SYLLABUS

TC20: Neurocritical Care

Monday, November 14, 2011 14:45 - 18:15 Hall L

Marrakesh, Morocco, November 12-17, 2011

XXth WORLD CONGRESS OF NEUROLOGY

XXth WCN 2011 MARRAKESH World Congress of Neurology

WFN

SMN SOCIETE MAROCAINE DE NEUROLOGIE

WCN Education Program

Monday, 14 November, 2011

14:45-18:15

NEUROCRITICAL CARE

Chairperson: **Lutz Harms**, *Germany*

INTRAVENTRICULAR HAEMORRHAGE
Stefan Schwab, *Germany*

ELECTROLYTES AND ENCEPHALOPATHY
Lutz Harms, *Germany*

SEVERE BRAIN DAMAGE AND DISORDERS OF CONSCIOUSNESS
Steven Laureys, *Belgium*

16:15-16:45 Coffee Break

Acute Treatment of Intracerebral Hemorrhage

Stefan Schwab

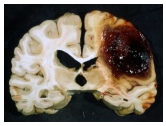
Department of Neurology

University of Erlangen-Nuremberg

Germany

ICH - Epidemiology

- ≈ 10-15% of all strokes
- 10-30 / 100.000 / year
- ≈ 2.000.000 / year woldwide
- Ventricular involvement ≈ 25-50%
- hydrocephalus ≈ 15-20%

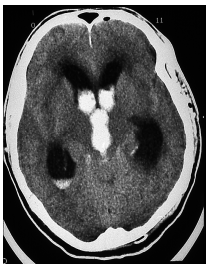


Weimar 2003 Cerebrovasc Dis

Qureshi 2009 Lancet

Ventricular hemorrhage (IVH)

- Primary IVH
  - headache
  - vomiting
  - Decreased consciousness
  - Focal neurological signs uncommon
- Secondary IVH
  - Decreased vigilance in combination with
  - Symptoms of ICH (e.g. hemiparesis)
- Diagnostic
  - CT
  - MRT (GRE-T2* / FLAIR)
  - DSA

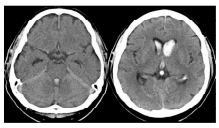


Tuhrim et al. Crit Care Med. 1999

Roos et al. JNNP 1995

Ventricular hemorrhage (IVH)

- **GRAEB score**



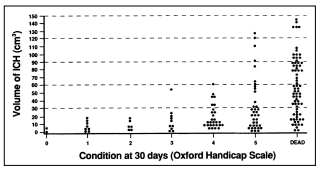
Lateral ventricle (each)
1 = trace of blood
2 = blood in < ½ Ventrikel
3 = blood in > ½ Ventrikel
4 = tamponade of ventricle, widened
3. und 4. Ventrikel (jeweils)
1 = evidence of blood but normal shape and size of ventricle
2 = tamponade of ventricle, widened

- **"LeRoux" Scale**
  - Each ventricle separately investigated
  - Maximum value 16
- **"Diringer" – Hydrocephalus-Scale:**
  - Each ventricle separately investigated
  - Maximum value 24

ICH – prognostic factors

not influencable:

- Initial hematoma volume
- age
- GCS on admission
- Location of ICH



influencable:

- Basic management
- Hemorrhage growth / re-bleeding
- Edema formation
- Intraventricular clot
- Hydrocephalus

Broderick 1993 Stroke
Davis 2006 Neurology
Hemphill 2001 Stroke
Tuhrim 1999 Crit Care Med
Ozdemir 2008 Neurol Res
Shapiro 1994 J Neurosurg
Diringer 1998 Stroke
Becker 2001 Neurology
Zurasky 2005 Neurology
Bhattathiri 2006 Acta Neurochir
Steiner 2006 Neurosurgery

ICH - Prognosis

- **Mortality**
  - ≈ 30-35% within 1 week
  - ≈ 60% within 1 year
  - ≈ 80% after 10 years
  - No difference between 1988 und 1998-2003
- **Functional Independence**

≈ 20% after 6 months

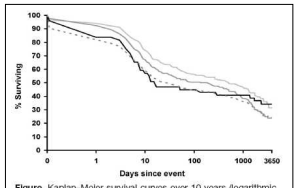
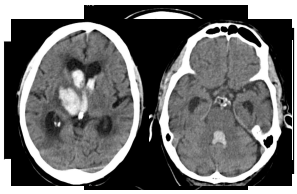


Figure. Kaplan–Meier survival curves over 10 years (logarithmic scale) in patients with deep (light grey line), lobar (dark grey line), or posterior fossa (black line) ICH (P=0.0947; log rank test). Data referring to all hemorrhages (dotted line) are given as reference and include cases of probable ICHs.

Sacco 2009 Stroke
Weimar 2003 Cerebrovasc Dis
Flaherty 2006 Neurology
Fogelholm 2005 JNNP
Broderick 1993 Stroke

ICH – treatment targets

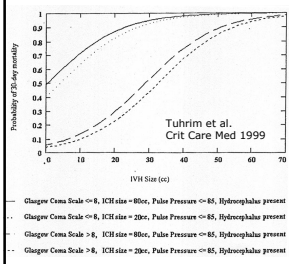
- Basic management
  - Tracheostomy
  - Prophylaxis DVT
  - BP
- ICH surgery
  - Hematoma evacuation
  - minimal invasive (MISTIE)
- ICH growth
  - Hemostasis
  - OAT-ICH – INR normalization
- Edema formation
  - ICP-monitoring
  - Decompressive surgery
  - Hypothermia
- Intraventricular hemorrhage and hydrocephalus
  - Intraventricular fibrinolysis
  - Lumbar drains



Treatment Target

„intraventricular hemorrhage and post-hemorrhagic hydrocephalus"

Treatment Target - intraventricular hemorrhage

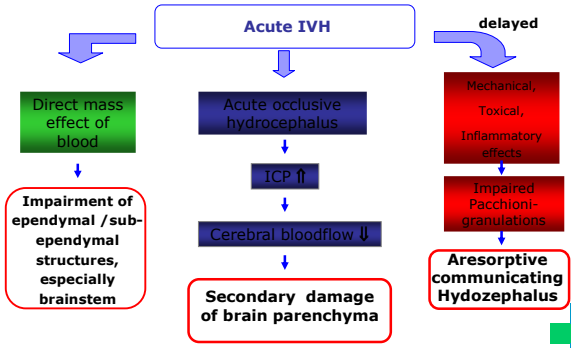


- IVH ≈ 25–45% after primary ICH
- IVH + hydrocephalus ≈ 15–30%
- Independent prognostic parameter
- Morbidity and mortality increased
- Lethality within 30 days:

  43-59% (vs. 9% without IVH)
- STICH, NOVO 7, FAST:

  poor Outcome in 70-90 %
- Optimal treatment so far unknown

Treatment Target - intraventricular hemorrhage



Intraventricular fibrinolysis

Metaanalyses of observational studies - Mortality

	n	Deaths			
		n	%	RR	95% CI
ICH	201				
Conservative	93	67	72	Ref.	–
EVD	75	42	56	0.78	0.53–1.14
EVD + Fibrinolysis	33	3	9	0.13	0.04–0.40

Metaanalyses of observational studies – functional outcome

		Poor outcome (mRS 4 und 5)			
		n	%	RR	95% CI
ICH	201				
Conservative	93	32/37	86	Ref.	–
EVD	75	65/75	87	1.00	0.66–1.53
EVD + Fibrinolysis	33	5/23	22	0.25	0.10–0.65

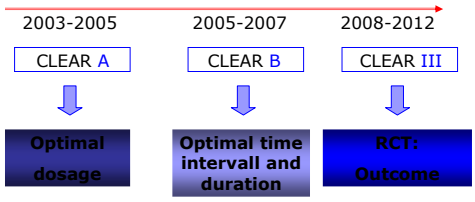
Nieuwkamp 2000 J Neurol

Intraventricular fibrinolysis

CLEAR IVH

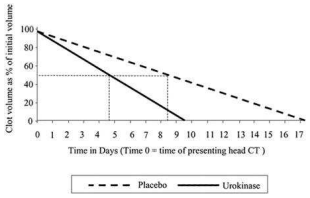
Clot Lysis: Evaluating Accelerated Resolution of Intraventricular Hemorrhage rt-PA Treatment of Brain Hemorrhage

A multicenter, randomized, double-blind, placebo-controlled trial



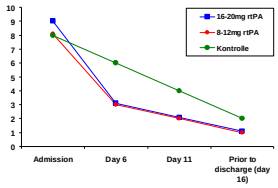
Intraventricular fibrinolysis
- what is sure? -

Fastened clot lysis



Urokinase

Naff et al. 2004

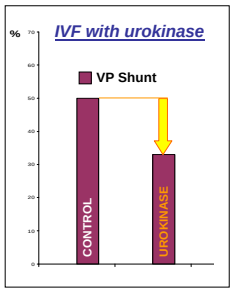


rt-PA

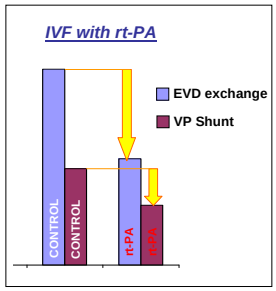
Huttner et al. 2008

Intraventricular fibrinolysis
- what is sure? -

Reduction of necessity of EVD-exchanges and VP-shunts



Tung 1998 Br J Neurosurg



Huttner 2008 Eur J Neurol

Intraventricular fibrinolysis

CLEAR-IVH
- Phase III -

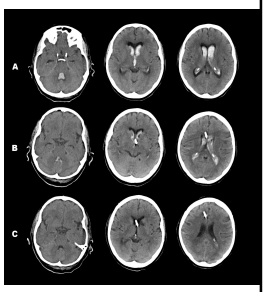
2009-2012?

CLEAR III

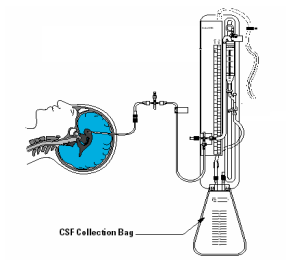
- Placebo-controlled
- Double blinded
- Randomized
- Planned patients: 500 (currently ≈ 87)
- Primary endpoint: mRS after 6 months
- Power-assumption: 15 % „Shift“ in Outcome mRS 0-3

Intraventricular fibrinolysis
- practical approach -

- Indication (according to CLEAR IVH)
  - ⇒ ICH < 30ml
  - ⇒ occlusive Hydrocephalus (tamponade of 3./4.Ventricles)
  - ⇒ necessity of EVD
- CT-Angio prior to IVF (rule out vascular malformation)
- >12h after symptom onset; >6h after EVD-placement
- Single dose 1mg (-4mg)
- Interval 8h (-12h) until „opening“ of 3./4. Ventricles



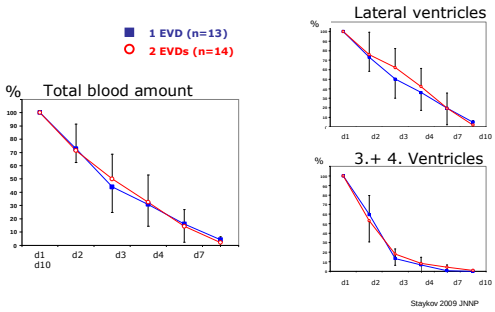
Intraventricular fibrinolysis
- practical approach -



- **CT for confirmation of EVD-location!**
- **Sterile work:**
  - rt-PA 1 mg/ml
  - aspirate 4 ml from EVD
  - slowly inject rt-PA
  - ca. 2ml NaCl (dead space)
- **then clamp EVD for 30-60 min** (ICP-Control)

Intraventricular fibrinolysis

1 *versus* 2 EVD:
Reduction of ventricular clot volume



Intraventricular fibrinolysis

No fear of re-bleeding!

all **37** published studies on IVF

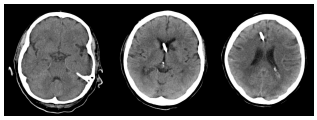
⇨ total n=502; IVF n=307, Controls n=195

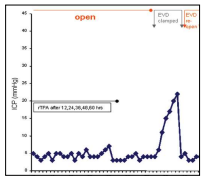
	Lysis		no Lysis	
	n	**re-bleeding**	**n**	**re-bleeding**
Alle	307	12 (3.9%)	195	3 (1.6%)
ICB	219	8 (3.6%)	170	2 (1.8%)
SAB	68	3 (4.4%)	25	1 (4%)
AVM	20	1 (5%)	-	-

3.9% vs. 1.6% !?
χ2 test: p=0.128

Post-hemorrhagic hydrocephalus

- 3d after admission: ventricles free from blood

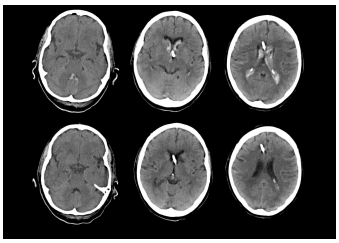




…..however, **ICP increase** after clamping of EVD

- in **>80%** of all patients in acute phase

Post-hemorrhagic hydrocephalus



Aresorptive comminicating hydrocephalus
Based on impairment of CSF-resorbing Pacchioni-Granulations of the Arachnoidea Mater by ventricular blood break down products

Post-hemorrhagic hydrocephalus

Problems of communicating hydrocephalus:

- continuous EVD-drainage necessary
  - Dislocation
  - Infection
  - Obstruction
- Permanent VP-Shunt – when?
  - decision on VP-Shunts usually after 2-3 weeks
- ≈25%-33% of patients with EVD and aresorptive hydrocephalus need VP-shunting (if not received IVF)
- VP-Shunt - Malfunction
  - In 1. year up to **40%** (even experienced neurosurgeons)
  - **70-80%** of pateints with VP-Shunt need revision
  - Causes both on proximal and distal end
  - Infection up to **8-10%**

Engelhard 2004 Surg Neurol

Post-hemorrhagic hydrocephalus - Lumbar drains -

Concept of lumbar drains

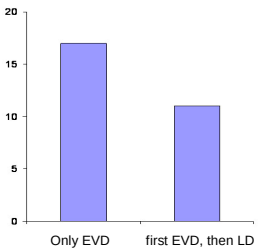
1) As soon as IVH is resorbed and „cleared"# 3. and 4. ventricles (CT-based) and
2) EVD-clamping fails ➔
3) Diagnosis of aresorptive hydrocephalus with communicating inner and outer CSF spaces

➡

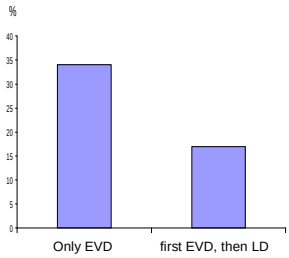
Placement of Lumbar drain should sufficiently drain CSF spaces – thereby replacing the EVD

Post-hemorrhagic hydrocephalus - Lumbar drains -

Duration of EVD (days)



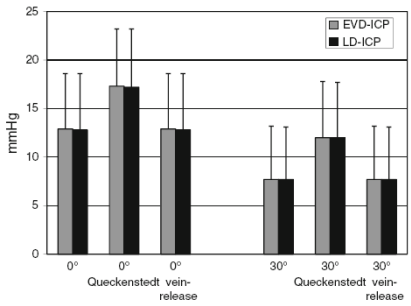
Nessessity of VP-Sunts (in %)



Huttner 2007 Stroke

Post-hemorrhagic hydrocephalus - Lumbar drains -

ICP monitoring via Lumbar drains



Speck et al NCC 2010

Combination of IVF and Lumbar drains

ICP curve during EVD and LD management

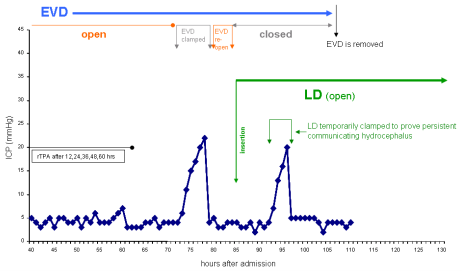
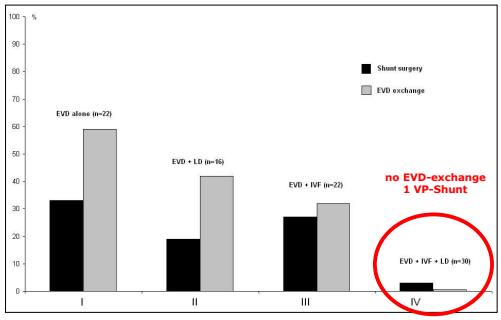


Fig. 1. External ventricular drainage (EVD) and lumbar drainage (LD) management shown exemplarily in patient 1. First peak in the ICP curve: after clearing of the third and fourth ventricle, attempt to clamp the EVD; increase in ICP verifies persistent hydrocephalus. Bottom between peaks: after LD was placed, EVD was branched off, proving that LD was capable of sufficient CSF drainage. Second peak in the ICP curve: to verify persisting hydrocephalus, LD was closed (while EVD remained closed), and there was a rise in ICP. rtPA , recombinant tissue plasminogen activator.

Huttner/Schab 2007 Neurocritical Care

Combination of IVF and Lumbar drains



Staykov et al. 2009 STROKE

AHA-recommendations

Ventricular drainage as treatment for hydrocephalus is reasonable in patients with decreased level of consciousness	Class IIa, Level of Evidence B New Recommendation
Although intraventricular administration of rt-PA in IVH appears to have a fairly low complication rate, efficacy and safety of this treatment is uncertain and is considered investigational	Class IIb, Level of Evidence B New Recommendation

2010 American Heart Association

Conclusion – Treatment of IVH

- EVD placement in occlusive hydrocephalus
- Intraventricular fibrinolysis speeds-up clot resolution
- Intraventricular fibrinolysis leads to
  - less EVD-exchanges
  - less VP-shunts
  - Influenes outcome? (CLEAR-IVH)
- As soon as aresorptive hydrocephalus is diagnosed → place LD
- Lumbar drainage leads to
  - Less EVD-exchanges
  - Less VP-shunts
- Combination of IVF and LD leads to
  - No EVD-exchanges
  - Almost no VP-shunts

Conclusions

BASIC MANAGEMENT

- Tracheostomy is frequently necessary in ICH volumes >30ml with IVH and hydrocephalus
- Early DVT prophylaxis using LMWH is safe
- BP management with SBP between 140-160 mmHg

HEMATOMA EVACUATION

- no general recommendation, probably useful in lobar-close-to-surface ICH and cerebellar hemorrhages; not recommended in basal ganglia and thalamic bleeds
- Minimal invasive OP currently studied (MISTIE)

Conclusions

PREVENTION HEMATOMA GROWTH

- FVIIa reduces ICH growth but does not improve outcome (maybe in subgroups currently studied)
- Warfarin-ICH needs immediate reversal of increased INR using PCC (and FFP´s) in combination with vitamine K

REDUCTION EDEMA FORMATION

- ICP-monitoring if ICP-lowering treatment is performed
- Decompressive Craniotomy (analogous to malignant MCA infarction)?
- Hypothermia as add-on to maximal conservative treatment with interesting preliminary findings

Conclusions

INTRAVENTRICULAR FIBRINOLYSIS

- Distinct evidence for hastened IVH-clot resorption
- Thereby reducing necessity of EVD-exchanges and VP-Shunts
- Effects on outcome currently studied (CLEAR-IVH)

POST-HEMORRHAGIC HYDROCEPHALUS and LUMBAR DRAINS

- LD are capable of replacing EVD and have further effects on EVD-exchanges and VP-shunts
- Combination of IVF and LD → no exchanges and VP-shunts any more!

Electolytes and encephalopathy

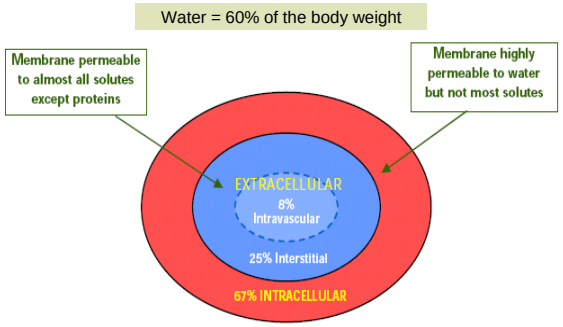
XXth World Congress of Neurology

Marrakesh

November 12-17, 2011

Lutz Harms.

Physiology , fluid balance



(B. Wills 2001)

Internal environment

- Composition of liquid surrounding cells
- Important for vital functions
- Components:
  - Constant volume
  - Constant tonicity and composition
  - Constant pH

Under normal coditions, the osmolarity and volume are regulated using informations from osmoreceptors and Baroreceptors and complex mechanisms

Osmolarity = 2 (Na+K) + BUN/2,8 + Gluc/18

BUN (blood urea nitrogen), glucose in mg/dl

Na, K in milliequvalents per liter – mEq/l

Refers to the number of solute particles dissolved in a solvent

-Is expressed as milliosmole per liter (mOsm/l)

-In the case BUN and glucose are normal, osmolarity can approximated by doubling the serum Na^+ plus 10

-Normal serum osmolarity: 290+/-5mOsm/l

Clinical importance of Hyponatremia

- The most common electrolyte disorder with a marked increase among hospitalised and nursing home patients
  - Acute care hospital: incidence 2,5%
  - Postoperative patients: 4,4%
  - Intensive care unit: 30,0%
- Chronic hyponatremia is more common than acute, acute hyponatremia is much more dangerous

Major causes of hyponatremia (<135 mmol/l)

- Iatrogenic
- SIADH / CSW
- Brain injury
- Isotonic fluid loss
- Drugs
- Water intoxication
- Endocrinopathy
- Paraneoplastic
- Pulmonary
- Renal
- Cardiac disease
- Other

Hyponatremia – important differences

Rapidity of development	Causes
• Acute	• Syndrom of Inapproprite Antidiuretic Hormon (SIADH)
• Chronic	• Cerebral Salt Wasting Syndrom - CSW
	• Other

Patients with levels belov 125 mOsm/l typically develop symptoms, especially in the setting of a rapid decrease.

When sodium concentration drops below 105 mOsm/l, life threatening complication are likely to occure.

SIADH

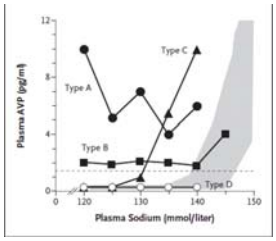
= **S**yndrom of **i**nappropriate **a**nti**d**iuretic **h**ormon secretion

May complicate neurological diseases of many types:

-Head trauma
-Bact. Meningitis
-Cerebral infarction
-Subarachnoid hemorrhage
-Neoplasm
-GBS

Roberts 1982

Types of osmoregulatory defects



- Typ A (30% of SIAD patients) fluctuating AVP secretion unrelated to plasma osmolarity or sodium level
- Typ B (30%) constant, non-supressible oversecretion of AVP despite hyponatremia
- Type C (30%) elevated AVP correlating with plasma osmolarity
- Typ D (10%) normal osmoregulation, but patients still fail to dilute urine

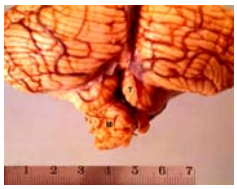
- **No correlation between the type of osmoregulation and underlying disease**

Roberts 1982

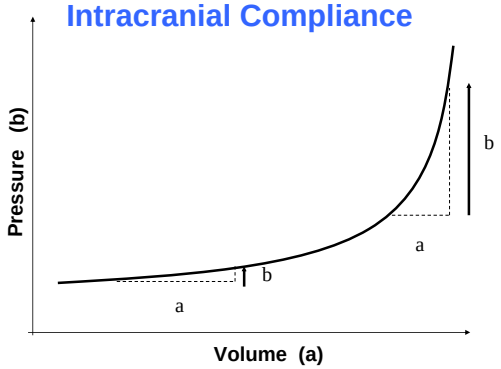
Pathophysiology of Hyponatremia

- Shift of water into brain cells start 20 minutes after acute reduction of sodium concentration
- **Increased level of vasopressin (in case of SIADH) causes a movement of water into brain cells itsself**
- Increased ICP reduces the cerebral blood flow
  (CBF = MAP – ICP)
- **Inhibitory effect of vasopressin and estrogen on the ATP synthesis** – resulting in an impaired Na/K pump

Herniation



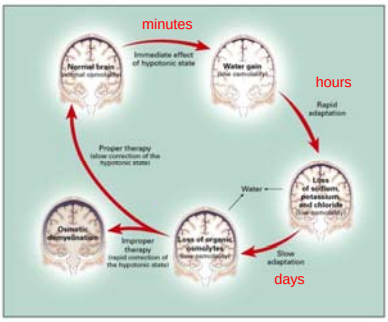
Intracranial Compliance



Clinical features of hyponatremic encephalopathy

Early	Advanced	Late
Headache	Impaired cognition	Decorticate postur.
Nausea	Inappr. behaviour	Bradycardia
Emesis	Hallucinations	Hypo/Hyperthermia
Muscular cramps	Asterixix	Dilated pupils
Weakness	Multifocal myoclon.	Epileptic seizures
	Respiratory insuff.	Coma

Effects of hyponatremia on the brain and adaptive responses



Adrogué et al. 2000

Diagnostic scheme in hyponatremia* a

Plasma osmolarity

High:
pseudohyponatremia /
renal failure

Low: „true“ hyponatremia

Urine sodium concentration

Low (<25 mmol/l):
-extrarenal sodium loss
-effective circulation volume depletion

High (>40 mmol/l):
-renal sodium loss (incl. CSW)
-increased effectiv circulationg volume (incl. SIADH)

*patients with intracranial disorders

Diagnostic scheme in hyponatremia* b

Volume status based on:
-clinical predictors of extracellular water
-laboratory findings
-central venous pressure measurement

Hypovolemia:
CSW
Diuretics
Extrarenal sodium loss
Salt losing nephritis
Mineralocorticoid deficiency
Osmotic diuresis

Normo / hypervolemia:
SIADH
Glucocorticoid deficiency
Hypothyreoidism
Hepatic cirrhosis
Heart failure
Renal failure

*patients with intracranial disorders

SIADH and CSW

- **Syndrom of inappropriate ADH secretion = SIADH**
- Water retention =dilutional Hyponatremia
- Urin hypertonic
- **Treatment: fluid restriction**

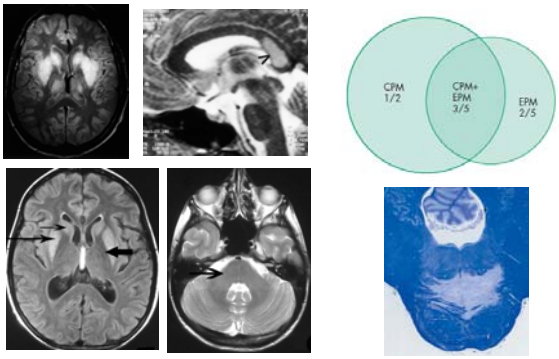
- **Salt wasting syndrom = CSW ***
- Hypovolemia and sodium deficit
- **Treatment: sodium and water administration**

* due to excessice secretion of natriuretic peptides and atrial natriuretic peptides

Pittfalls in Hyponatremia

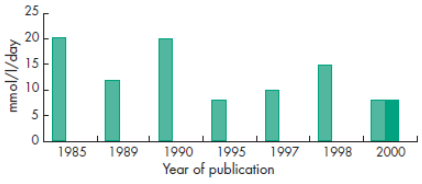
- Correcting hyponatremia too rapidly may result in CPM with permanent neurological deficits
- Do not neglect to consider laboratory error as a cause of hyponatremia
- Because of the association with small cell carcinoma of the lung, aggressive workup for occult SCC in patients without an alternative explanation for their SIADH may be warrented

Pontine and extrapontine myelinolysis



Sajith et al. 2007, Martin et al. 2004,Behrens et al. 2001, Menger et al.

Maximal suggested correction of hyponatremia



Martin et al. 2004

Management of hyponatremia

- **Sodium requirement:**
  Na deficit = (desired Na - measured Na) x 0.6 x Kg BW
- Administration of 3% NaCl only if level of less than 110mmol/l
- Acute hyponatremia – correction: up to 1-2 mmol/l
- Chronic hyponatremia – correction: 0,5 mmol/l
- < 8-(12) mmol/l first 24 h (chronic cases)

-stopp when symptoms disappear or serum sodium of 125-130 m0smol/l is achieved

- Furosemide 1mg/Kg, if fluid load exist (cardiac failure)
- Normalize potassium level
- Monitoring serum and urine electrolyte levels

Conclusions

- Symptoms of encephalopathy caused by disorders of electrolytes
  - are induced by many causes, complex pathophysiology
  - are unspecific (delirium, confusionel state, seizures etc.)
  - depending from severity and dynamic of abnormality
  - may be life threatening
- underlying disease or cause should be clarified
- causal treatment is necessary beside treatment of symptoms

Severe brain damage & disorders of consciousness: *Improving pain assessment*

Steven Laureys MD PhD
Coma Science Group
Cyclotron Research Centre &
Neurology Dept
University & University Hospital of Liège
Belgium

World Congress of Neurology
Marrakesh, November 14, 2011

WFN

COMA SCIENCE GROUP

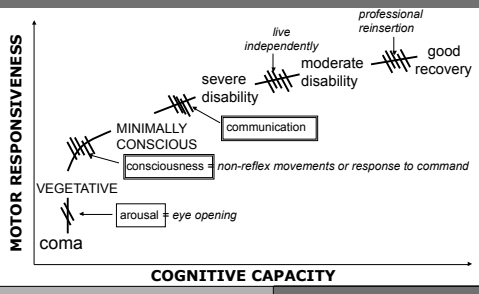
Université de Liège

CHU de Liège

www.comascience.org

1

Quantifying consciousness



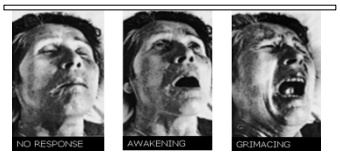
Laureys et al., Current Opinion in Neurology, 2005

www.comascience.org

2

Pain without words ?

Pain is a subjective first-person experience
which has to be communicated to be accurately assessed



Only motor response considered indicative of conscious perception
is localization to noxious stimulation

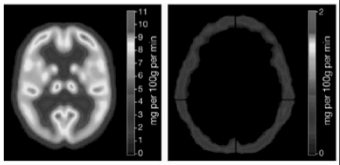
Laureys et al What it like to be vegetative or minimally conscious? *Curr Opin Neurol 20 (2007) 609-13*

www.comascience.org

3

No brain, no pain

NORMAL BRAIN DEATH



Laureys, 2005

Motor response without pain

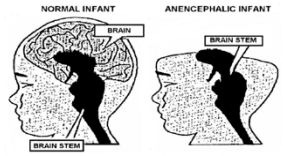
BRAIN DEATH

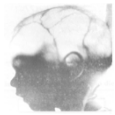
Bueri et al Mov Disord. 2000, 15:583-6

Spinal reflexes 75%

extension-pronation
plantar responses
muscle stretch reflexes
abdominal reflexes
undulating toe flexion sign
"Lazarus' sign

No cortex, no pain



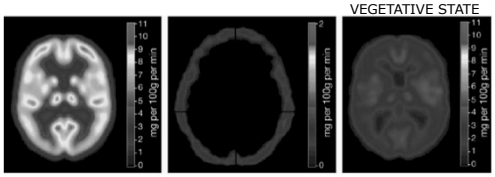


Consciousness in congenitally decorticate children: developmental vegetative state as self-fulfilling prophecy

Shewmon et al Dev Med Child Neurol. 1999

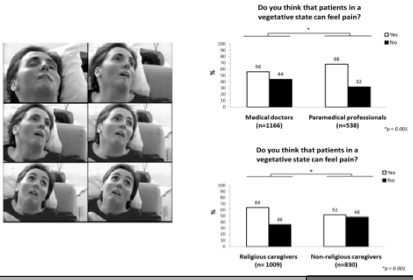
Some cortex, some pain?

NORMAL BRAIN DEATH COMA VEGETATIVE STATE



Laureys, 2005

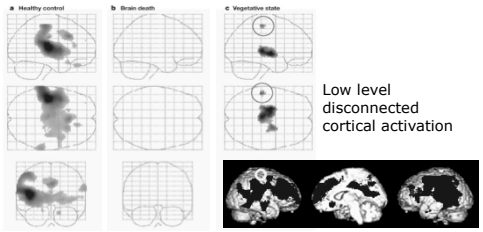
Pain in the vegetative state?



Demertzi et al, *Prog Brain Res,* 2009

Brain activation to pain

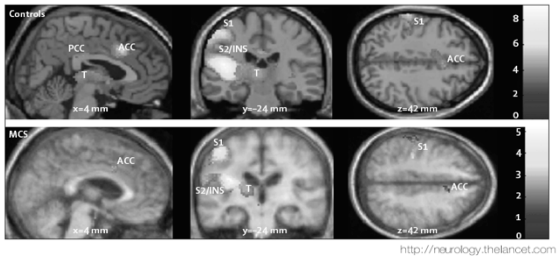
Noxious electrical stimulation



Low level disconnected cortical activation

Laureys et al, *Neuroimage,* 2002
Laureys, *Nature Reviews Neuroscience,* 2005

Pain in minimally conscious state



http://neurology.thelancet.com

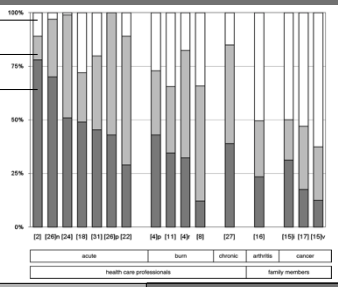
Boly et al *Lancet Neurology*, 2008

Assessing pain

overestimation

agreement

underestimation



Kappesser and Williams, *Pain* 2010

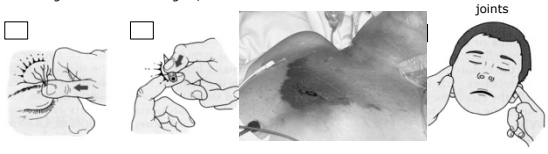
Standardized stimulation

Supraorbital ridge

Nail beds of fingers/toes

Sternum

Temporo-mandibular joints



Standardized assessment

Standardized stimulation

Table 1
Protocol of the Nociception Coma Scale (detailed administration guidelines in Complementary online material).

Motor response
3 – Localization to noxious stimulation
2 – Flexion withdrawal
1 – Abnormal posturing
0 – None/flaccid

Verbal response
3 – Verbalisation (intelligible)
2 – Vocalisation
1 – Groaning
0 – None

Visual response
3 – Fixation
2 – Eyes movements
1 – Startle
0 – None

Facial expression
3 – Cry
2 – Grimace
1 – Oral reflexive movement/startle response
0 – None

Schnakers et al, *Pain* 2010

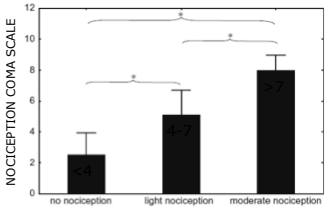
Pain in infants & demented

Ethical Implications: Pain, Coma, and Related Disorders *Encyclopedia of Consciousness* (2009), vol. 1, pp. 243-250

Table 1 Selection of behavioral scales which assess acute pain in noncommunicative patients

Infants	NIPS: Neonatal Infant Pain Scale
	FLACC: Faces, Legs, Activity, Cry, Consolability Observational Tool
	PIPP: Premature Infant Pain Profile
	CRIES
	CHEOPS: Children's Hospital of Eastern Ontario Pain Scale
Demented elderly	PAINAD: Pain Assessment In Advanced Dementia
	CNPI: Checklist of Nonverbal Pain Indicators
	DOLOPLUS 2
	ADD: The Assessment of Discomfort in Dementia Protocol
	PACSLAC : Pain Assessment Checklist for Seniors with Limited Ability to Communicate

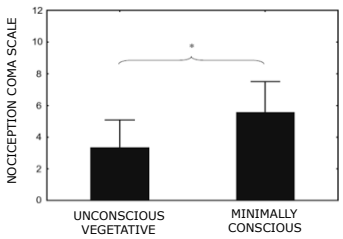
Nociception coma scale



Checklist of Non-verbal Pain Indicators

Schnakers et al, *Pain* 2010

Nociception coma scale



Schnakers et al, *Pain* 2010

www.comascience.org

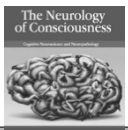
16

Nociception Coma Scale

- New "pain scale" for disorders of consciousness after coma
- Assesses motor, verbal (vocal), visual (ocular), and facial responses on scales from 0 (no response) to 3 (total scores 0 – 12) to a quantified standard stimulus
- Brief time required (1–5 min) to conduct and rate the examination
- More sensitive compared with 4 other "pain" scales
- Permits detect, communicate & follow non-communicative patient's behaviors and their management
- Allows monitoring treatment avoiding sedative effects & under-uses of analgesics

www.comascience.org

17



THANK YOU

Université de Liège
CHU de Liège
fnrs.be
Cyclotron research centre
James S. McDonnell Foundation
MIND SCIENCE

www.comascience.org

18