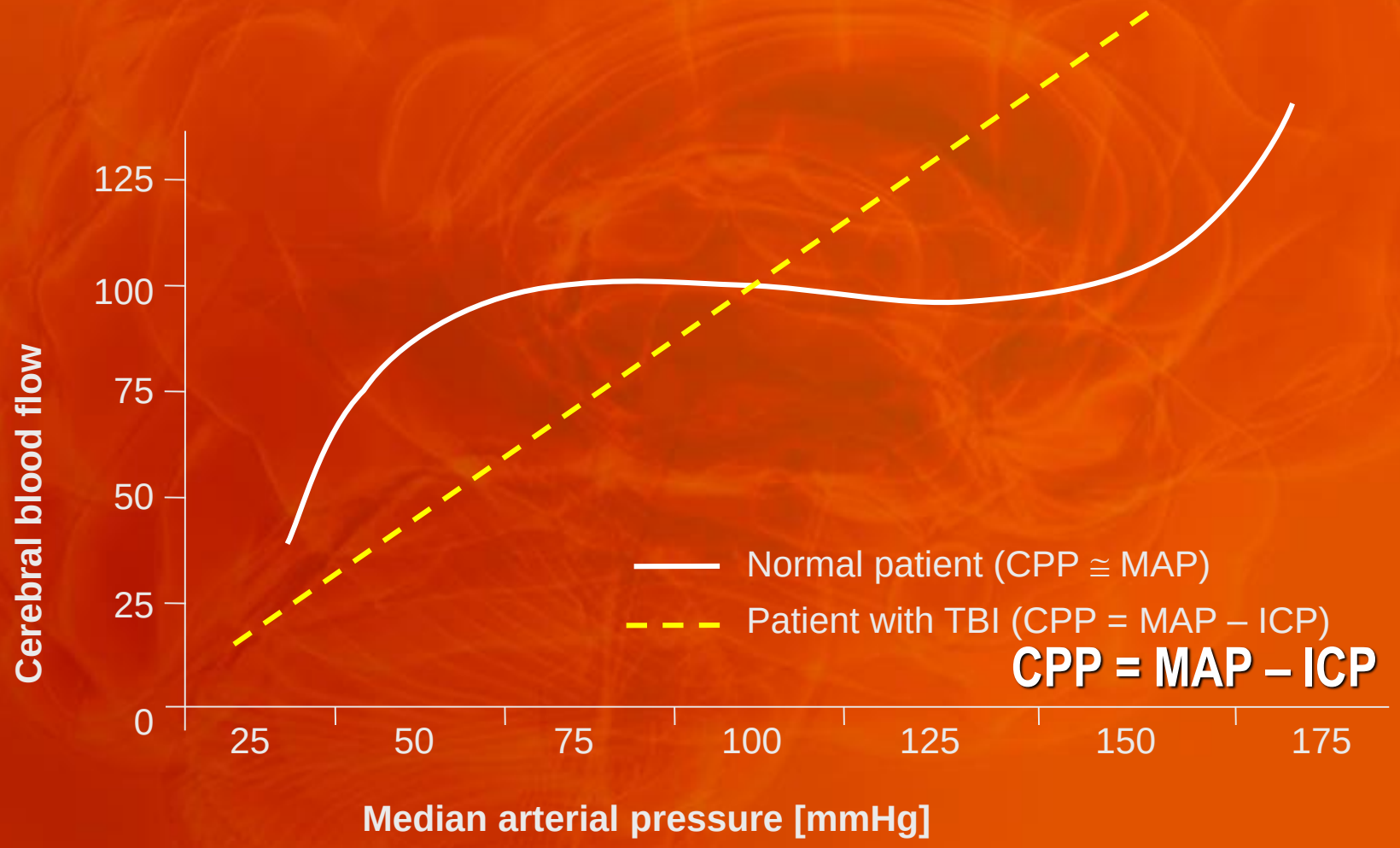








Cerebral blood flow in head trauma



Cerebral Perfusion: Thresholds

ml/100g/min

50 – 55	normal value
20 – 25	changes in consciousness and EEG pattern
18 – 20	severe neurological deficit, EEG flat
12 – 17	disappearance of evoked potentials, partial brake down of Na^+/K^+-pump
< 10 – 12	complete brake down of Na^+/K^+ pump within minutes, cell death

ICP Monitoring

CPP = MAP - ICP

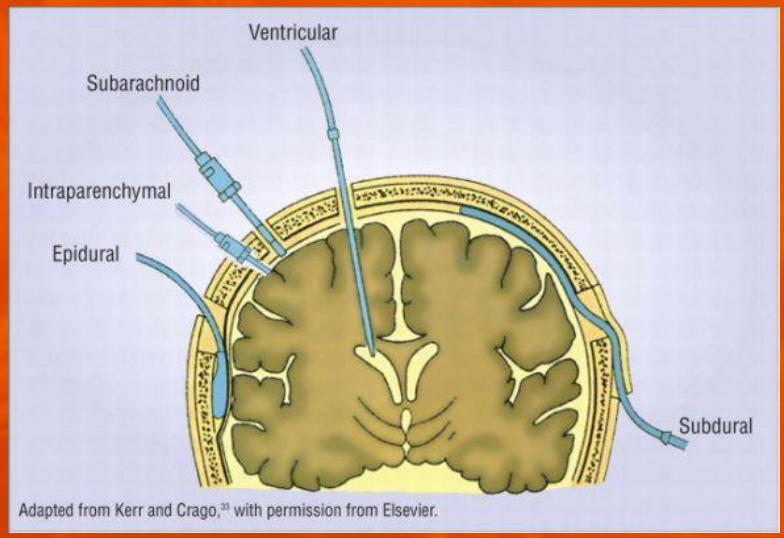
Indications:

- GCS ≤ 8 if CT pathological
- GCS > 8 if CT pathological and neurologic reassessment impossible
- neurologic deficit if neurologic reassessment impossible, independent of CT scan
- Severe TBI with normal CT and associate 2 of the following:
  - > 40 years,
  - uni-/bilateral posturing
  - systolic arterial pressure < 90 mmHg

ICP > 20 mmHg, > 5 min = intracranial hypertension

Brain Injury Foundation, American Association of Neurological Surgeons, Joint Section on Neurotrauma and Critical Care (1996) Guidelines for the management of severe head injury. J Neurotrauma 13:641-734 Stocker R, Bernays R, Kossmann T, Imhof HG (2001) Monitoring and treatment of acute head injury

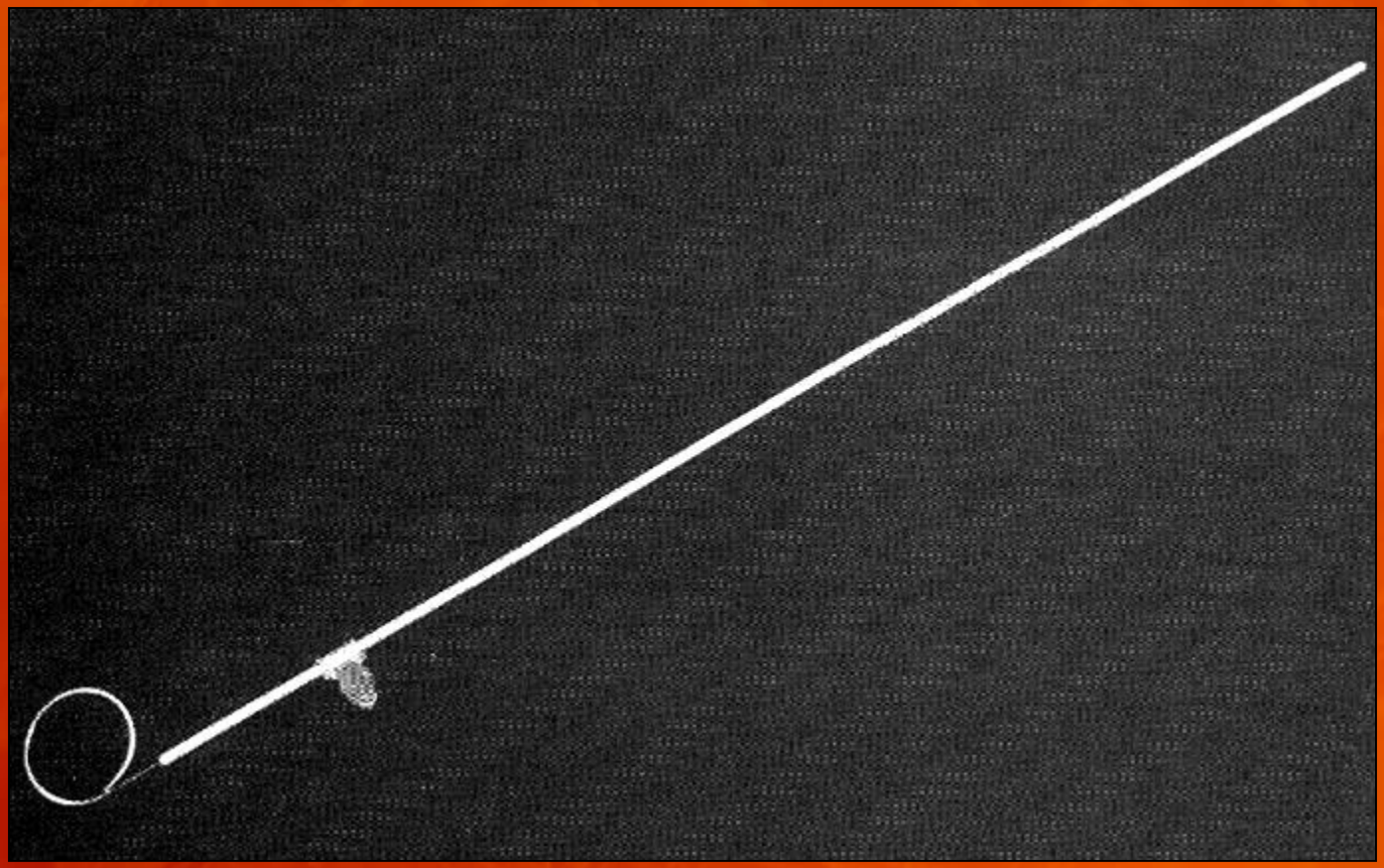
ICP Monitoring Devices



Adapted from Kerr and Crago,[33] with permission from Elsevier.

- **Parenchymal**
  fiberoptic, “Tip”-manometric (intraparenchymal/subdural/intraventricular). No Drainage. Minimal invasive, no in vivo calibration possible (Camino, **Codmann**):
- **Ventricular catheter**
  “Drained CSF possibly> CSF-production => net drainage. Measuring of brain compliance possible
- **Subdural Probe**
  No Drainage. Minimal lesions, narrow ventricle system, midline-Shift
- **Epidural Screw**

Intraventricular Catheter

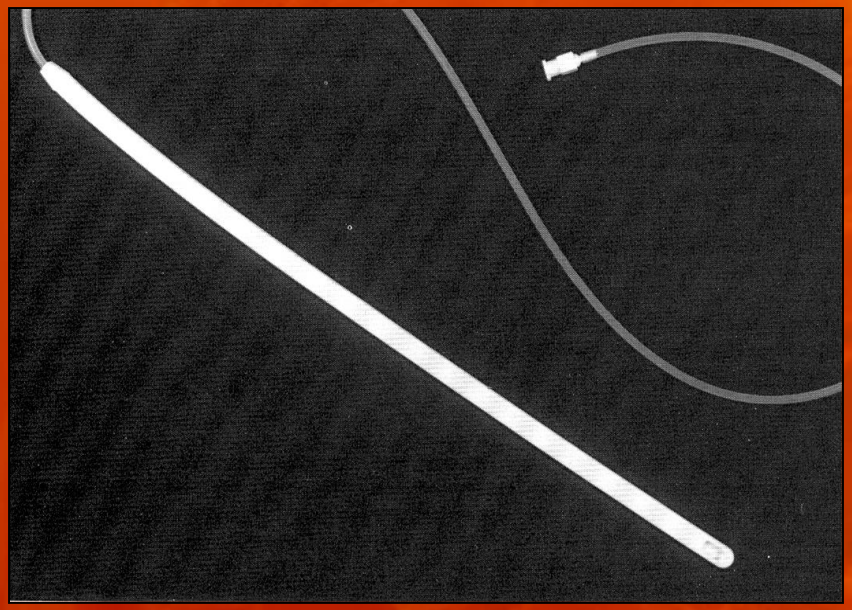


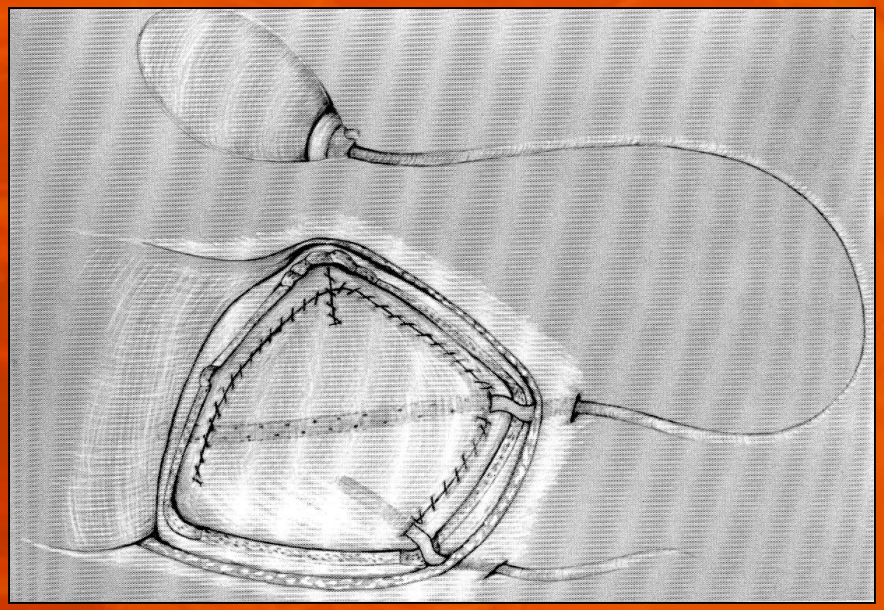
Advantages: accurate measurements, CSF-drainage (therapy), in-vivo-calibration possible.

Disadvantage: invasive, risk for infections

Stocker R, Bernays R, Kossmann T, Imhof HG (2001) Monitoring and treatment of acute head injury

Subdural Probe



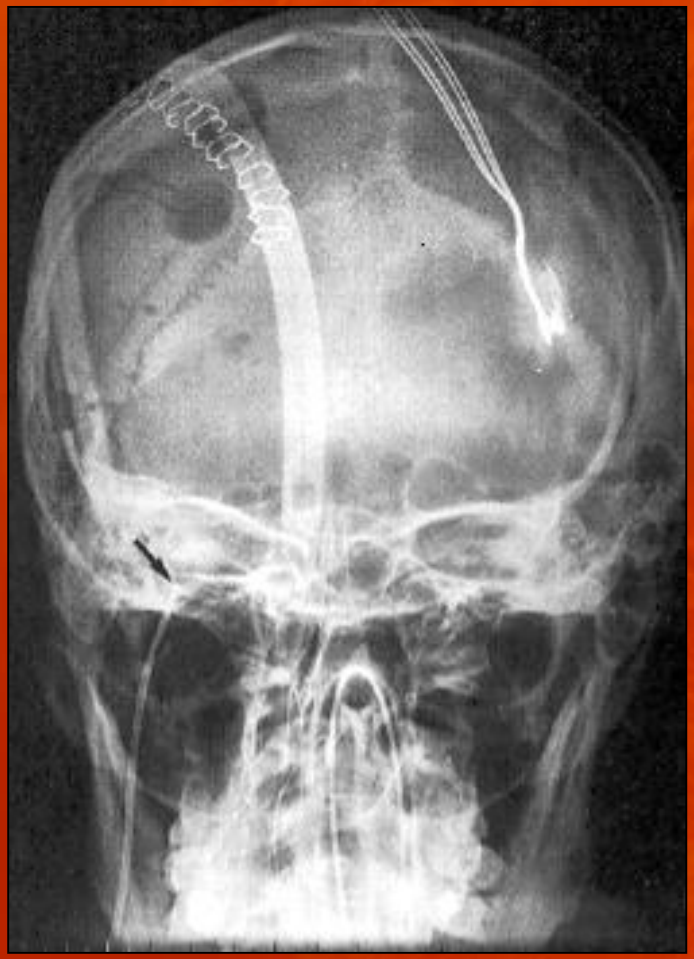


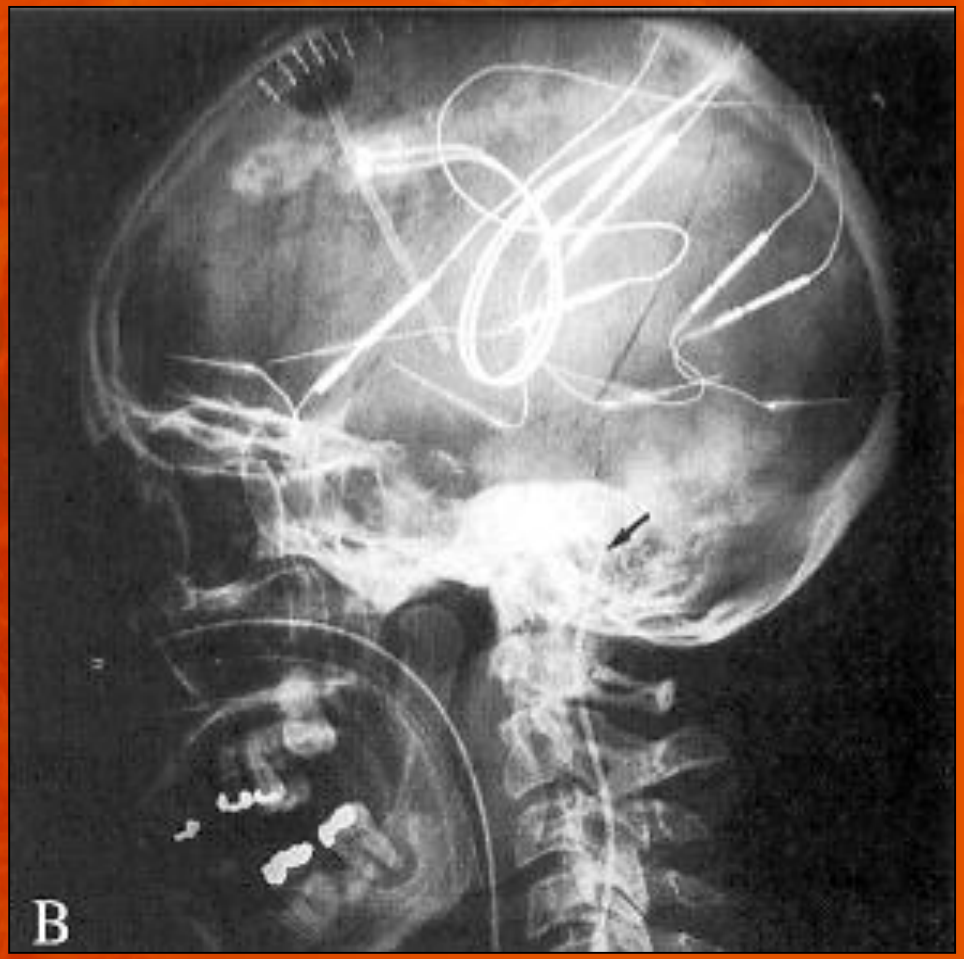
Advantages: low complication rate (<1%), in vivo-calibration possible, low infection rate (<5%)

Disadvantages: no CSF-drainage

Stocker R, Bernays R, Kossmann T, Imhof HG (2001) Monitoring and treatment of acute head injury

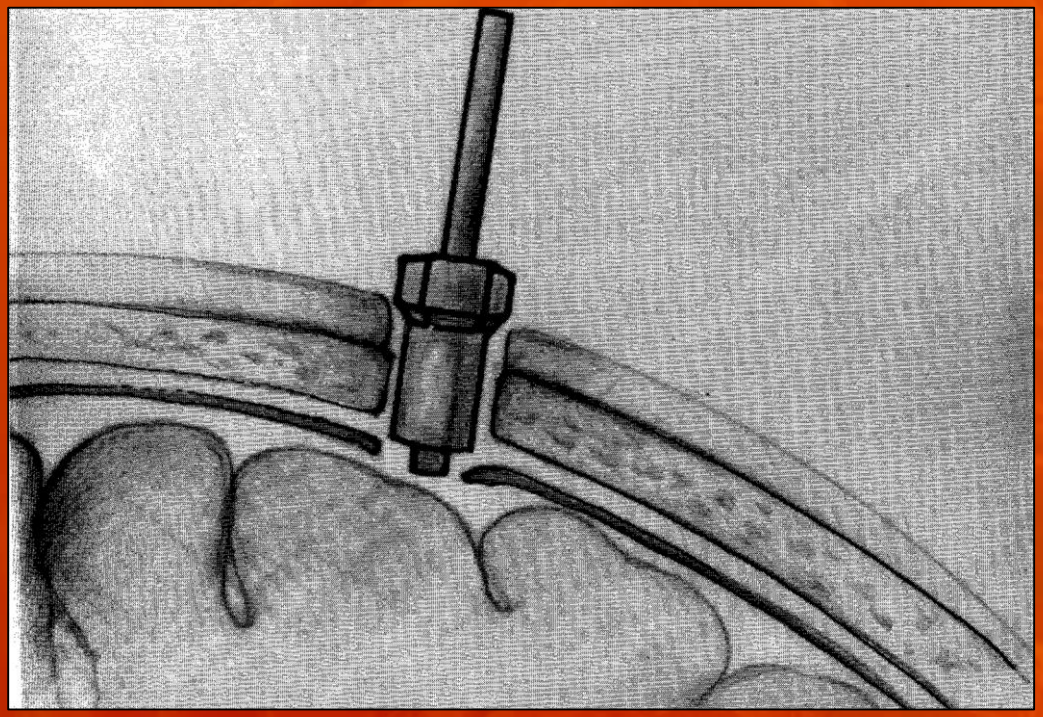
ICP Monitoring
Subdural / intraventricular ICP Monitoring





Stocker R, Bernays R, Kossmann T, Imhof HG (2001) Monitoring and treatment of acute head injury

Subdural Screw

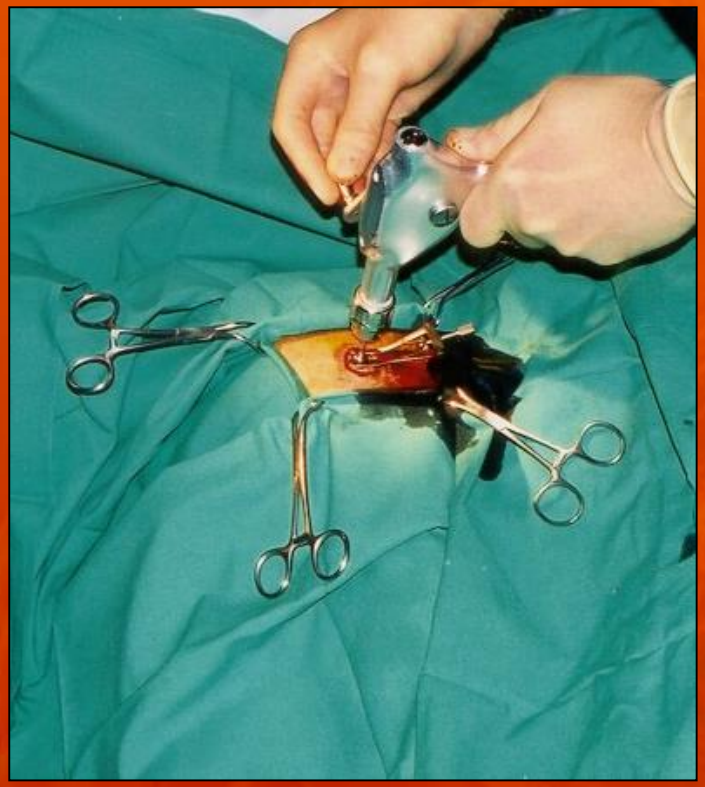


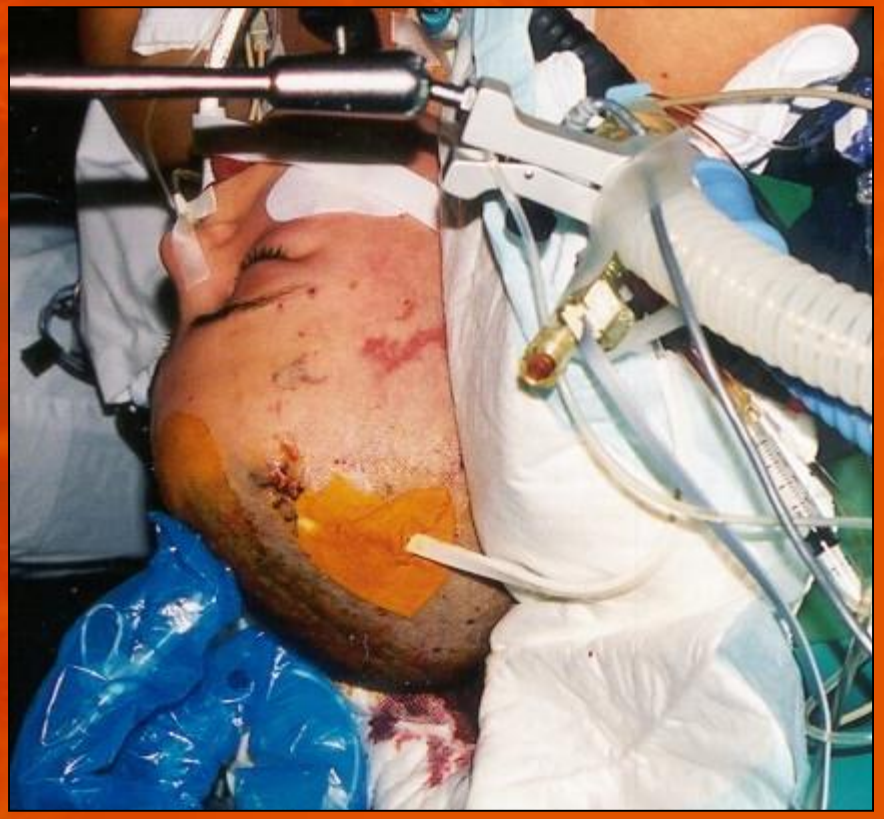
Insertion and correct placement of subdural screw

Advantages: accuracy, in-vivo-calibration possible

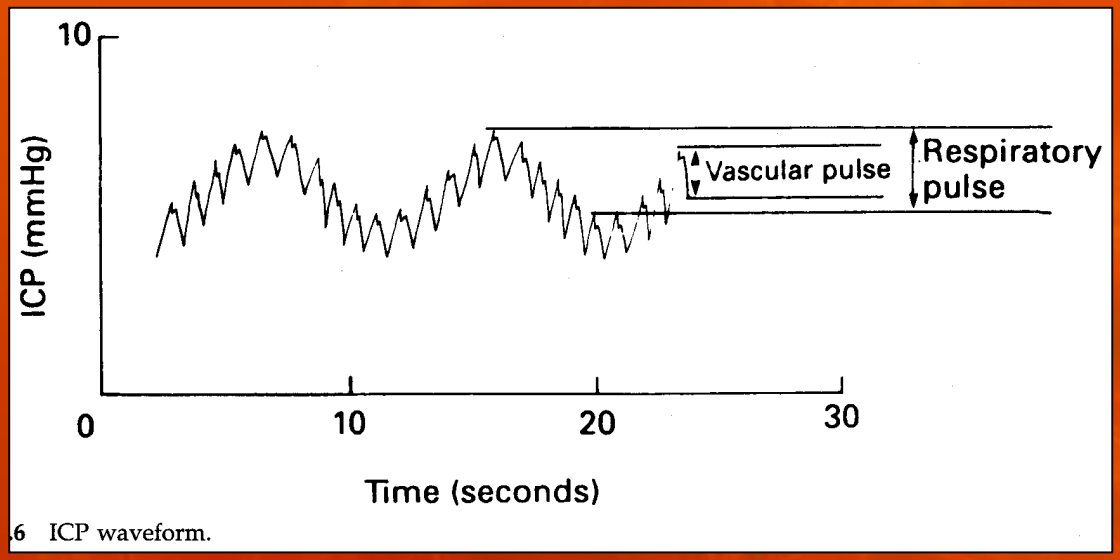
Disadvantages: no CSF-drainage

Stocker R, Bernays R, Kossmann T, Imhof HG (2001) Monitoring and treatment of acute head injury

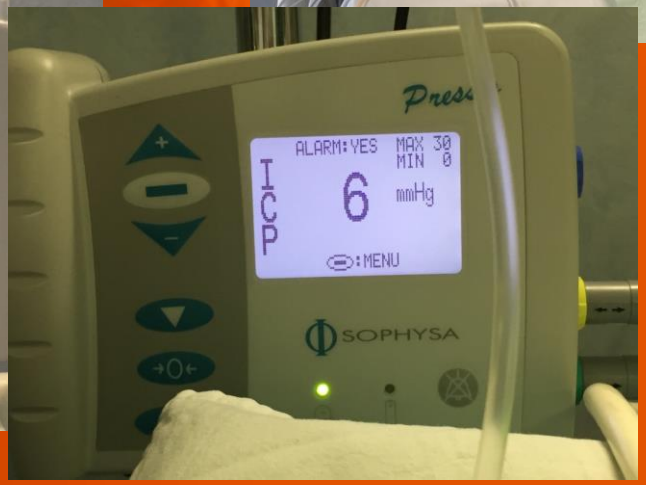




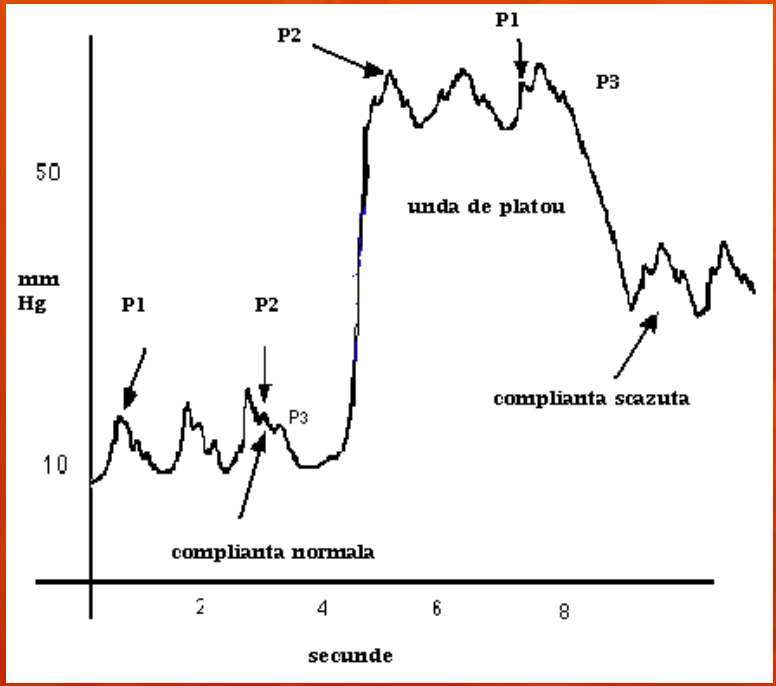
ICP-Curves



.6 ICP waveform.



ICP-Curves



Measurements of ICP

- normal ranging in a supine adult – ***7 - 15mmHG***
- lack of data supporting an absolute threshold for criticaly elevated ***ICP > 20 – 25 mmHg***
- ***refractory elevations of ICP >20mmHg*** -to aggressive treatament – stong predictor of mortality

- ICP utilized as a tool to monitor CPP, wich has offen been seep as a surrogate for CBF

- CBF better predicted by MMM rather than ICP or CPPalone

ICP Monitoring

- "Guidelines Group" with ICP-Monitoring and Therapy according Guidelines *versus*
- "Non Guidelines Group" with prophylactic barbiturate application, blind administration of osmo diuretics, routine hyperventilation

Results

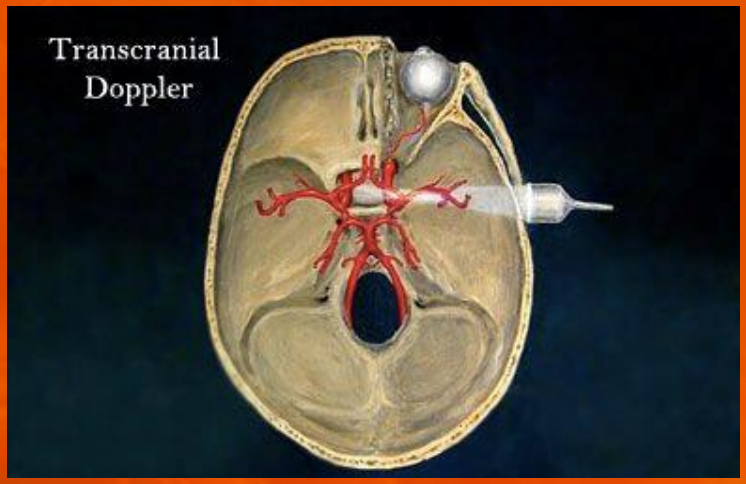
GOS	Guidelines (incl. ICP)	Non-Guidelines (without ICP)
	%	%
1 (dead)	30	44
2-3	21	31
4-5	49	25

Vukic-M et al. The effect of implementation of guidelines for the management of severe head injury on patient treatment and outcome. Acta Neurochir Wien. 2007

Non-Invasive Intracranial Pressure Monitoring

- transcranial Doppler (TCD)
  - pulsatility index (PI) – systolic and diastolic velocity
- pupillometry
- ultrasound measurement of optic nerve sheath diameter (ONSD)

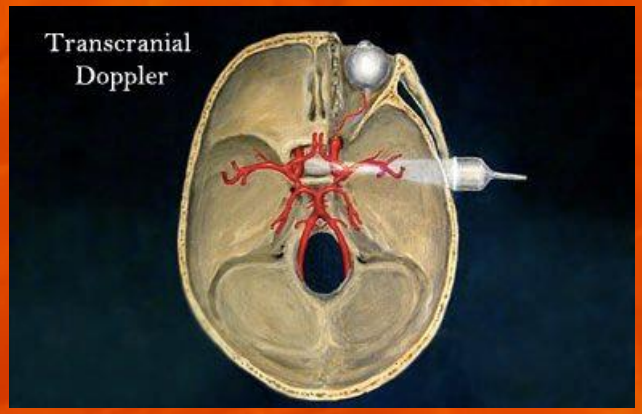
Transcranial Doppler (TCD)



- TCD noninvasively measures blood flow velocity by emitting and receiving high-frequency energy. The change in frequency - velocity and direction of CBF

- Mainstay in detecting vasospasm following SAH
  - evaluating the anterior circulation, particularly the MCA and ICA arteries
  - high degree of correlation with angiography when using a peak mean flow velocity threshold of >200 cm/s

Miller C, Armonda R. Neurocrit Care. 2014; 21(Suppl 2):S121–8.
Suarez JI, et al. Crit Care Med. 2002; 30:1348–55.



- **Regarding posterior circulation** velocity thresholds - conflicting,
  - recent guidelines - 85 cm/s as a threshold for vasospasm detection

    Le Roux P, et al. Neurocrit Care. 2014; 21(Suppl 2):S282–96.
  - high flow velocity can be a reflection of decreased vessel diameter (vasospasm) or increased blood volume (hyperemia).

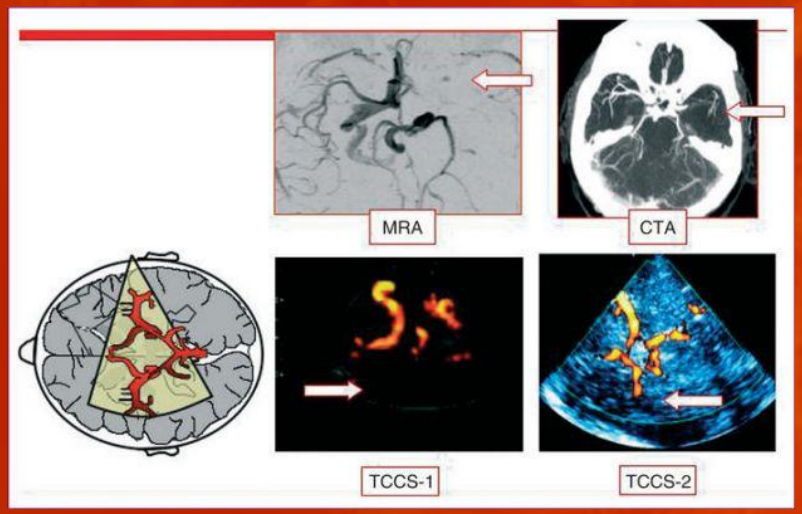
- **The Lindegaard ratio (LR)** between the middle cerebral artery and external carotid artery velocities ⟶ differentiate between vasospasm and hyperemia

  - >3 have been accurate in differentiating clinical and radiographic vasospasm from hyperemia

Gonzalez NR, Boscardin WJ, Glenn T, Vinuela F, Martin NA. J Neurosurg. 2007; 107:1101–12.
Nakae R, Yokota H, Yoshida D, Teramoto A. Neurosurgery. 2011; 69:876–83. disc 883

Transcranial color-coded duplex sonography (TCCS)

- Ultrasound-derived blood flow velocity detection → visualizes arteries with angle-corrected flow velocities
  - vessels previously thought to be difficult to insonate with conventional TCD (ICA and ACA)
  - better correlation to angiographic vasospasm than TCD alone



Proust F, et al. Stroke J Cereb Circ. 1999; 30:1091–8.

Brain Oxygenation

Invasive parenchymal catheter brain tissue oxygen (PbtO2)

Jugular bulb venous oxygen saturation (SjvO2)

→ continuous real-time evaluation of the balance of brain tissue oxygenation + treatment targets for CPP and triggers for systemic evaluation.

- Oxygenation - vital to the maintenance of cellular homeostasis,
- Marker for tissue at risk for secondary injury - neuronal integrity and its values

1. ***BTF guidelines have recommended placement of brain oxygenation monitoring when hyperventilatory strategies are employed after TBI***
2. ***more recent MMM guidelines recommending its placement in patients at risk for ischemia***

Brain Trauma Foundation, American Association of Neurological Surgeons & Congress of Neurological Surgeons. *J Neurotrauma*. 2007; 24(Suppl 1):S1–106.
Le Roux P, et al. *Neurocrit Care*. 2014; 21(Suppl 2):S282–96.

Guidelines for the management of TBI

Oxygenation should be monitored and hypoxia avoided

Prophylactic hyperventilation ($PaCO_2$<25 mmHg) is not recomanded

Hyperventilation is recommended as a temporizing measure for the reduction of elevated intracranial pressure (ICP)

Hyperventilation should be avoided during the first 24 hours after injury when CBF is often critically reduced

If hiperventilation is used, jugular SjO_2 or $PbrO_2$ measurements are recommended to monitor oxygen delivery

Bratton SL et al. J neurotrauam 2007

The international Multidisciplinary Consensus Conference on

Multimodality Monitoring in Neurocritical Care

We recommend monitoring brain oxygen in patients with or at risk of cerebral ischemia and/or hypoxia, using brain tissue ($PbtO_2$) or / and jugular venous bulb oximetry ($SjvO_2$)

A $PbtO_2$ < 20 mm Hg be considered a threshold at wich to initiate therapy

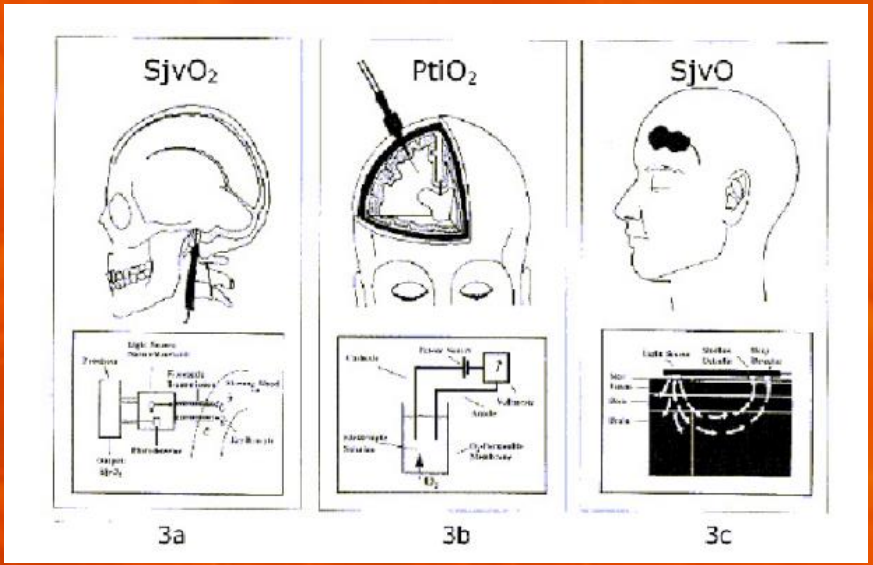
An $SjvO_2$ <55% can be considered as the threshold for abnormality and to start intervention

Le Roux P.et al Neurocrit. Care 2014

Methods

Commercially available invasive probes measuring oxygen content:

Licox system (Integra neurosciences)
Neurovent-PTO system (Raumedic).



- Provide: continuous regional monitoring via a Clark-type membrane electrode or a quenching process of fluorescence → measures the oxygen content present within the adjacent white matter.

- Studies
  - *safety and efficacy of these catheters*
  - *mechanical caveats that values are dependent on patient temperature, location/depth, and calibration time*

Stewart C, et al.. Neurosurgery. 2008; 63:1159–64. discuss 1164–1165.

PbtO2 (Licox)

- Normal ranges 20–35 mmHg

Pennings FA, Schuurman PR, van den Munckhof P, Bouma GJ.. J Neurotrauma. 2008; 25:1173–7

- MMM guidelines→ treatment threshold of 20 mmHg

Le Roux P, et al. Neurocrit Care. 2014; 21(Suppl 2):S282–96

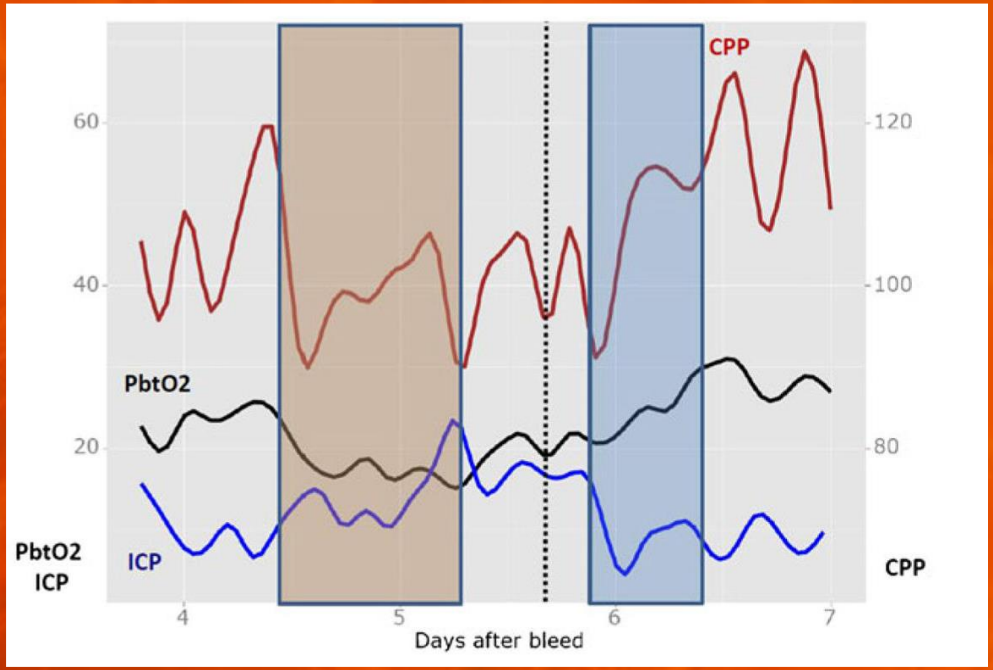
- **↓PbtO2 levels < 10 mmHg → morbidity, mortality, and extracellular evidence of metabolic crises have been associated**

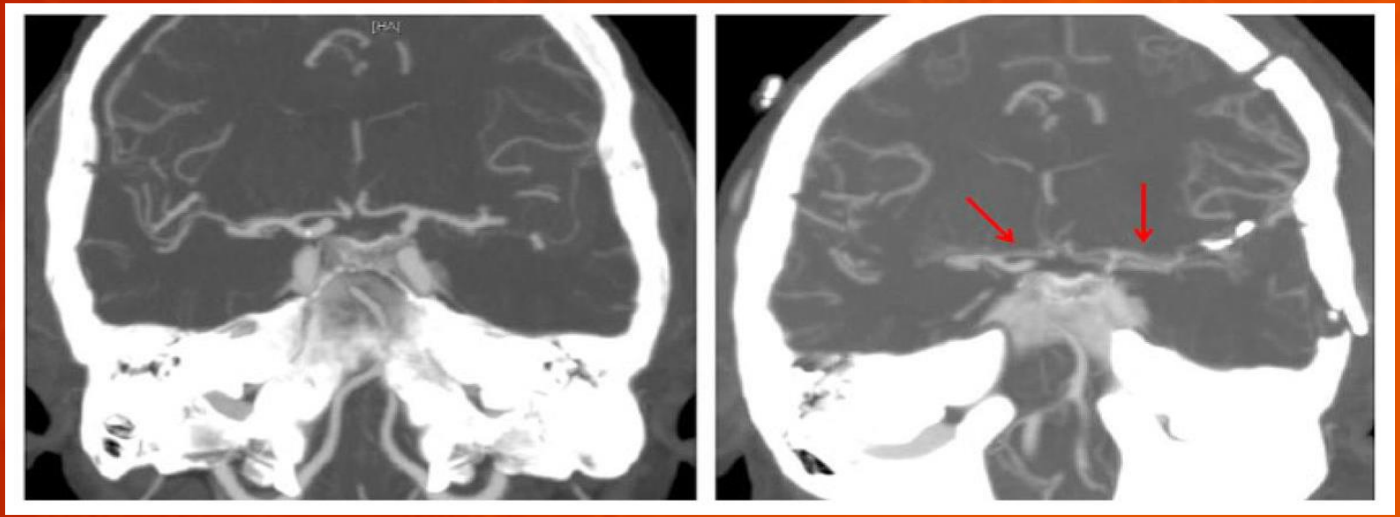
- **PbtO2 - target for CPP-driven therapy with evidence for improved long-term outcomes in both TBI and SAH**

Maloney-Wilensky E, et al. Crit Care Med. 2009; 37:2057–63.
Hlatky R, Valadka AB, Goodman JC, Contant CF, Robertson CS. J Neurotrauma. 2004; 21:894–906.
Bohman L-E, et al. Neurocrit Care. 2013; 19:320–8.

Clinical Case

MMM in SAH patient with vasospasm





PbtO2 (Licox)

- ↓PbtO2 = not specific for simple perfusion failure.
  - Influencing factors - CO2, O2, hypermetabolic states (fever, shivering, seizures)

Stiefel MF, et al. *J Neurosurg*. 2006; 105:568–75.

Jaeger M, Schuhmann MU, Soehle M, Nagel C, Meixensberger J. *Stroke J Cereb Circ*. 2007; 38:981–6.

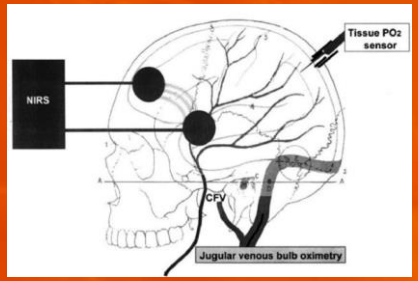
- PbtO2 = CBF X arteriovenous tension of O2 → indicating brain oxygenation relies on both adequate oxygen supply (perfusion/ oxygenation) and extraction (diffusion)

Rosenthal G, et al. *Crit Care Med*. 2008; 36:1917–24.

- PbtO2 monitoring - provide information:
  - assess for adequate oxygenation delivery when targeting optimal CPP ranges, and
  - reveal non-perfusion-related brain hypoxia when CPP is at goal / regional area in which the probe is placed.

- Based on the underlying etiology of ABI, the preferred location of probe placement will vary

Jugular bulb venous oxygen saturation (SjvO2)



- Information on global cerebral utilization of oxygen.
- Catheter placement - in the dominant internal jugular vein (when possible) ⟶ superiorly into the jugular bulb

Sheinberg M, et al.. J Neurosurg. 1992; 76:212–7.

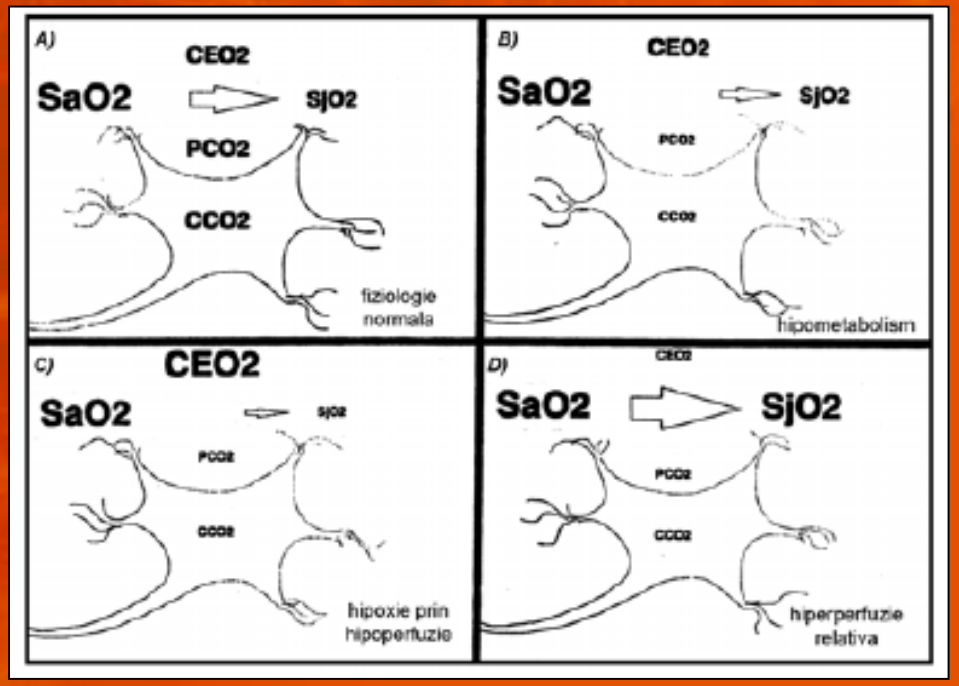
- Normal values - 55 and 75 %.
- < 55 % - increased oxygen extraction and tissue at risk for ischemia ⟶ poor outcomes especially when there is a failure to improve values with CBF-directed treatment

Gopinath SP, et al. J Neurol Neurosurg Psychiatry. 1994; 57:717–23.
Le Roux PD, Newell DW, Lam AM, Grady MS, Winn HR. J Neurosurg. 1997; 87:1–8.

Jugular Venous Oxygen Saturation ($SvjO_2$, ajDL)

Relation CBF ~ $CMRO_2$ ⇒ 3 scenarios

1. CBF is equally reduce as CMRO2
   - CEO2 ct
   - **SvjO2 normal**
2. "cerebral hypoxia and hypoperfusion"
   - CBF ↓ ↓, and CMRO2 ↓
   - CEO2 ↑, and **SvjO2 ↓**
3. "hyperemia or luxurious perfusion"
   - CBF ↑, and CMRO2 ↓
   - CEO2 ↓, and **SvjO2 ↑**



$SjvO_2$

- Cerebral compensatory mechanism for either decreased oxygen delivery or increased demand is an increase in oxygen extraction
- Exhausted compensatory mechanism → ischemia & ↓SjvO2.

- SjvO2 > 75 % - hyperemia, decreased metabolic demand, or even cell death

Cormio M, Valadka AB, Robertson CS. *J Neurosurg*. 1999; 90:9–15

- Its accuracy and safety is limited in comparison to PbtO2 monitoring

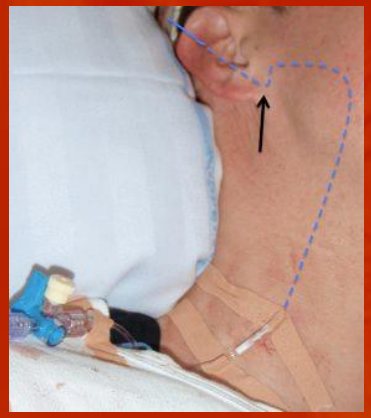
Gupta AK, et al. *Anesth Analg*. 1999; 88:549–53.

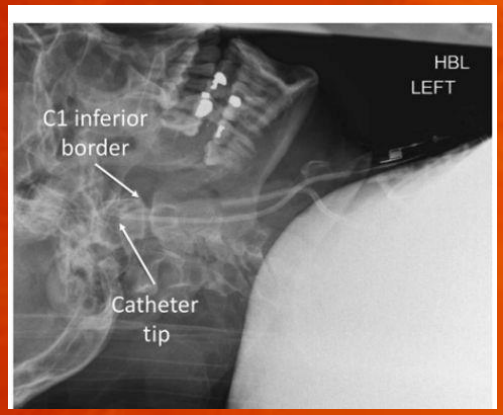
- Similar to PbtO2 monitoring - nonspecific nature, BUT ability to trigger suspicion of a subclinical state change.

Treatment strategies

- Focused on optimizing a twofold approach to brain oxygenation: delivery and demand.
- Efforts to optimize CPP
  - oxygenation delivery in addition to identifying,
  - treating hypermetabolic demand states - fevers and seizures
- Regional (PbtO2) + global (SjvO2) monitoring + more traditional ICP/CPP monitoring → promise for improved outcomes

Stiefel MF, et al. J Neurosurg. 2005; 103:805–11.





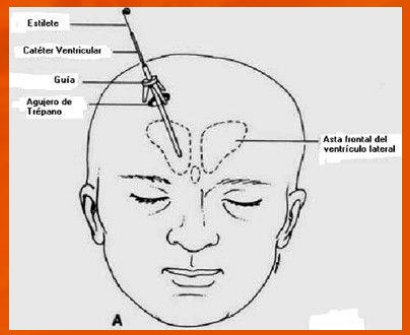
Cerebral Metabolism

Cerebral microdialysis (MD)

Analyses substrates within extracellular fluid of regional subcortical white matter → real-time monitoring of brain chemistry and detect energy crisis.

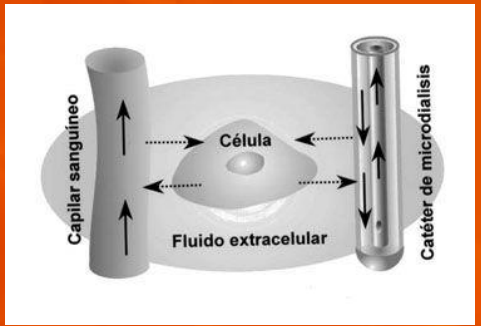
Artificial CSF dialysate - through a MD catheter with a semipermeable membrane → allowing molecules of a certain size or smaller to equilibrate down its concentration gradient.

Perilesional placement - recommended for focal injuries



Diffuse injuries – TBI - right frontal placement is recommended to favor less eloquent brain regions.

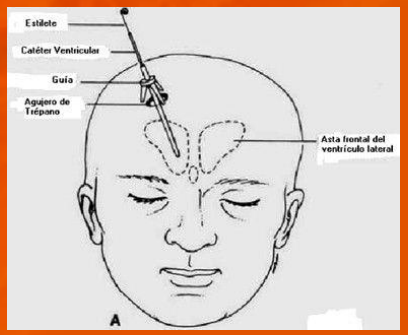
Cerebral Metabolism



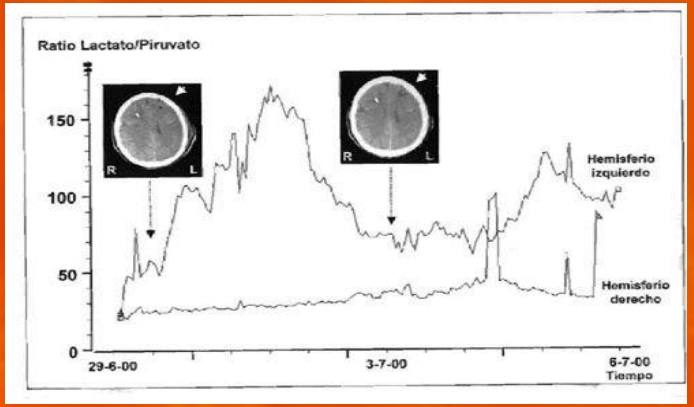
- **The extracellular substrates typically measured**
  - lactate
  - pyruvate
  - glucose
  - glutamate
  - glycerol.

- **Glutamate**
  excitatory neurotransmitter
  associated with injury and inflammatory cascade responses.

- **Glycerol**
  lipid-rich component of neurons
  marker of CNS cellular breakdown.
  ↑- associated with irreversible cellular death/ischemia.



Cerebral Metabolism



Lactate, pyruvate, and the lactate to pyruvate ratio (LPR)

- markers of hypoxia or ischemia → utilize as targets for perfusion optimization.
- LPR of >40 and >25 have both been reported as thresholds of metabolic distress
- Observational studies have suggested LPR >25 in the first 72 h is associated with poor outcome in TBI.

Timofeev I, et al. Brain J Neurol. 2011; 134:484–94.
Hutchinson P, O'Phelan K. Neurocrit Care. 2014; 21(Suppl 2):S148–58.

Mitochondrial dysfunction - significant role in LPR derangement;
LPR and lactate levels can be elevated in the absence of hypoxia or ischemia

Vespa PM, et al. *Crit Care Med*. 2007; 35:1153–60.

MMM Bioinformatics Integration Systems

A temporal, integrative analytic approach to multiple components of neuromonitoring - necessary to identify subclinical events - to intervene in a timely fashion.

Translate MMM data into a timely treatment regimen - out of reach of the typical **neuroICU workflow.**

An integration system relying on bioinformatics - **treat the complex multivariable disease which is SBI.**

The key steps for integrating these multiple parameters are data acquisition, integration, processing, and visualization in a single, user friendly interface

Individualized to practice environments and **include bedside integration systems or centralized database solutions**

Roh D and Pars S 2016

Conclusion

- Strides must be taken to utilize the myriad of moving **physiologic variables in a centralized, real-time montage in order to create an information interface** that can influence real-time treatment decisions.

- However, these treatment strategies and future trial designs must step away from a “one size fits all” treatment threshold utilizing a single component of MMM.

- Rather individual modes of MMM that can reveal cerebral and cerebrovascular physiology should i**ntegrate information from multiple modalities to reveal the patient-specific “injury profile” and vascular compliance** in order to formulate an optimal treatment plan.

- **It is not the device itself that will improve outcomes, but early recognition of these injury patterns and timely administration of individually tailored treatments.**

THANK YOU !!!