ACID BASE AND NEUROTRAUMA: unravelling the effects of hypertonic saline

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CASE

- ♂ 78y – fall from stairs, 6 meter, found after unknown time delay
- No previous medical history
- SpO2 unmeasurable, normotensive
- Lethargic, external bleeding head wound, light reactive pupils

--> Intubation and transport to hospital

Hypotensive during transport: what fluids to give?

WHAT DO THE GUIDELINES RECOMMEND?

Brain Trauma Foundation TBI Guidelines

Prehospital Guidelines for the Management of Traumatic Brain Injury – 3rd Edition

Al Lulla, Angela Lumba-Brown, Annette M. Totten, Patrick J. Maher, Neeraj Badjatia, Randy Bell, ...show all

TREATMENT: fluid resuscitation

Strong: Prevent hypotension & resuscitate with isotonic/blood products

Weak: *Hypertonic fluid resuscitation* for GCS<8 with suspected ICP↑

TREATMENT: hyperosmolar therapy for suspected increased intracranial pressure

Weak: *No prophylactic hypertonic fluids* for suspected ICP↑/cerebral herniation

But: studies on which the guidelines are based use different concentrations and protocols

3%, 7.2%, 7.5%, 10%, and 23.4% ⟶ no evidence for optimal %

HYPEROSMOLAR SOLUTIONS: MANNITOL VS. HYPERTONIC SALINE

Hypertonic Saline Versus Mannitol for Traumatic Brain Injury: A Systematic Review and Meta-analysis With Trial Sequential Analysis

Schwimmbeck, Franz[*]; Voellger, Benjamin MD[†]; Chappell, Daniel MD[*]; Eberhart, Leopold MD[‡]

- No statistical differences in mortality and neurological outcomes
- But significantly lower ICP & higher CPP higher with hypertonic saline
- *Conclusion*: **Hypertonic saline might be superior** and is safe & well-tolerated

TABLE 1. Characteristics of Included Studies

References	Design	N (ep.)	Patients	Fluids	Main Results
Du et al[36]	RCT	132	Severe TBI ICP > 20 mm Hg	3% HS 20% M	HS was better than M in reducing ICP. Clinical outcome was not significantly improved
Cottenceau et al[40]	RCT	47 (165)	Severe TBI ICP > 15 mm Hg	7.5% HS 20% M	HS and M both reduced ICP and increased CPP
Francony et al[41]	RCT	20	TBI and stroke ICP > 20 mm Hg > 10 min	7.45% HS 20% M	HS and M both reduced ICP effectively
Hendoui et al[42]	RCT	33	Moderate to severe TBI Scheduled therapy	5% HS bolus 5% HS cont. 20% M	S100B useful for treatment monitoring HS safe and effective in TBI
Huang and Yang[43]	RCT	33 (238)	Severe TBI ICP > 20 mm Hg > 5 min	15% HS 20% M	HS and M similar on maximum ICP reduction, action onset, and duration of action
Ichai et al[44]	RCT	34 (69)	Severe TBI ICP > 25 mm Hg > 5 min	HSL 20% M	HSL is superior in reducing ICP Better neurological outcome in HSL group
Jagannatha et al[45]	RCT	38 (488)	Severe TBI ICP > 20 mm Hg > 10 min	3% HS 20% M	HS: shorter duration of increased ICP and inotrope requirement
Mao et al[37]	RCT*	14 (56)	Severe TBI, after decompressive craniectomy ICP > 20 mm Hg > 5 min	3% HS 20% M	HS and M rapidly decrease ICP; HS has a longer duration of action
Qin et al[38]	RCT	48	Severe TBI, after decompressive craniectomy ICP > 15 mm Hg > 30 min	3% HS 20% M	HS can decrease postoperative complications, and improve the prognosis of patients
Sakellaridis et al[46]	RCT	29 (199)	Severe TBI ICP > 20 mm Hg > 5 min	15% HS 20% M	HS and M equal on ICP reduction and duration of action
Upadhyay et al[48]	Quasi RCT†	200	Neurocritically ill children Symptoms of increased ICP	3% HS 20% M	HS is a safe and effective alternative to M
Vialet et al[47]	RCT	20	Severe TBI ICP > 25 mm Hg > 5 min	7.5% HS 20% M	Less ICP episodes and treatment failure in HS group
Yan et al[39]	RCT*	16 (64)	Severe TBI, after decompressive craniectomy ICP > 25 mm Hg > 5 min	3% HS 7.5% HS 20% M	HS can rapidly decrease ICP and increase MAP without obvious side-effects
Cheng et al[64]	NCT‡§	60	TBI, after decompressive craniectomy ICP > 20 mm Hg > 5 min	3% HS 20% M	Greater reduction of ICP and lower daily ICP burden after HS therapy
Colton et al[49]	NCT‡	117 (289)	Severe TBI ICP > 20 mm Hg > 5 min	3/7.5% HS M	HS superior to M in reducing ICP
Fletcher et al[50]	NCT‡‖	330	Neurocritically ill	HS 20% M	No difference in venous thromboembolisms
Gallesio et al[51]	NCT‡	36	Severe TBI	HS M	HS corrects ICP better HS is effective after M failure
Grimmer and Tesoro[52]	NCT‡	105	Neurocritically ill	23.4% HS 20% M	No difference in ICP control and mortality
Kerwin et al [53]	NCT‡	22 (210)	Severe TBI ICP > 20 mm Hg > 5 min	HS M	HS is more effective in reducing ICP
Larive et al[54]	NCT‡	27	Neurocritically ill Target sodium 145-155 mmol/L	3% HSAc cont. M	No differences in adverse events
Mangat et al[55]	NCT‡§	50	Severe TBI	3/23.4% HS 20% M	HS is more effective in lowering duration of daily elevated ICP
Mehta et al[56]	NCT‡	13	Children with severe TBI	3% HS/3% HS	Sodium and osmolality strongly correlate in serum

Fluid	Osmolarity
Mannitol (20%)	1000 mOsm/L
NaCl (3%)	1026 mOsm/L
NaCl (10%)	3420 mOsm/L
NaCl (20%)	6840 mOsm/L

TO GIVE OR NOT TO GIVE HYPERTONIC SALINE?

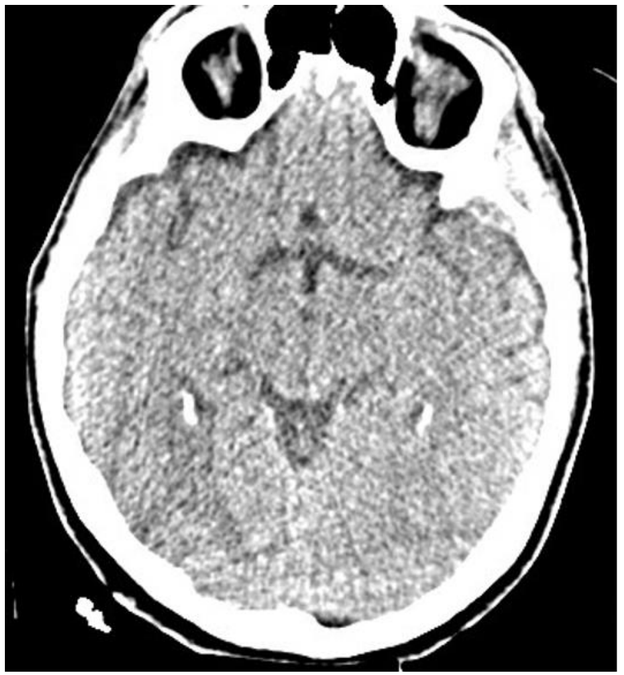
↓↓ ICP
↑↑ CPP
Safe and well tolerated

No improvement in survival and neurology
What concentration and volume?
What population?

CASE

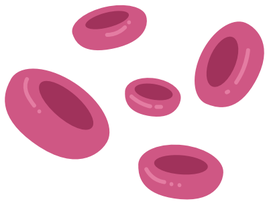
78y, 6m fall from stairs
2 x 100cc 10% NaCl

- Chest X ray: traumatic hemopneumothorax ⟶ chest tube
- During admission unexpected IHCA ⟶ dead after 20 minutes



- Post-mortem CT:

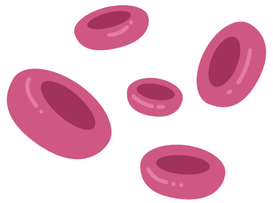
Hemopneumothorax, lung contusion, adequately placed chest tube
Femur fracture
Non-displaced temporal bone fracture
Small epidural hematoma + small trace of subarachnoid bleeding



CASE

Severe combined respiratory and metabolic acidosis

	Value	Normal values
pH	6.84	7.33 – 7.43
pCO_2, venous (kPA)	8.0	5.5 – 6.8
pO_2, venous (kPA)	2.3	4.0 – 5.3
HCO_3^- (mmol/L)	10.2	24.0 – 28.0
Base Excess (mmol/L)	-21.8	0 – 4.0
Lactate (mmol/L)	10.4	0.5 – 1.5
Na^+ (mmol/L)	158	135 – 145
K^+ (mmol/L)	4.9	4.0 – 5.0
Cl^- (mmol/L)	126	96 – 106
Glucose (mmol/L)	11.6	4.0 – 8.0
Hb (mmol/L)	4.1	8.5 – 11.0



CASE

1

SID
158 – 126 = 32
(corrected normal value = 43, so 43-32=11 mmol explained by chloride)

Compare Na-Cl with 34 mM

(apply correction to 34 if pH is extreme: +1.5 for pH -0.1)

2

Albumin is unknown, presumably normal

Add 3mM to predicted SBE for each 10g/L below 40 g/L

3

BE -21.8, of which 10.4 explained by lactate ⟶ 11.4 remaining acid

Compare BE on BG strip with BE predicted, Look at lactate

	Value	Normal values
pH	6.84	7.33 – 7.43
pCO_2, venous (kPA)	8.0	5.5 – 6.8
pO_2, venous (kPA)	2.3	4.0 – 5.3
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Hb (mmol/L)	4.1	8.5 – 11.0

Also:

- Anion gap = 158 - 126 - 10.2 = 21.8, but < 12 (normal) corrected for lactate → NAGMA from hyperchloremia
- Hypernatremia 158 with calculated osmolality of 337

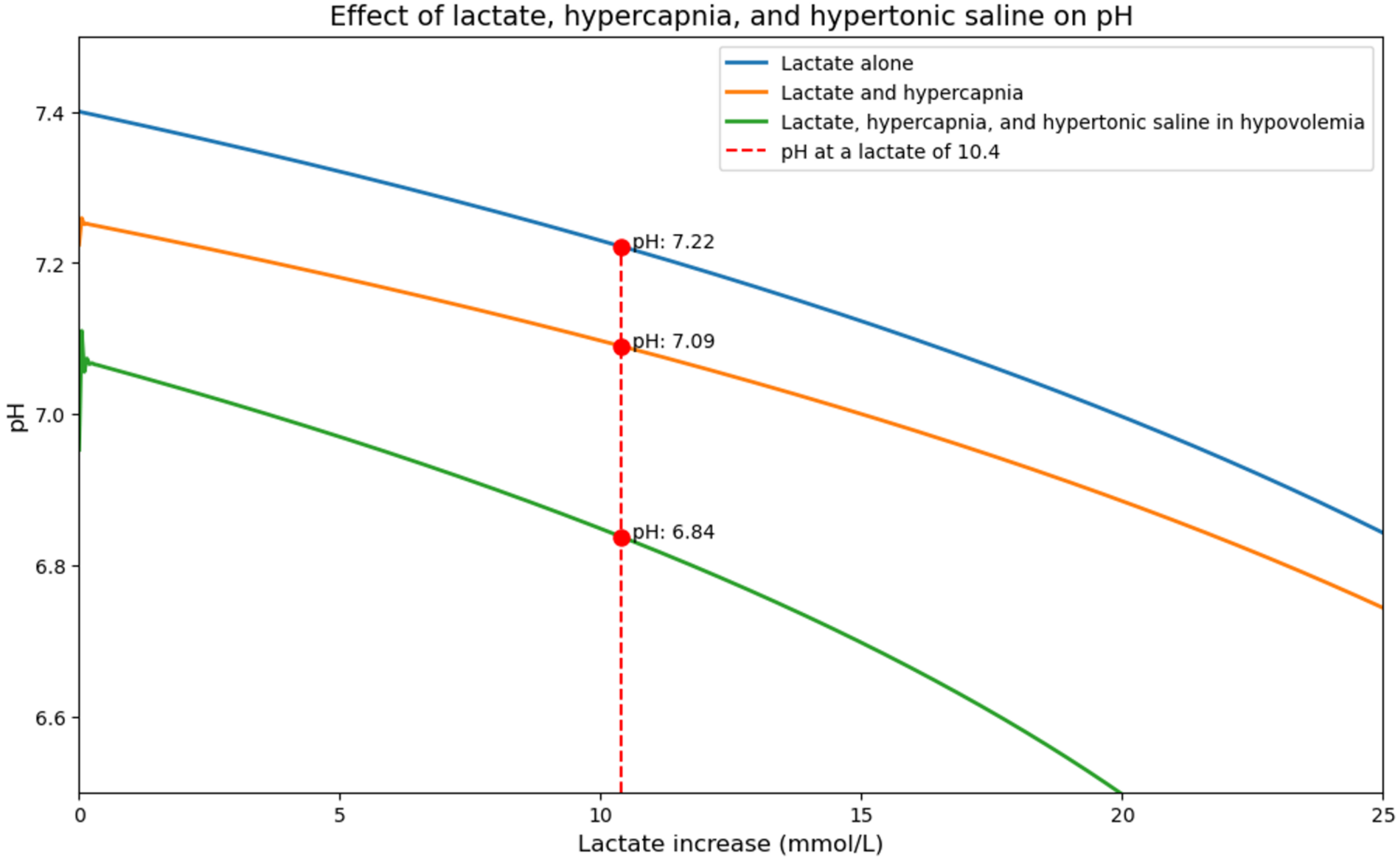
How to simulate the individual effects of every acid-base disturbance in this case?

$$pH = 6.1 + log_{10} \frac{[SID] - [A^-] - [SIG]}{0.03\, pCO_2}$$

$$pH = 6.1 + log_{10} \frac{([SID] - \text{chloride effect}) - [A^-] - ([SIG] + lactate)}{0.03\, pCO_2}$$

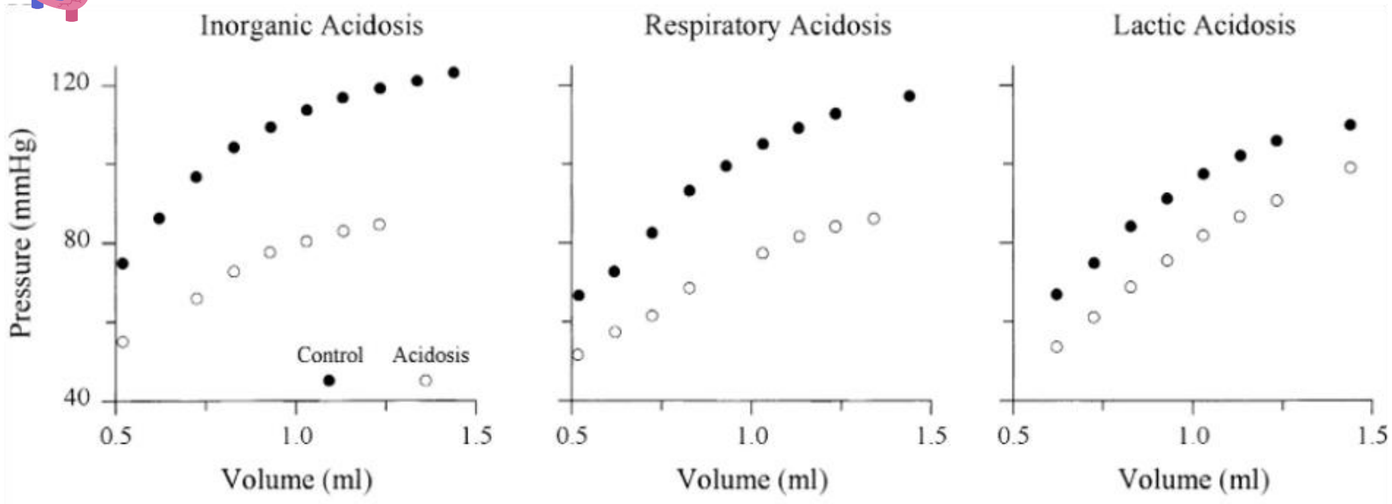
- SID / chloride effect based on Base Excess contribution of 11.4
- pCO2 based on the case
- Atot based on minimal dilution and healthy invidual

--> simulate as a function of lactate

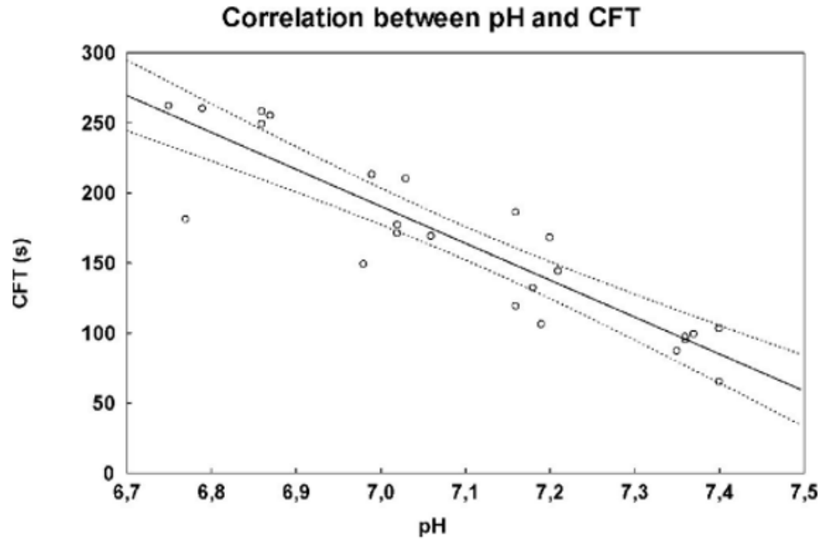

Effect of lactate, hypercapnia, and hypertonic saline on pH
Lactate alone
Lactate and hypercapnia
Lactate, hypercapnia, and hypertonic saline in hypovolemia
pH at a lactate of 10.4
pH: 7.22
pH: 7.09
pH: 6.84
pH
7.4
7.2
7.0
6.8
6.6
0
5
10
15
20
25
Lactate increase (mmol/L)

Does acidosis matter?

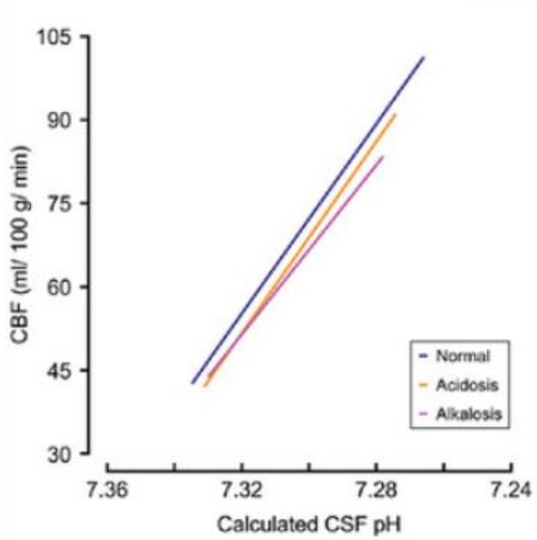
Cardiac contractility



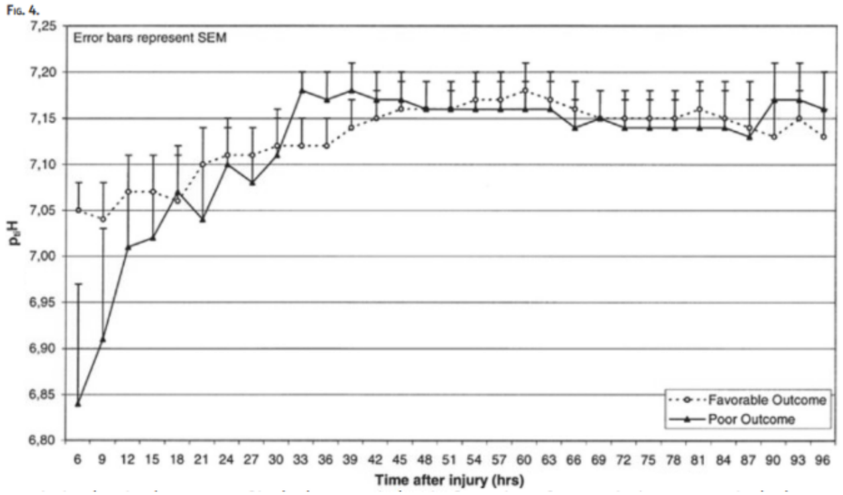
Coagulation



ICP
CPP
CBF

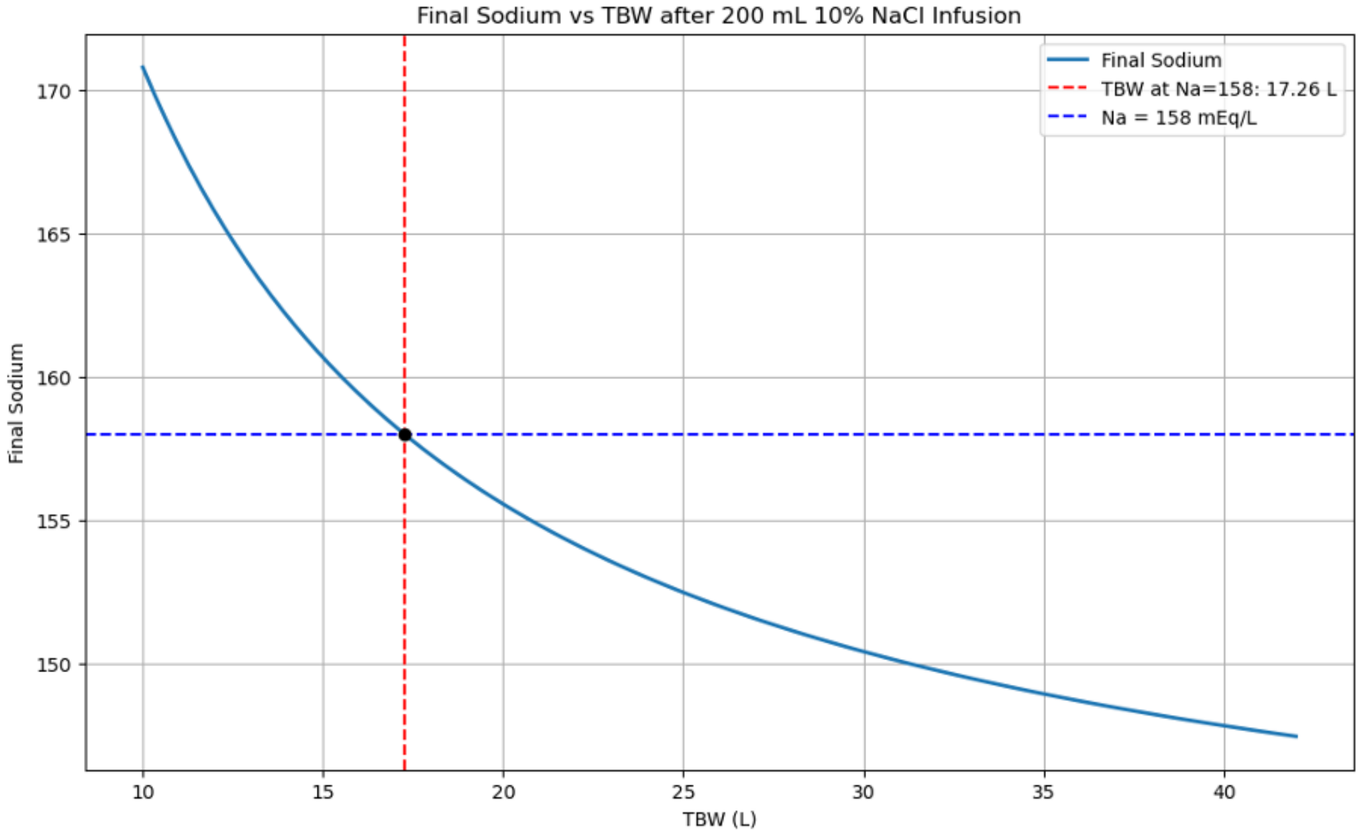


Neuronal damage



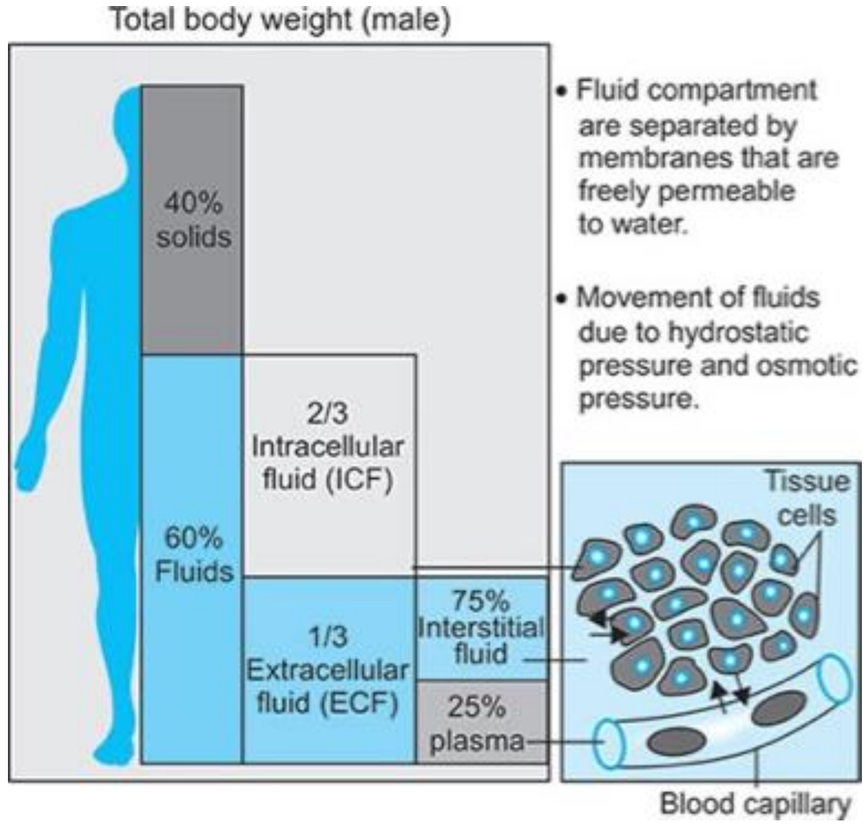
Does the osmolality rise matter?

$$\Delta[Na^+] = \frac{Infused\ [Na^+] - serum\ [Na^+]}{Total\ body\ water + 1}$$



Unlikely this much TBW was lost in this case

⟶ **Delayed equilibration of Na in shock**



Does the osmolality rise matter?

- Too rapid correction of chronic hyponatremia --> osmotic demyelination syndrome
- Maximum increase of Na 10 mOsm/L per 24 hours
- Osmolality rise in this case was >42 mOsm/L in just hours

Alternatives?

1) 3% hypertonic saline

No difference when compared with other outcomes

Potentially better ΔICP en ΔGCS

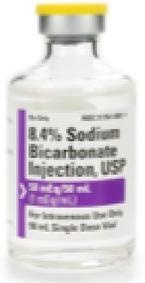
Less metabolic consequences

2) 8.4% $NaHCO3^-$

High osmolarity

Alkalinising

Frequently present in prehospital equipment

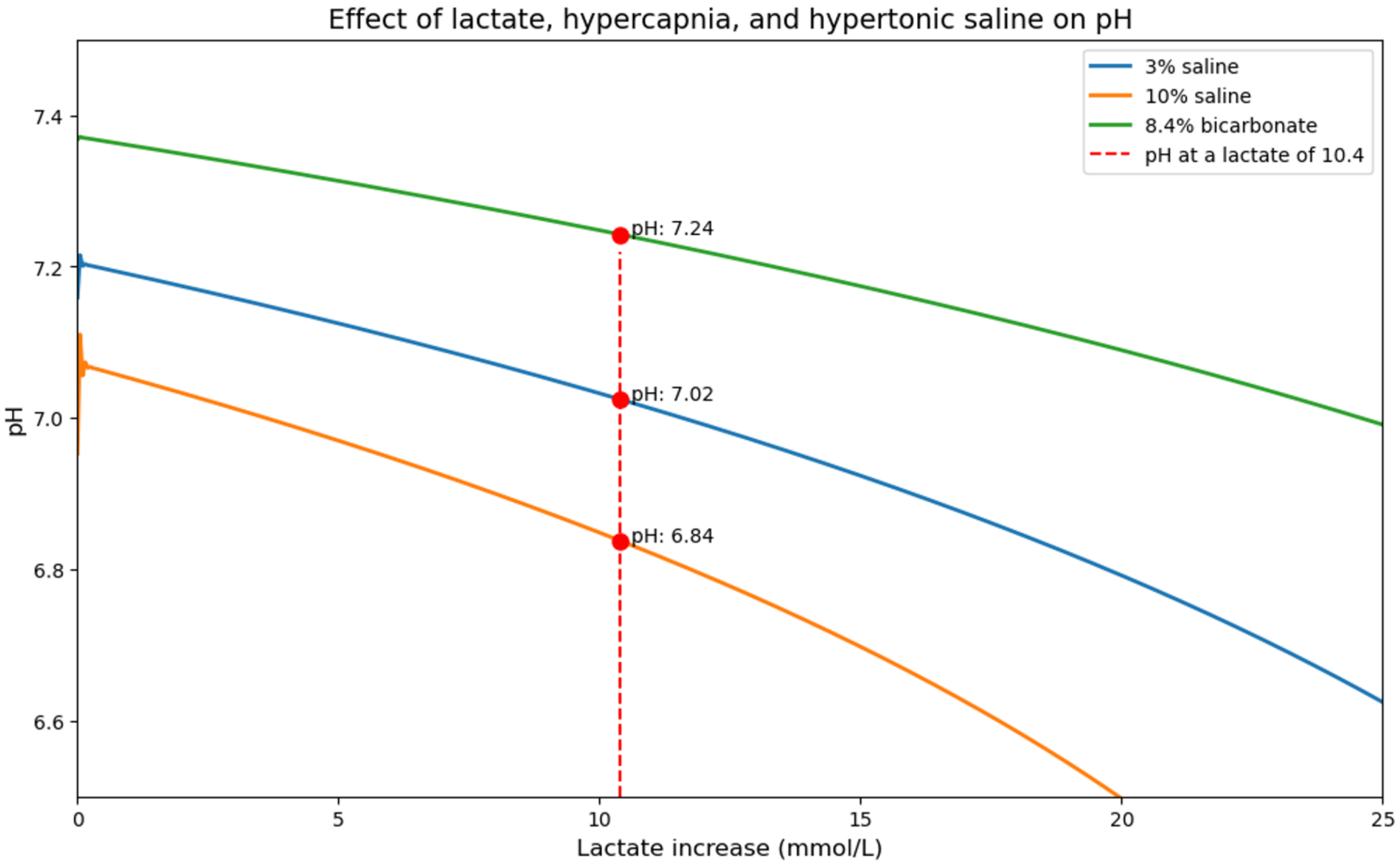


3) Hypertonic lactate / acetate / beta hydroxy buterate

Less risk of acidosis

Neuroprotective due to high available energyflux

Decrease in ICP when compared with mannitol


Effect of lactate, hypercapnia, and hypertonic saline on pH
3% saline
10% saline
8.4% bicarbonate
pH at a lactate of 10.4
pH: 7.24
pH: 7.02
pH: 6.84
pH
7.4
7.2
7.0
6.8
6.6
0
5
10
15
20
25
Lactate increase (mmol/L)

Not just one case

Trauma mechanism	ISS	Received dose HTS (mL)	Lactate (mmol/L)	Base excess	Ion contribution (mmol/L)	pH	pH without HTS contribution
Fall	35	200	10.4	-21.8	11.4	6.84	7.09
Fall	59	100	3.5	-6.5	3.0	7.18	7.23
Fall	75	100	7.4	-18.1	10.7	6.92	7.11
Fall	48	200	2.2	-7.6	4.8	7.20	7.27
Traffic	36	200	2.2	-7.2	2.5	7.23	7.27
Traffic	34	200	3.0	-11.4	8.4	7.15	7.29
Traffic	57	200	2.7	-13.2	7.6	7.07	7.20
Fall	57	100	8.3	-20.9	10.9	6.89	7.10
Fall	34	200	3.0	-12.8	6.8	7.13	7.24
Fall	59	200	6.0	-15.3	6.6	7.07	7.19
Traffic	25	100	1.4	-6.2	4.2	7.30	7.37

Injury Severity Score (ISS); Hypertonic Saline (HTS)

Conclusion

- **Stewart light** helps us to understand acid-base disturbances caused by fluids

- Very **limited evidence of prehospital 10% NaCl** in TBI

⟶ Improved markers ICP & CPP, no improvement in neurology and survival

- Attributable to properties of hypertonic saline?

⟶ **Hyperchloremic acidosis**

⟶ Osmolarity rise

⟶ Both particularly prominent in hypovolemia

- Alternatives?

⟶ NaCl 3%

⟶ NaHCO3, NaLac, NaBHB?