The trouble with guidelines
why we struggle

- Too complex
  - more information than need
- Too simple
- They don’t say anything useful
- Contradictory
- …..Evidence-based?
Diagnostic algorithms
what’s new?

- **Design**
  - user-sensitive
- **Evidence-based approach**
  - weighting proportionate to diagnostic utility
    - urine osmolality
    - urine Na⁺
    - volume status

Traditional algorithms
clinical assessment of volume status is not reliable

- **How good is assessment of volume status?**
  - hypovolemia, euvoelema, hypervolemia
    - sensitivity 0.49
    - specificity 0.47
    - independent of Na⁺ status
- **How useful is assessment of volume status?**
  - do algorithms based on volume status work?
    - frequent misdiagnosis
  - impact of removing ECF assessment
    - substituting urate excretion improves accuracy

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Hyponatremia diagnostic pathway

Exclude non-hypotonic hyponatremia

Acute or severe symptoms?

Yes

Consider immediate treatment with 3% NaCl

No

Urine osmolality

< 100 mOsm/kg

≥ 100 mOsm/kg

Yes

Consider diuretics

No

Consider all other processes

Patient on diuretics?

No

Acute or severe symptoms?

Yes

Low effective arterial volume

< 30 mmol/L

≥ 30 mmol/L

No

Consider all other processes

Yes

Hyponatremia

< 100 mOsm/kg

≥ 100 mOsm/kg

Hyponatremia

< 30 mmol/l

≥ 30 mmol/l

Consider

Primary polydipsia

Low solute intake

Beer potomania

IF ECF contracted consider

Heart Failure

Liver cirrhosis

Nephrotic syndrome

IF ECF expanded consider

GI loss

e.g. vomiting

IF ECF normal consider

SIADH

Secondary adrenal failure

Hypothyroidism

Consider occult diuretics

Diagnostic algorithm

is it really hyponatremia?

Exclude non-hypotonic hyponatremia

e.g. hyperglycemia

Acute or severe symptoms?

Yes

Consider immediate treatment with 3% NaCl

No

Urine osmolality
Pseudohyponatremia causes

<table>
<thead>
<tr>
<th>Context</th>
<th>Serum osmolality</th>
<th>Agent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effective</td>
<td>Isotonic/hypertonic</td>
<td>Glucose, Mannitol, Glycine, Sorbitol, HTK, Hyperosmolar contrast media</td>
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<tr>
<td>osmolytes</td>
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<tr>
<td>Ineffective</td>
<td>Isotonic/hypertonic</td>
<td>Urea, Alcohols, Ethylene Glycol, Lactate</td>
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<tr>
<td>Artifact</td>
<td>Isotonic</td>
<td>Lipids, Immunoglobulin</td>
</tr>
</tbody>
</table>

Effect of solid-phase components
low Na\(^+\) artifacts in dilution-based methods

Normal solid-phase fraction
- Aqueous phase
- Solid phase

Increased solid-phase fraction
- Aqueous phase
- Solid phase
Hyponatremia
Na⁺ measurement by direct potentiometry

- No dilution step
  - independent of solid phase fraction

![Diagram of Aqueous phase and Solid phase](image1)

Diagnostic algorithm
urine osmolality

- **Excess water intake**
  + uOsm <100 mOsm/kg
- **AVP action**
  + uOsm >pOsm
- **The 'grey area'**
  + SIAD & excess water intake?

![Diagnostic algorithm diagram](image2)

References:
  Biochemical and etiological characteristics of acute hyponatremia in the emergency department
  The Journal of Emergency Medicine 29: 369-374
Diagnostic algorithm

why urine Na\(^+\) is central

**Urine Na\(^+\)**

- <30 mmol/L
  - Low effective arterial volume
  - If ECF expanded consider
  - If ECF contracted consider
- ≥30 mmol/L
  - Patient on diuretics?
  - Yes
    - Consider diuretics
    - Consider all other processes
  - No
    - If ECF contracted consider
    - If ECF normal consider
    - Consider occult diuretics

Diagnostic algorithm

hypovolemia vs. euvolemia by uNa\(^+\)

- **Thresholds & cut-offs**
  - uNa\(^+\) <30 mmol/L
    - Sensitivity 0.87-1.0
    - Specificity 0.52-0.83
  - uNa\(^+\) <20 or <50 mmol/L
    - Lower sensitivity
    - Lower specificity

- **Ti**

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Fenske W, Maior SKG, Bleichschmidt A, Lücks B, Stark S. 2010
Utility and limitations of the traditional diagnostic approach to hyponatremia: a diagnostic study
The American Journal of Medicine 123: 652-657

Hato T, Hellman R, Ng R. 2010
Additional diagnostic testing
serum urate & fractional urate excretion

- **Diuretics**
  - Serum urate <4 mg/dl
  - Fractional urate excretion >12%

- **SIAD in patients on diuretics**
  - Serum urate <4 mg/dl
  - Fractional urate excretion >12%


Diagnosis of SIAD
AVP fingerprint when there should be none

- **Supporting features**
  - Serum urea <3.6 mmol/L
  - Fractional Na+ excretion >0.5-1%
  - Fractional urea excretion >55%
  - Serum urate <0.24 mmol/L

FIG. 7 Fluid intake, urine sodium, serum sodium concentration, and body weight during a 7-day study of W. F. Arnheiter. Accuracy of urine dilution on 2 X [Na] + [K] ranged from 280 to 440 mmol/L on days 4 through 7.
Cerebral salt wasting
natriuresis, hyponatremia & volume depletion

- History
- CSW vs. SIADH
- Mechanisms
  - sympathetic NS
  - pressure natriuresis
  - natriuretic peptides
- Problems
  - definition
  - diagnosis
  - mechanism
  - absence of understanding vs. evidence of absence

Hyponatremia diagnostic pathway

Exclude non-hypotonic hyponatremia

Acute or severe symptoms?

≥300 mOsm/kg

<30 mOsm/kg

≥30 mmol/L

<30 mmol/L

Low effective arterial volume

Patient on diuretics?

Yes

Consider immediate treatment with 3% NaCl

No

Consider diuretics

Consider all other processes

If ECF expanded consider
- Heart Failure
- Liver cirrhosis
- Nephrotic syndrome

If ECF contracted consider
- Dehydration
- Third space loss
- Previous diuretic use

If ECF normal consider
- SIADH
- Secondary adrenal failure (Addison's disease)
- Cerebral salt wasting

Consider occult diuretics

Hyponatremia

No

< 100 mOsm/kg

≥ 100 mOsm/kg

< 30 mmol/L

≥ 30 mmol/L

Consider
- Primary polydipsia
- Low solute intake
- Nephrogenic diabetes insipidus
- Other causes

Patient on diuretics?

Acute or severe symptoms?

No

Yes

Exclude other causes