

ACPN x TSN
5 December 2025

Update on dysnatremia

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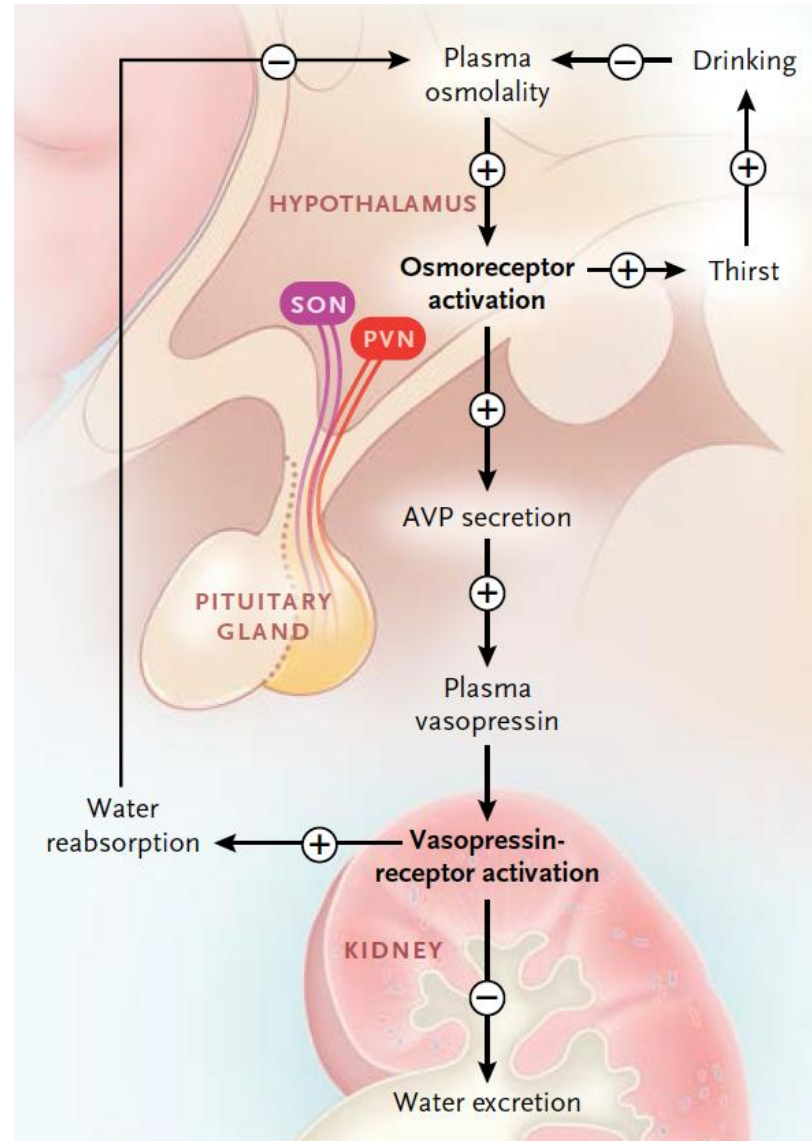
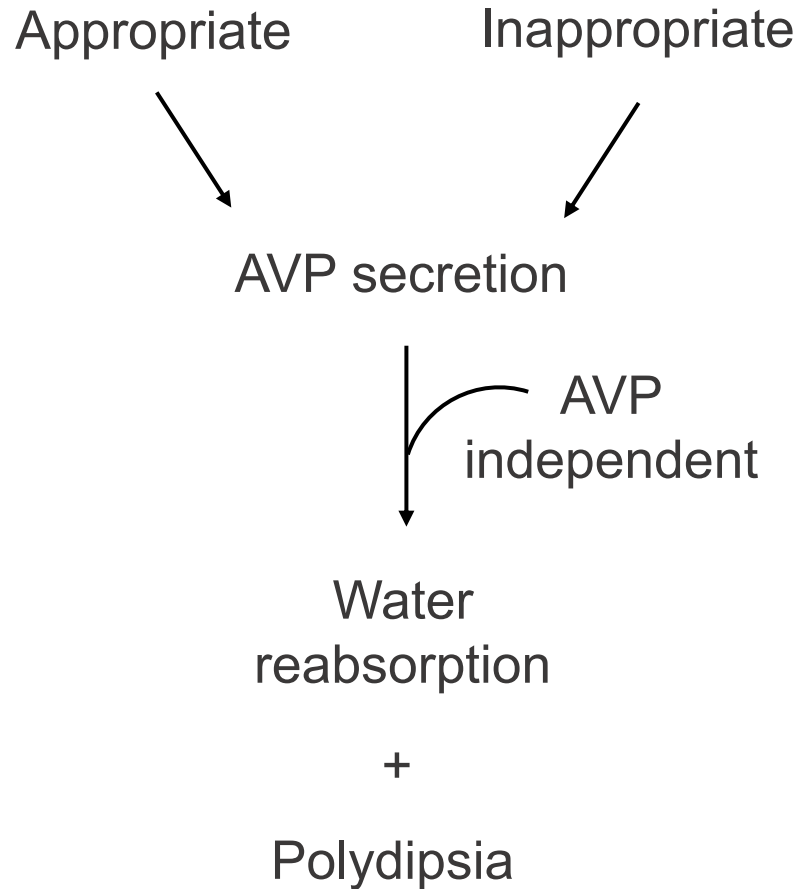


Update on dysnatremia

1. Pathophysiology
2. Hyponatremia
3. Hypernatremia

Osmoregulation: brain-kidney axis

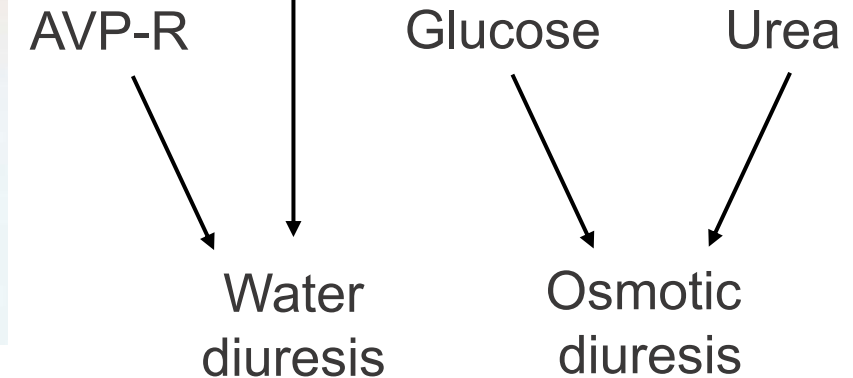
Hyponatremia
(plasma $\text{Na}^+ \leq 135$)



Hypernatremia
(plasma $\text{Na}^+ \geq 145$)

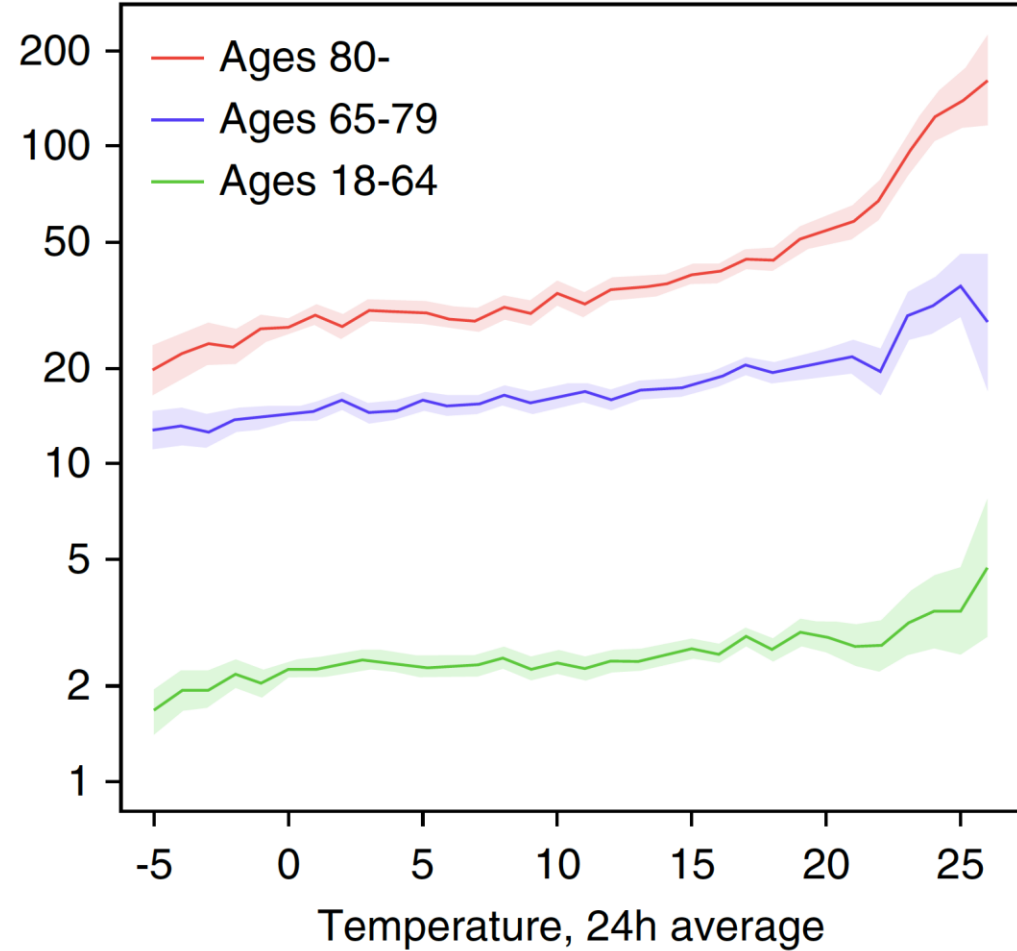
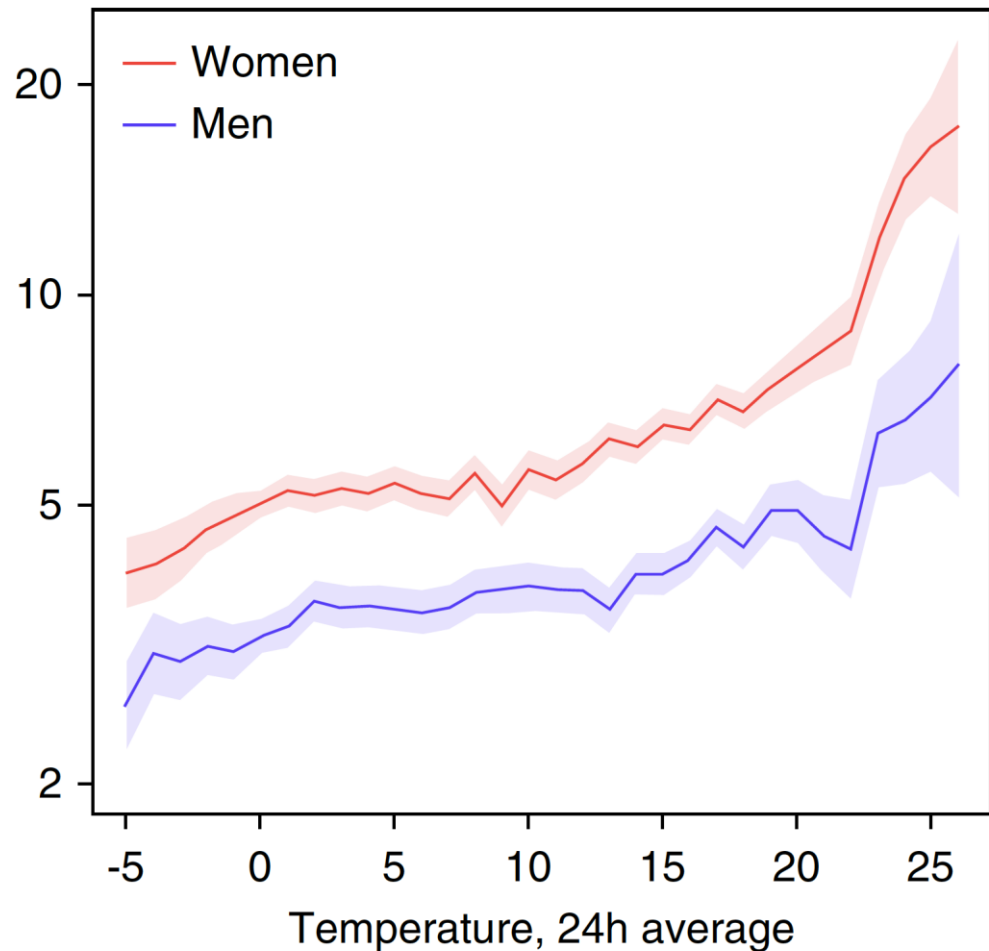
Adipsia/hypodipsia

AVP deficiency



Heat-related hyponatremia

Cases of severe hyponatremia per 1 million person-days



Complications of hyponatremia

Rare

Acute or
symptomatic
hyponatremia

Majority of patients

Usually chronic,
no or mild symptoms

Rare

Overcorrection
of chronic
hyponatremia



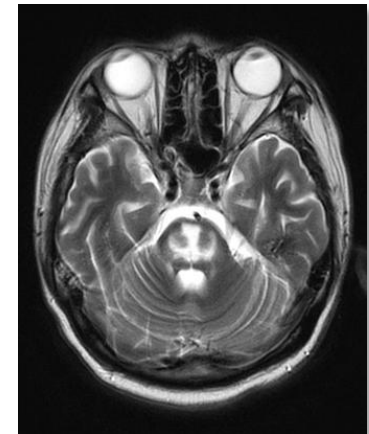
Danger:
Cerebral edema



Association with mortality:
Mechanism? Modifiable?



Danger:
Osmotic demyelination



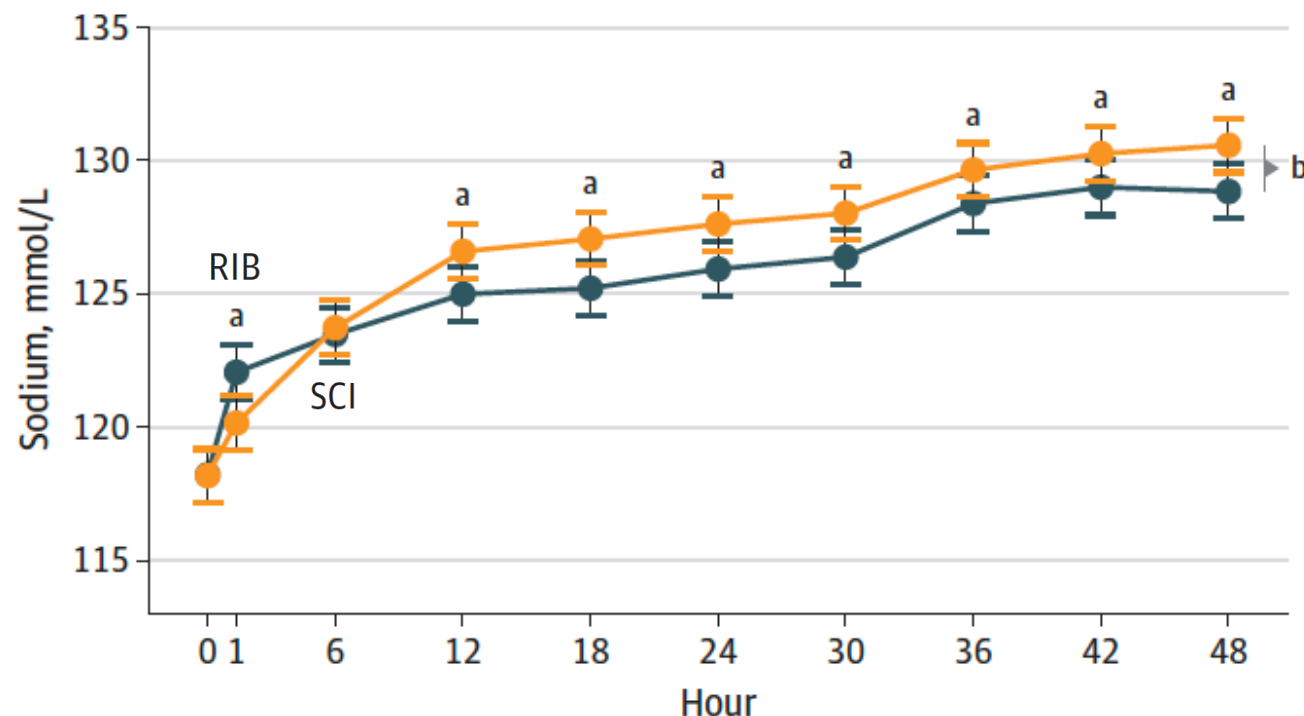
Case of acute hyponatremia

- Natural healer for ayahuasca ceremony
- Also drank 8 liters of water
- Glasgow Coma Scale: E1M3V1
- Plasma sodium 110 mmol/L

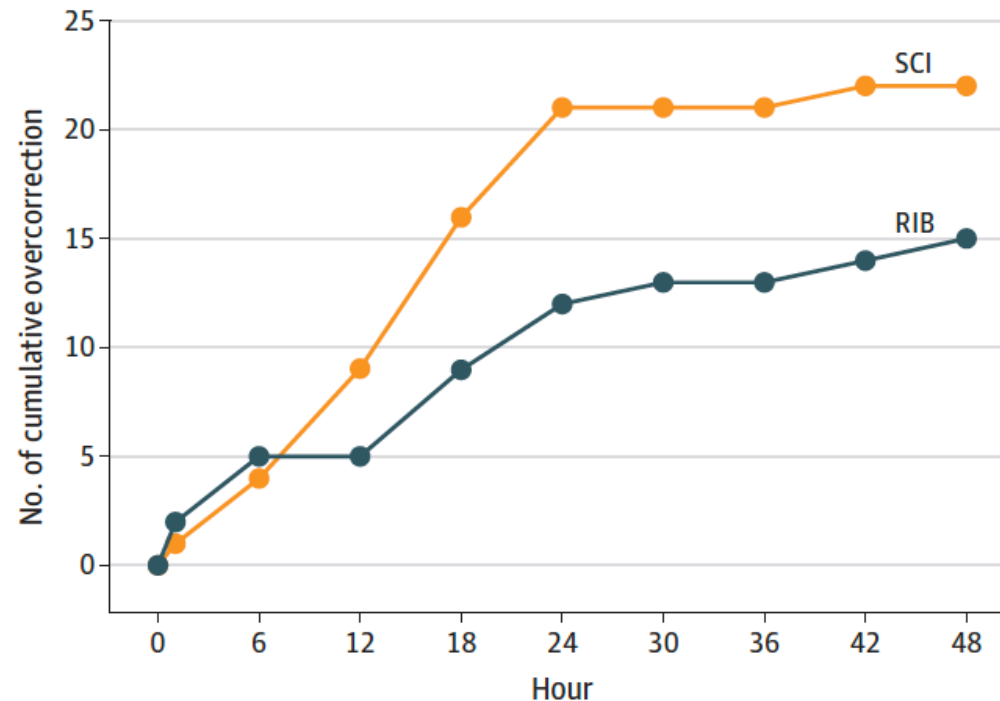


Hypertonic saline: slow continuous infusion vs. rapid intermittent bolus

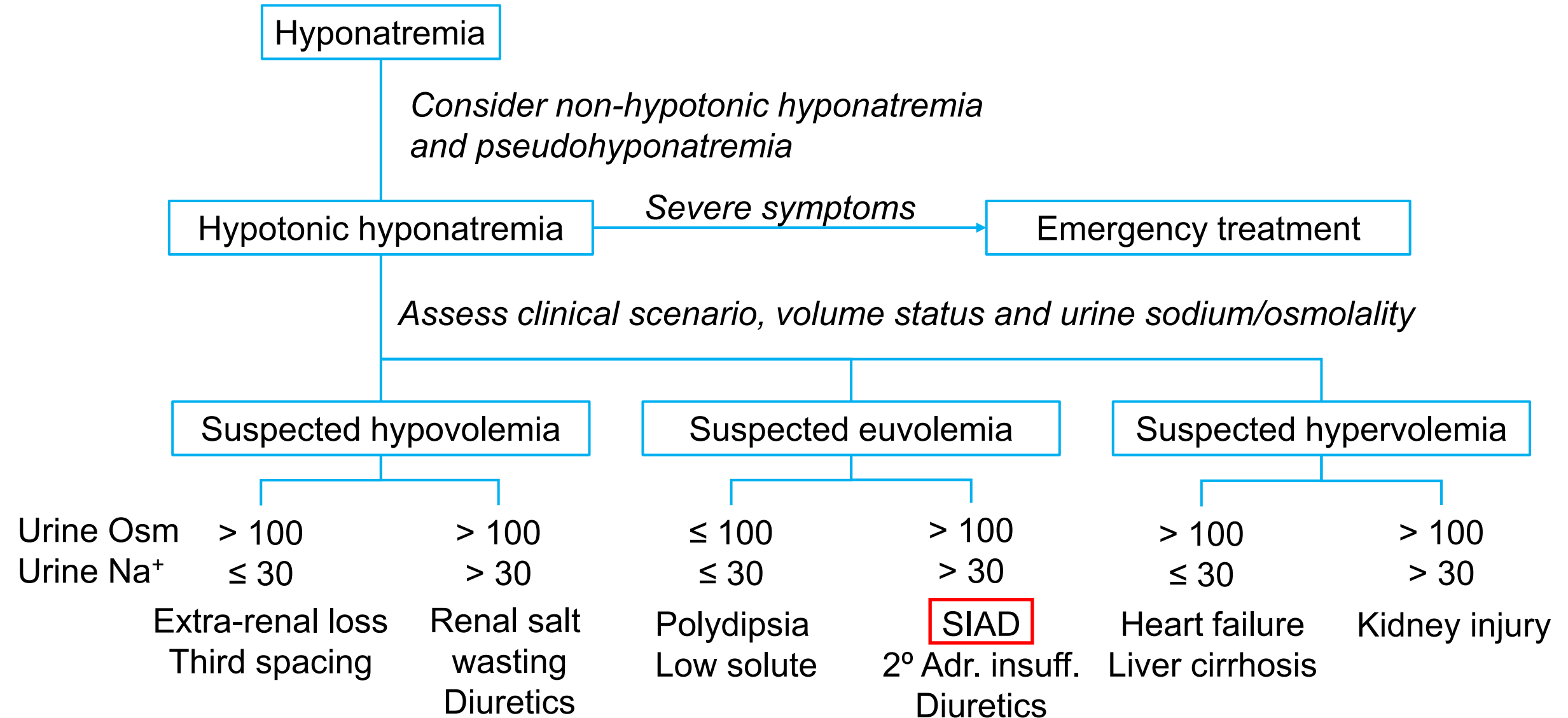
Serum sodium



Overcorrection

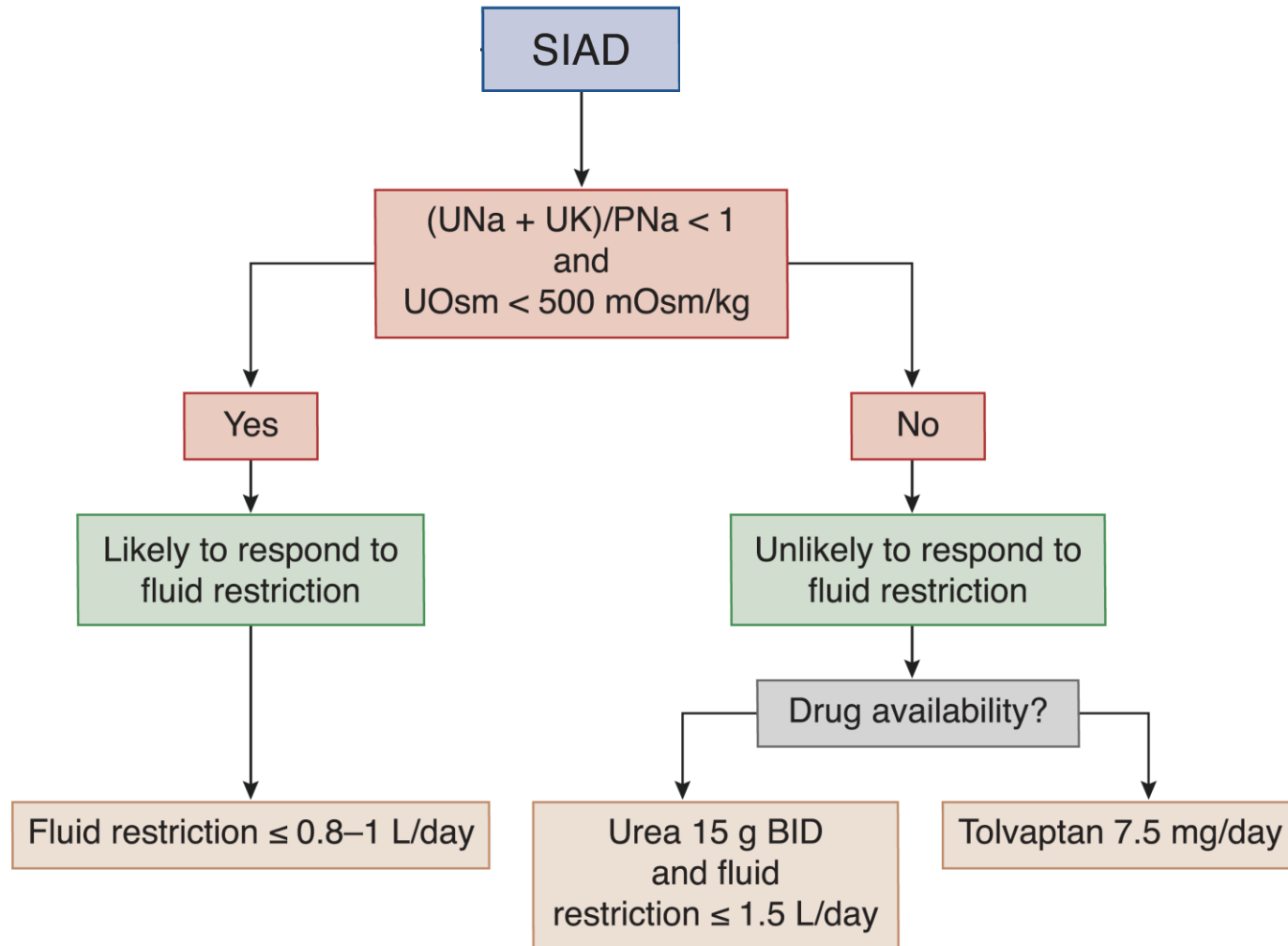


Hyponatremia: diagnostic approach



Christie Turin (on behalf of the ESA-ERA guideline committee)

Treatment of the syndrome of inappropriate antidiuresis



Emerging treatment options

Clinically tested

- SGLT2 inhibitors
- Protein supplementation

Experimental

- Apelin-17 analog
- Mambaquaretin toxin
- Urea transporter A1 inhibitor

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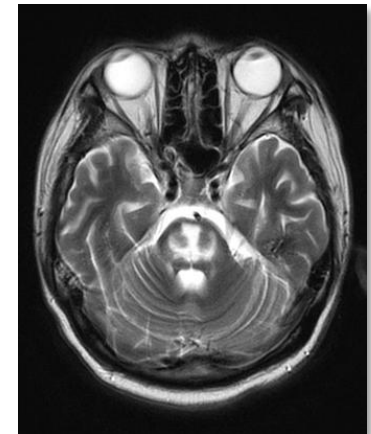
Danger:
Cerebral edema



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Mechanism? Modifiable?

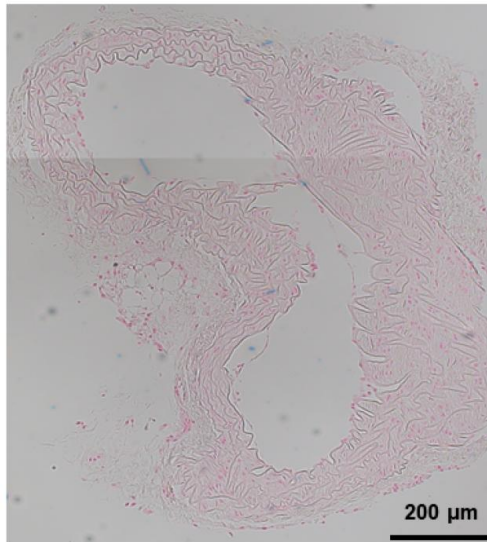


Danger:
Osmotic demyelination

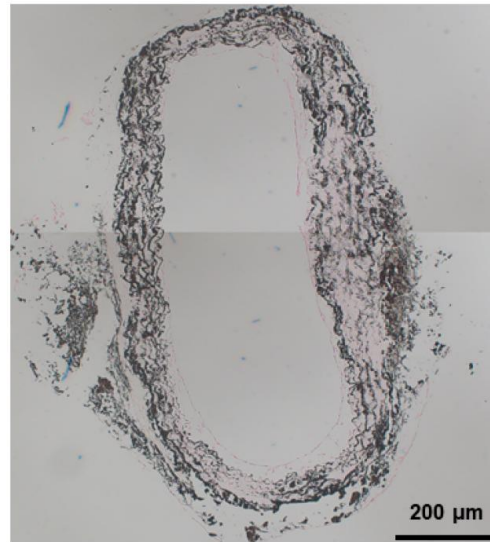


Experimental hyponatremia causes vascular calcification, NETosis and thrombosis

Mouse aortic rings



Low Na
(non-CM)



Low Na
Calcifying medium

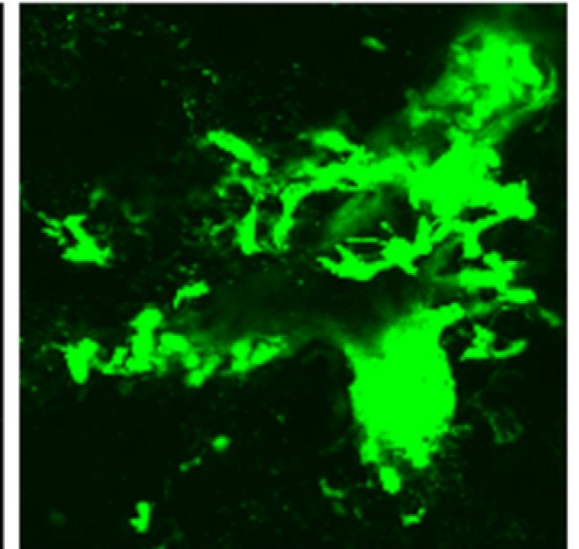
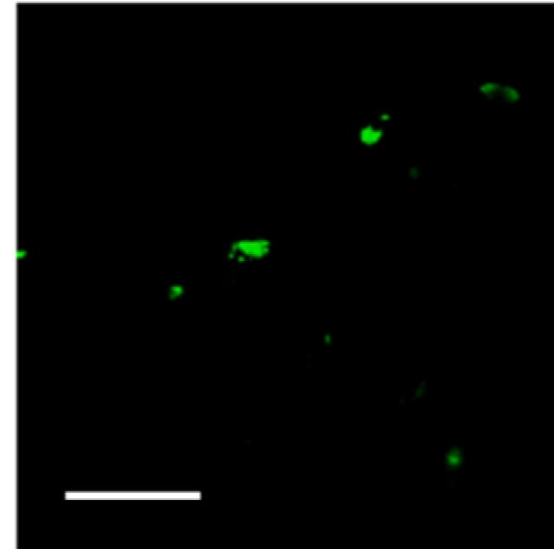
Matsueda et al., ATVB 2024

Lung

Normonatremia

Hyponatremia

Sytox Green



Inoue et al., PNAS USA 2024

Correction rates and outcomes

JAMA Internal Medicine | [Original Investigation](#)

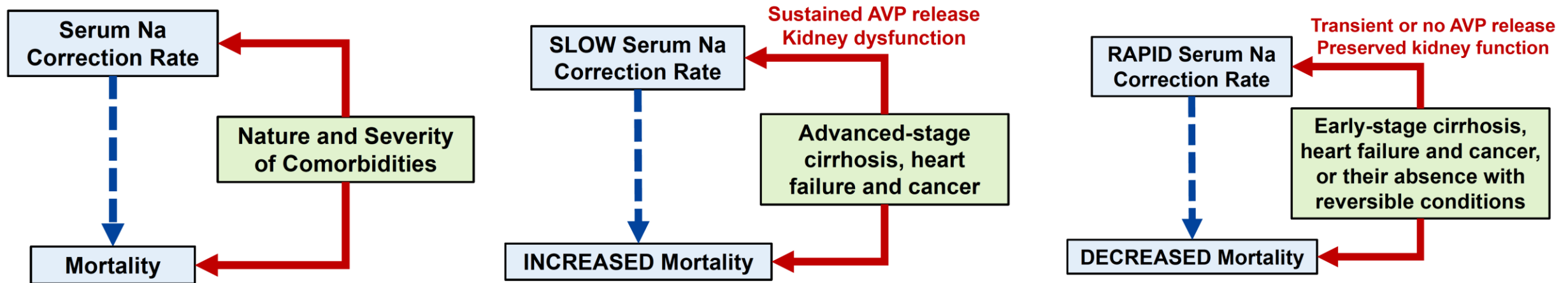
Correction Rates and Clinical Outcomes in Hospitalized Adults With Severe Hyponatremia

A Systematic Review and Meta-Analysis

Juan Carlos Ayus, MD; Michael L. Moritz, MD; Nora Angélica Fuentes, MD; Jhonatan R. Mejia, MD;
Juan Martín Alfonso, MD; Saeha Shin, MPH; Michael Fralick, MD, PhD, SM; Agustín Ciapponi, MD, MSc, PhD

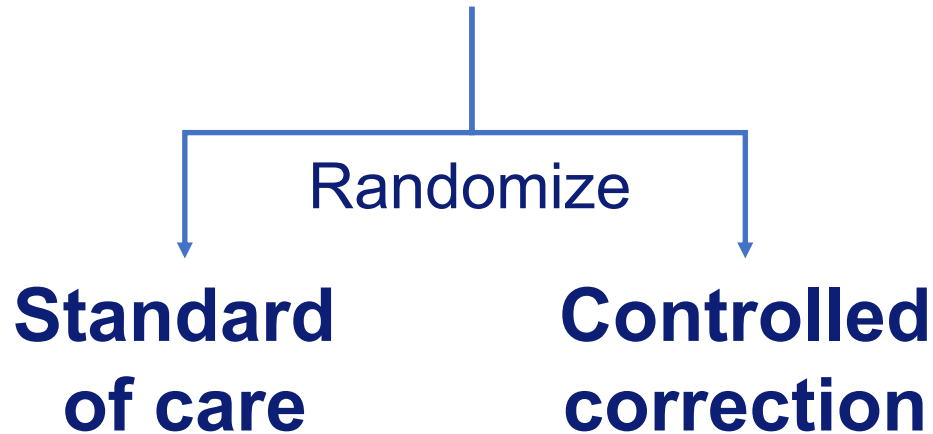
JAMA Intern Med 2024

Potential confounders in associations plasma sodium correction rates and mortality



Hyponatremia Intervention Trial (HIT)

Hospitalized patients
plasma sodium < 130 mmol/L



Mirjam
Christ-Crain

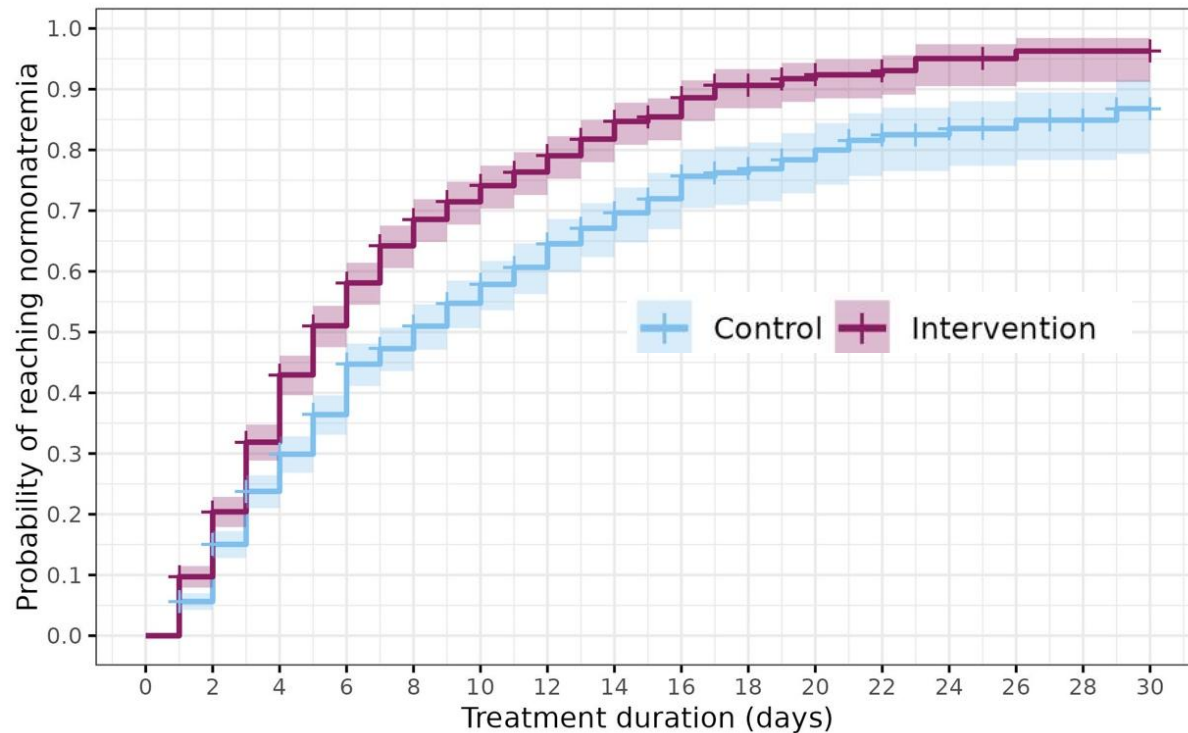
Julie
Refardt

Primary endpoint

30-day mortality or hospital readmission
n = 2,173 patients

Hyponatremia Intervention Trial (HIT)

Probability of reaching normonatremia Probability of reaching endpoint



Primary endpoint: intervention 20.8% vs. control 22.1%.
Normonatremia at discharge: 25% lower chance of endpoint.

Refardt et al., ASN Kidney Week 2024; manuscript under review

Osmotic demyelination syndrome



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[DOI: 10.1056/EVIDoa2200215](https://doi.org/10.1056/EVIDoa2200215)

ORIGINAL ARTICLE

Osmotic Demyelination Syndrome in Patients Hospitalized with Hyponatremia

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Adina Weinerman, M.D., M.H.Sc.,^{1,6} Terence Tang, M.D., M.Sc.,^{1,7} Afsaneh Raissi, B.Sc.(Hon.),³ Radha Koppula, M.B.B.S.,³
Fahad Razak, M.D., M.Sc.,^{1,3,8} Amol A. Verma, M.D., M.Phil.,^{1,3,8} and Michael Fralick, M.D., Ph.D.^{1,5}



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[DOI: 10.1056/EVIDe2300014](https://doi.org/10.1056/EVIDe2300014)

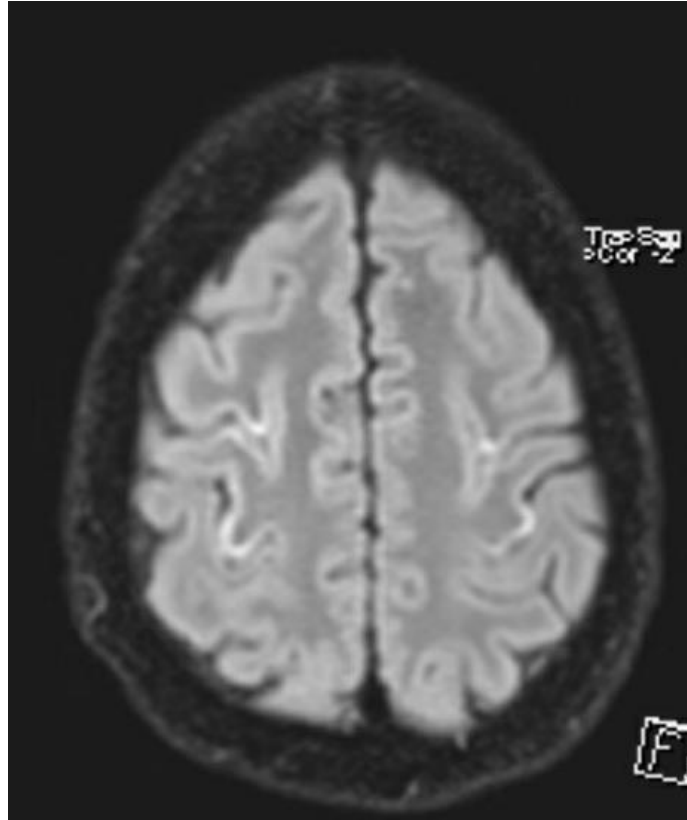
EDITORIAL

Hyponatremia Treatment Guidelines — Have They Gone Too Far?

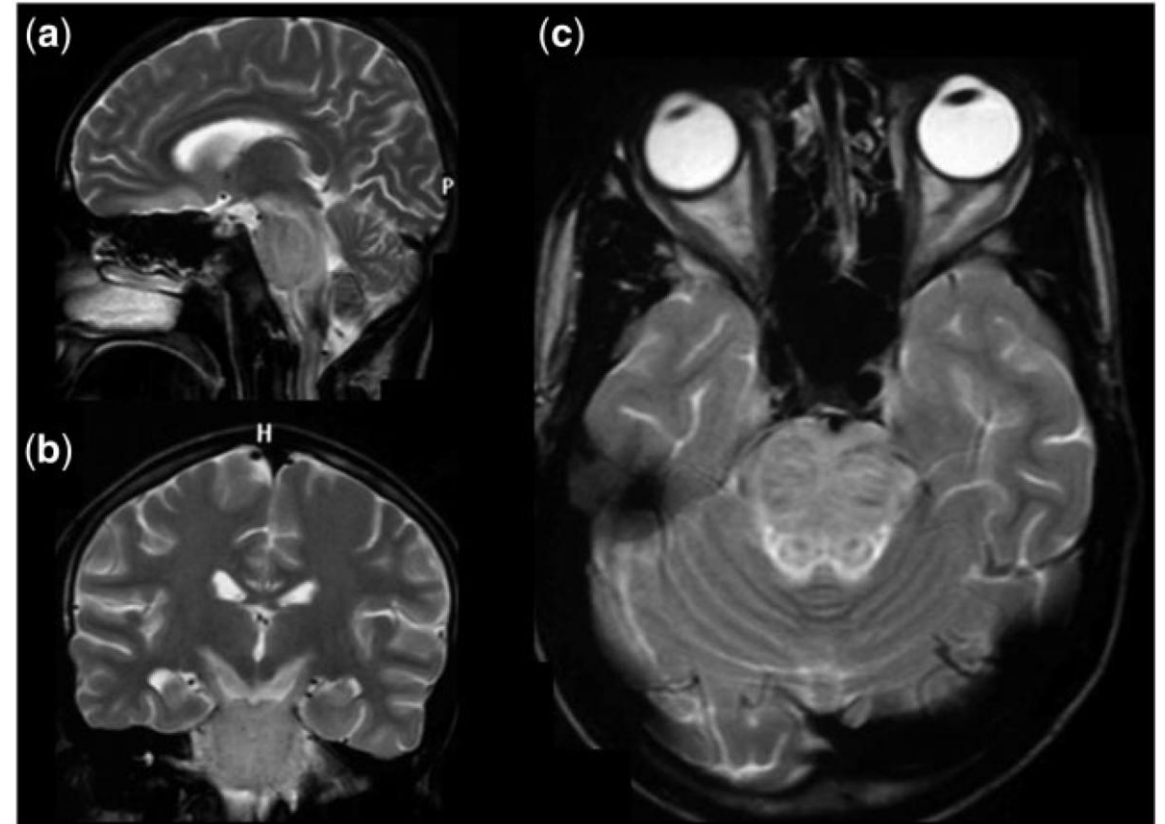
Juan C. Ayus, M.D.,¹ and Michael L. Moritz, M.D.²

Osmotic demyelination syndrome

43 year-old man with AVP deficiency



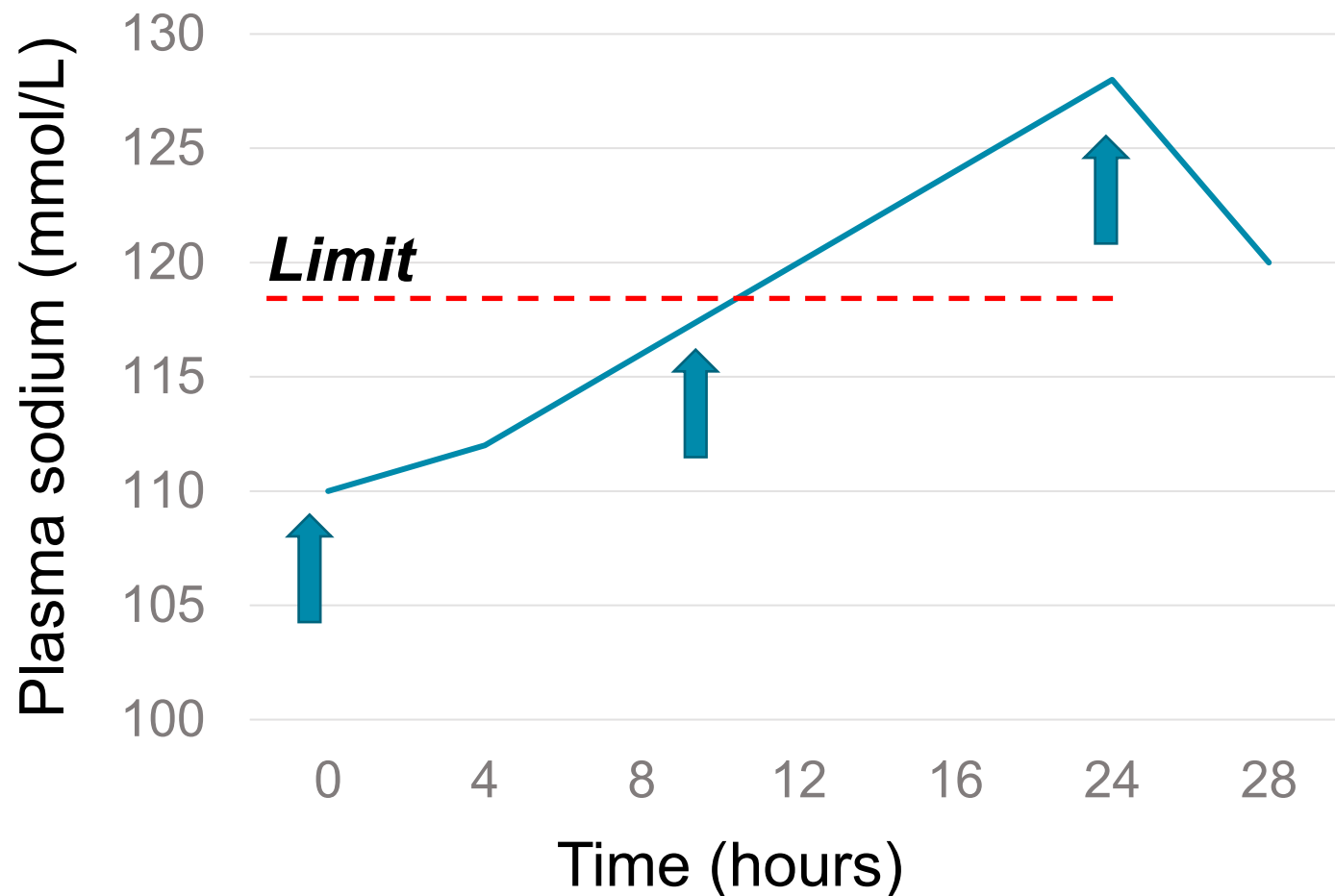
55 year-old man on thiazides



Plasma Na^+ 112 to 128 mmol/L in 13 hours

Plasma Na^+ 106 to 138 mmol/L in 3 days

Preventing or treating overcorrection



Rescue (relowering)

Desmopressin 2-4 μg every 6-8 h
+ D5W 3 mL/kg/h

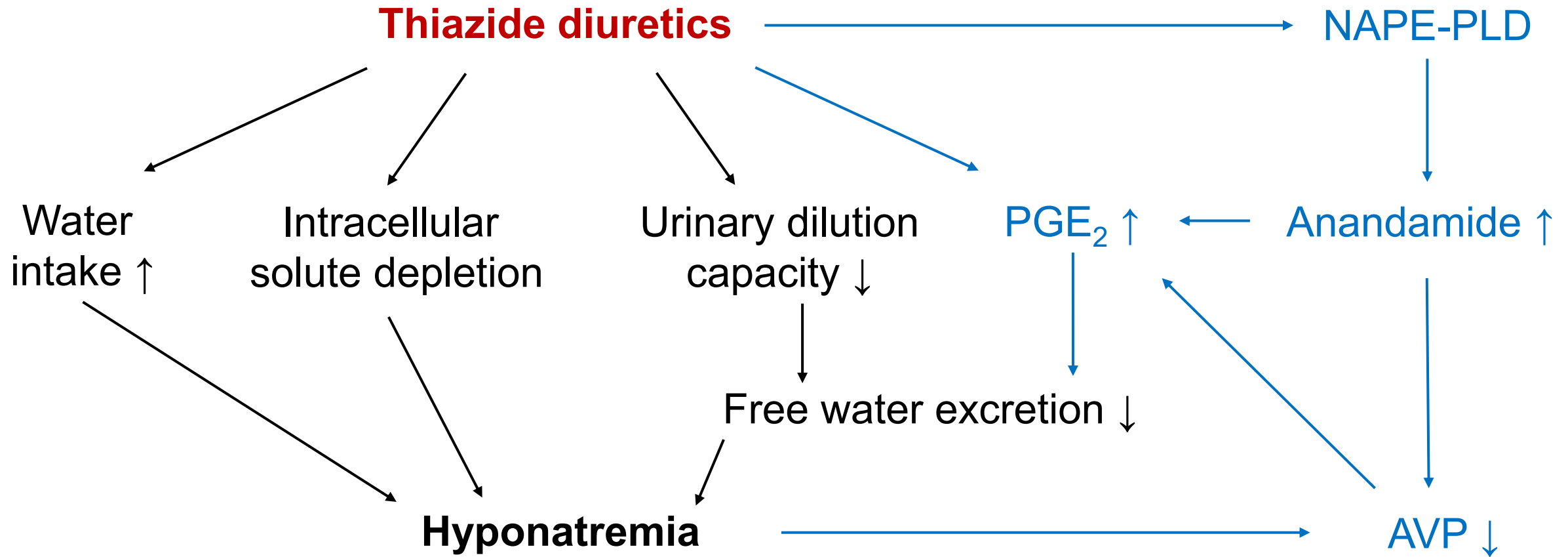
Reactive

Desmopressin 2-4 μg every 6-8 h

Proactive (desmopressin clamp)

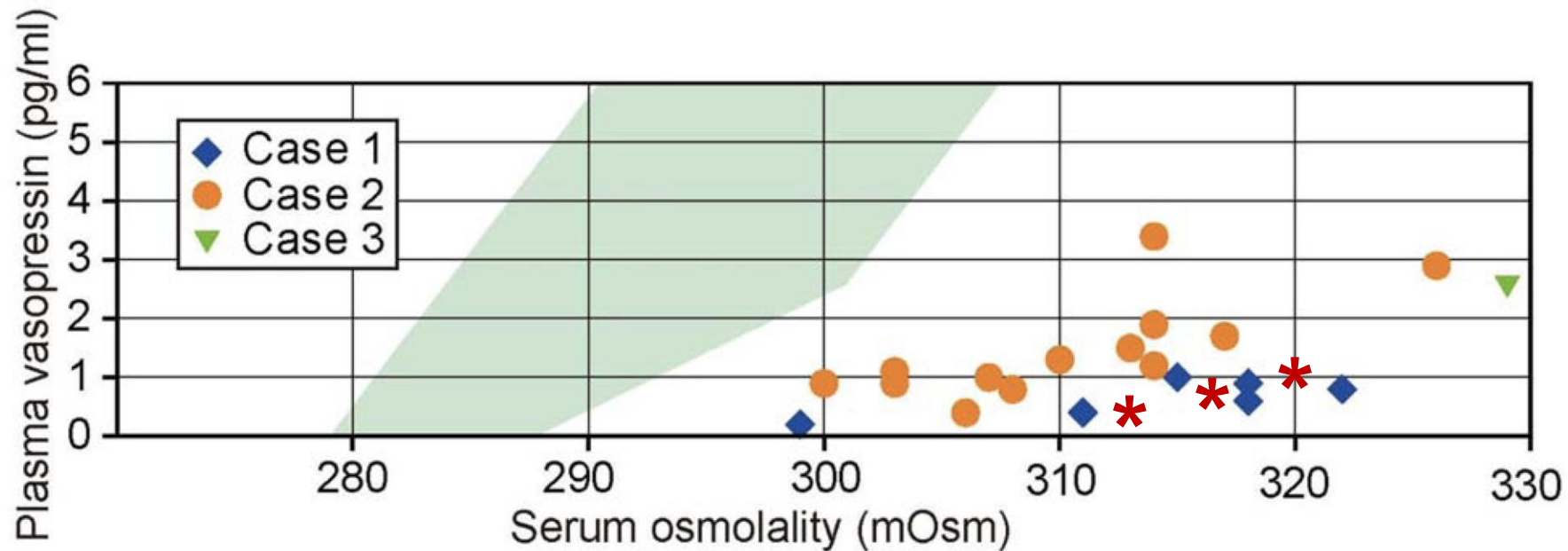
Desmopressin 2-4 μg every 6-8 h
+ 3% NaCl

Thiazide-induced hyponatremia



Hypernatremia

32 year-old female is referred for unexplained hypernatremia:
Plasma Na^+ 151, urine Na^+ 104 mmol/L, urine osmolality 740 mOsm/kg



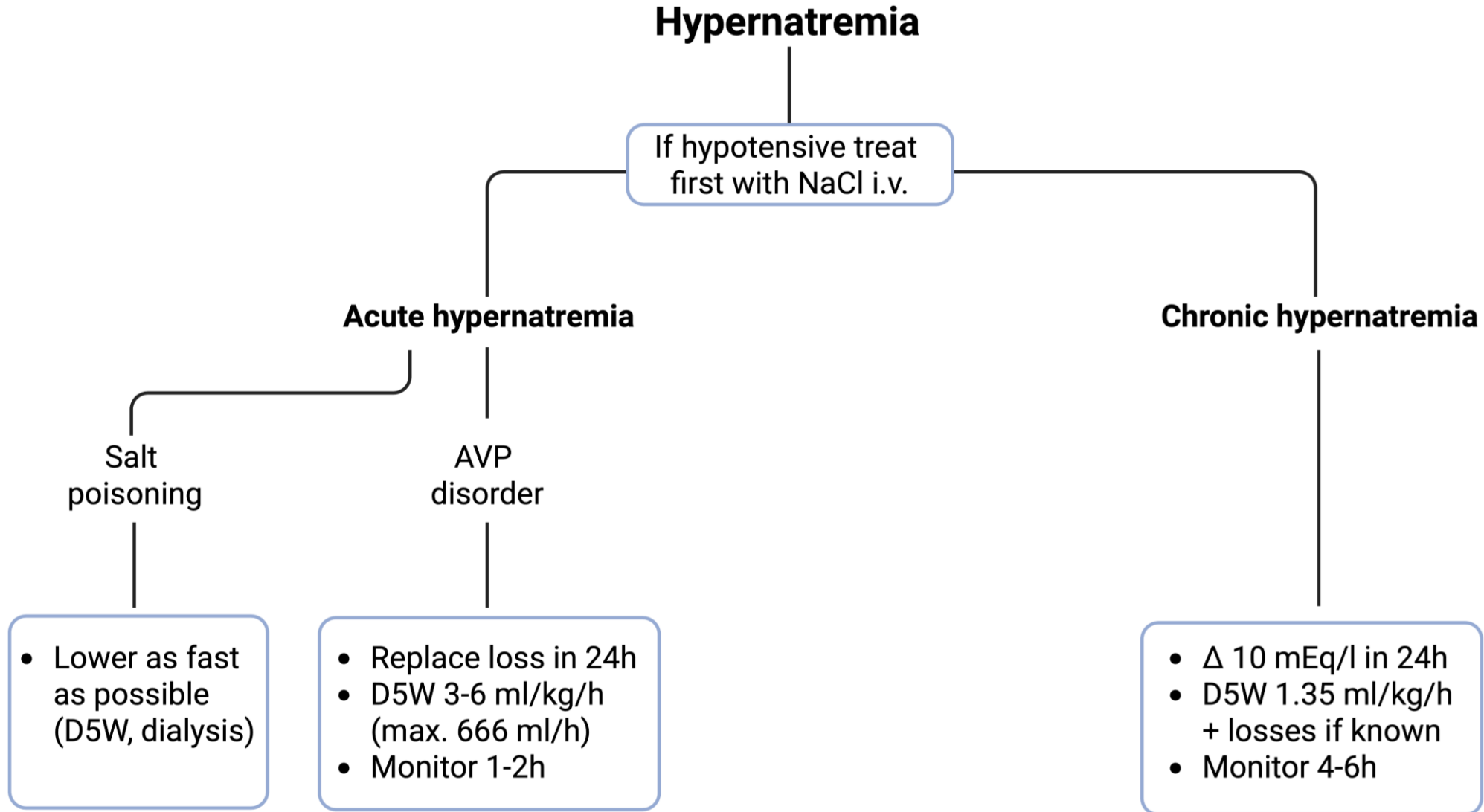
Hiyama et al.,
Brain Pathol 2016

AVP deficiency without thirst (adipsic diabetes insipidus)
due to autoantibodies against the subfornical organ

Diagnostic approach to hypernatremia

*Determine why no thirst
or access to water*

Treatment of hypernatremia





Update on dysnatremia

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2026 ESA-ERA hyponatremia guideline



In memory of Mitchell Halperin



1937 – 2025

Thank you!

