Dysnatremia v1.0: Table of Contents

Patients At Risk for High or Low Sodium

- Postop Neurosurgery At Risk for Hyponatremia
- Periop Neurosurgery At Risk for Diabetes Insipidus
- Postop Neurosurgery At Risk for Diabetes Insipidus

Patients with Diabetes Insipidus

- Periop Known Diabetes Insipidus
- ED or Acute Care Known Diabetes Insipidus

Background

- How Dysnatremia Occurs
Dysnatremia v1.0: Postop Neurosurgery At Risk for Hyponatremia

**Inclusion Criteria**
- Patients with procedure at high risk for low sodium

**Exclusion Criteria**
- Age <1 year

**Monitoring**
- Serum sodium and serum osmolality qam x 3 days
- Daily weight
- Strict intake and output
- If no void over 8 hours, bladder scan or ask patient to void

**Orders**
- Sodium <135
- Intake and output positive > 40 ml/kg over 8 hours
- Urine output <0.5 ml/kg/hr or no void over 8 hours
- Urine output >4 ml/kg/hour x 2 voids in a row
- Mental status change (particularly decreased responsiveness)

**Sodium**
- Sodium >135 Continue monitoring
- Sodium <135 (if not patient’s normal baseline)

**Serum Osm?**
- Serum osm <275
- No, volume down (see triangle)
- Yes, euvolemic/volume overload

**Euvolemic?**
- Serum Osm ≥275

**SIADH**
- Treatment options
  - Restrict fluids, take into account volume status, IV medication volume, and medications that cause low sodium
  - Do not add sodium (not a problem of sodium deficiency)
  - Do not give NS bolus to raise serum sodium
  - If sodium is 120 or less → go to PICU, consider hypertonic saline
  - If sodium dose not improve, consider alternative diagnoses

**Assessment**
- Continue to assess volume status, heart rate, etc

**Cerebral Salt Wasting?**
- Serum sodium <135, serum osm <275,
- Intravascular depletion
  - Consider cerebral salt wasting
  - Run normal saline fluids at maintenance rate, or increase fluid rate if already running NS fluids

**Pseudohyponatremia?**
- Serum sodium <135 and serum osm ≥275
  - Consider pseudohyponatremia
  - Check glucose and lipids

**Diagnostic Criteria for SIADH**
- Serum sodium <135 mEq/L AND
- Serum osm ≥275 mOsm/kg AND
- Euvolemic or volume overload

**Sodium >135 Continue monitoring**

**Procedures at High Risk for Low Sodium**
- Cranietomy
- Craniotomies repair/cranial vault expansion/frontal orbital advancement
- Hemispherectomy/lobectomy
- Placement of Grid and strip
- Tumor resection/biopsy
- Endoscopic 3rd ventriculostomy (ETV)
- Insertion of lumbar drain
- Laser ablation
- Subgaleal shunt insertion
- VP shunt externalization/external ventricular drain

**Diagnosis**
- Mental status change (particularly decreased responsiveness)

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Last Updated: October 2018
Next Expected Review: October 2023
PASS Clinic
- **Assess for history of DI**
  - Is patient awakening at night to urinate?
  - Labs
    - Serum sodium
    - Serum osmolality
    - Urine osmolality
    - Intake and output

Operating Room
- Insert temporary central IJ line
- Foley catheter
- Treat diabetes insipidus if criteria met
  - A higher sodium level may be appropriate if mannitol was given
  - Start vasopressin infusion at 0.5 milliUnit/kg/hr. Increase 0.5 milliUnit/kg/hr every 10-15 minutes to urine output 0.5 to 2 ml/kg/hr.
  - NS IV 1/3 maintenance
  - Anesthesiologist checks sodium and manages fluids to avoid hyponatremia
    - Do not replace urine output if on vasopressin infusion
    - Replace operative losses as required

To PICU

Endocrine Clinic Visit
- Known DI → use **Preop Known DI page**

Suspicious Or has Diagnosis Of DI

Diagnostic Criteria for Diabetes Insipidus (DI)
All are present:
- Serum sodium > 145 mEq/L
- Serum osmolality > 300 mOsm/kg
- Urine osmolality < 300 mOsm/kg
- Urine output > 4 ml/kg/hr

Procedures at High Risk for Dysnatremia
High risk for diabetes insipidus (DI)
- Transphenoidal hypophysectomy

How Dysnatremia Occurs

Inclusion Criteria
- Postop brain tumor for known craniopharyngioma or transsphenoidal hypophysectomy or any other transcranial surgery involving pituitary or hypothalamus

Exclusion Criteria
- Age <1 year

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Monitoring (PICU)
- Serum Sodium q4h
- Strict intake and output
- Daily weight
- Call for urine output >4 ml/kg/hr or serum sodium >145, and:
  - Obtain serum sodium, serum osm, urine osm, urine sodium
  - Consider ordering vasopressin for DI to bedside
  - If urine output >6 ml/kg/hr, may start vasopressin infusion while waiting for lab results after discussing with PICU attending

Inclusion Criteria
- Postop brain tumor for known craniopharyngioma or transsphenoidal hypophysectomy or any other transcranial surgery involving pituitary or hypothalamus

Exclusion Criteria
- Age <1 year
- Acute neurologic injury
- Acute or chronic kidney injury

Urine specific gravity
- At least
- Urine output

Diagnostic Criteria for Diabetes Insipidus (DI)
All are present:
- Serum sodium > 145 mEq/L
- Serum osmolality >300 mOsm/kg
- Urine osmolality <300 mOsm/kg
- Urine output > 4 ml/kg/hr

Vasopressin IV
- Start vasopressin infusion at 0.5 milliUnit/kg/hr
- Increase 0.5 milliUnit/kg/hr every 10-15 minutes until urine output <2 ml/kg/hr
- If NPO, use NS IV 1/3 maintenance rate
  - Be judicious in giving additional fluids, use only for clear intravascular depletion
  - Serum sodium in 2 hours, then q4h
  - Call for
    - Serum sodium <140
    - Urine output <0.5 or >2 ml/kg/hr x 2 hours in a row
    - Discuss with PICU attending whether to change infusion rate or stop IV fluids
  - Consult Endocrine
  - If tolerating PO
    - Allow PO intake to thirst
    - Discontinue IV fluids
    - Discontinue vasopressin starting at 0800 on postop day 2

Phase 1 (PICU)

Urine output > 4 mL/kg/hr and urine specific gravity < 1.010

Desmopressin PRN
- First dose desmopressin typically 50-100 mcg
- Serum sodium q4h, urine specific gravity each void (max 1/ hour; q4h if Foley in place)
- When *criteria for next desmopressin dose met, call Endocrine to discuss timing and size of dose

Phase 2 (PICU or acute care)

Endocrine determines it is appropriate to schedule desmopressin

Desmopressin Scheduled
- Desmopressin BID (sometimes TID)
- Serum sodium BID 2 hours prior to scheduled dose
- Hold dose for sodium <135 and call Endocrine
- When planning for discharge, call Endocrine to discuss plan for home fluid balance and sodium monitoring

Phase 3

*Criteria for next desmopressin dose
1. Urine output > 4 mL/kg/hr
   AND
2. At least 4 hours from last desmopressin dose
   AND
3. Urine specific gravity < 1.010 OR serum sodium rising over the last two checks

Acute Care (Floor) Criteria
- Tolerating PO
- If patient has NO intact thirst drive, establish fluid intake plan
- Manageable sodium monitoring
- Has tolerated oral desmopressin for 24 hours

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Dysnatremia v1.0: Periop Known Diabetes Insipidus

**Inclusion Criteria**
- Known diabetes insipidus on scheduled desmopressin at home

**Exclusion Criteria**
- Age <1 year
- Acute or chronic kidney injury

**PASS Clinic**
- Assess patient
  - What is desmopressin dose/frequency
  - How much patient is urinating (how well is DI controlled)
  - Any special feeding needs, oral intake
- Include in PASS clinic visit summary
  - Most recent sodium
  - Procedure details
    - Date/time (first case preferred)
    - Length of case
    - Planned disposition
  - Patient instructions
    - Take usual desmopressin dose before procedure
    - Clears until 2 hours before procedure
- Labs
  - Serum sodium

Contact Endocrinologist via message center to develop plan for DI management

**Default Plan of Care**
- Schedule as first case in the morning
- Give usual desmopressin morning dose
- Include length of case and disposition (home, acute care, critical care) and admitting service
- If long case, plan for desmopressin during case (suggested IV desmopressin dose)
- Anesthesiologist
  - Run IV fluids at 2/3 maintenance plus intraoperative losses, unless otherwise specified (i.e., g-tube feeding plan)
  - Do not replace urine output
  - Check sodium and manage fluids to avoid hyponatremia
**ED Assessment**
- Is patient tolerating oral intake (can keep down liquids after ondansetron)?
- Any decreased input or increased losses (vomiting, diarrhea, dehydration)?
- Any mental status change?
- Any history of adrenal insufficiency?
- Assess volume status and perfusion
- What is time and dose of last desmopressin?
- What is time of last void?
- **Chart and calculate I/O**
- Check serum sodium (ePOC)
- Discuss with Endocrinology
  - What is target sodium (typically 140-150)
  - If history of adrenal insufficiency, consider stress dose hydrocortisone

**Management**
- **Strict intake and output**
- What should happen before patient leaves ED?
  - Give desmopressin if necessary
  - Start IV fluids if necessary
  - Enter acute care orders

### Inclusion Criteria
- **Known neurogenic diabetes insipidus on scheduled desmopressin at home**
- **Concern for acute illness**

### Exclusion Criteria
- **Age <1 year**
  - Acute or chronic kidney injury

**Free Water Deficit Equation**
Free water deficit = 60% × weight, kg × (1 – target Na/current Na)

**Plan for Initial Management**

<table>
<thead>
<tr>
<th>Sodium</th>
<th>Consult Endocrine</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;135</td>
<td>!</td>
</tr>
</tbody>
</table>
| 0-5 above target sodium | ! | Tolerating Enteral Intake
  - Give desmopressin if due per home schedule
  - Enteral intake water to thirst (if no intact thirst: per home feeding plan) |
| 5-10 above target sodium | ! | Tolerating Enteral Intake
  - Give desmopressin if due per home schedule
  - Enteral intake water to thirst (if no intact thirst: per home feeding plan)
  - Consider goal enteral water intake over next 6 hours |
| 11-20 above target sodium | ! | Tolerating Enteral Intake
  - Give desmopressin if due per home schedule, or urine output > 4 ml/kg/hour and > 4 hours from the last dose
  - Enteral Intake water with calculated max sodium decrease serum sodium 10 mmol/L in 24 hours
  - Serum sodium q4h |
| ≥21 above target sodium | ! | Tolerating Enteral Intake
  - If abnormal mental status, go to PICU
  - Give enteral water to decrease sodium 10 mmol/L in 24 hours
  - Serum sodium q4h
  - Consider PICU admission |
| Not Tolerating Enteral Intake | ! | Give desmopressin if due per home schedule
  - D5%/NS at 2/3 maintenance rate (may not need overnight fluids) |
| Not Tolerating Enteral Intake | ! | Give desmopressin if due per home schedule
  - D5%/NS to replace water deficit over 24 hours
  - Replace urine output > 2 ml/kg/hour over the next 2 hours
  - Serum sodium q4h
  - If sodium not decreasing, add insensibles and replace full urine output |
| Not Tolerating Enteral Intake | ! | Give desmopressin if due per home schedule, or urine output > 4 ml/kg/hour and > 4 hours from the last dose
  - D5%/NS to decrease serum sodium 10 mmol/L in 24 hours
  - Replace urine output > 2ml/kg/hour over the next 2 hours
  - Serum sodium q4h
  - If sodium not decreasing, add insensibles and replace full urine output |
| Not Tolerating Enteral Intake or No Intact Thirst | ! | Transfer to PICU for vasopressin infusion |

**Be cautious giving fluid bolus: may cause rapid drop in sodium or rapid increase in urine output.**
How Dysnatremia Occurs

Nausea, emesis, and/or diarrhea

Output > Intake

Mild hypernatremia

Abnormal sodium level not detected or no change in plan

Severe hypernatremia

Rapid change in sodium

Underlying risk for seizure

- History of seizures
- Intracranial hemorrhage

AMS, Seizure

Rapid change in sodium

Severe hyponatremia

Abnormal sodium level not detected or no change in plan

Mild hyponatremia

Delays in care related to uncertainty regarding plan, lack of knowledge regarding likelihood of further sodium change

Increased risk of patient harm

DI

INcreased urine output

Delay in diagnosis and management due to provider uncertainty

SIADH

DEcreased urine output

Intake > Output

Cerebral Salt Wasting

IV fluids in addition to PO intake

Return to Periop Risk
Periop Neurosurgery at risk for DI: “Assess for History of DI”

- Diabetes insipidus (DI) is a condition characterized by polyuria, and typically, corresponding polydipsia

- Neurogenic DI is due to a deficiency of anti-diuretic hormone (ADH)
  - ADH is produced in the pituitary gland
  - Deficiency can occur due to growth of a mass near the pituitary, due to surgery near the pituitary gland, or due to any other traumatic injury to the pituitary gland

- Untreated patients with DI produce large volumes of dilute urine, day and night, and many of them are often thirsty as well

- Untreated patients with DI often have a serum osmolality > 300 mOsm/kg, urine osmolality < 300 mOsm/Kg, and they may have an elevated serum sodium.

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Return to Periop Risk
Periop Known Diabetes Insipidus: Suggested IV desmopressin dose

- While conversion from oral desmopressin to IV desmopressin is inexact for any individual patient, literature supports a range of $1/100 - 1/800$ for a dose conversion.

- A rule of thumb: an IV dose of $1/500^{th}$ the oral dose provides anti-diuresis for a period of time without overtreatment.
Phase 2: Desmopressin PRN

• Patients with a new diagnosis of DI after neurosurgery are known to have one of three outcomes over the next 10-14 days:
  1. Their DI is transient and it self-resolves
  2. They develop syndrome of inappropriate antidiuretic hormone (SIADH), which causes low urine output and a declining serum sodium
  3. They have permanent DI and will require lifelong treatment

• Giving a dose of desmopressin to a patient who has outcome #1 or #2 could place them at risk for a large decline in their serum sodium and dangerous hyponatremia

• The PRN desmopressin phase is designed to follow urine output and serum sodium closely so that desmopressin is only given when it is safe to do so
Phase 3: Scheduled Desmopressin

- Once a patient has been established to have permanent DI, they can have their desmopressin scheduled, rather than given PRN.
- The goal of this phase is to establish safe dosing of desmopressin in preparation for discharge home.
- When planning for discharge, it is important to determine lab follow-up and whether the family will monitor intake and output at home.
“Call Fors” for patients at risk for hyponatremia

- Patients recovering from neurosurgery who have a large positive imbalance of intake and output or low overall urine output are at high risk to develop hyponatremia.

- The “call fors” and labs that they trigger are designed to detect hyponatremia and to intervene before it becomes severe (sodium < 125).

- It is also important to consider that, although rare, some patients may develop DI which will be detected due to polyuria (urine output >4mL/kg/hr).
SIADH vs Cerebral Salt-Wasting (CSW)

- SIADH and Cerebral Salt-Wasting can be difficult to distinguish diagnostically, and they require different methods of treatment.

- CSW patients should have evidence of volume depletion, because their sodium level is low due to inappropriate loss of sodium in the urine:
  - Tachycardia
  - Delayed capillary refill
  - Decrease in weight
  - Other signs of dehydration appropriate for the age (i.e. sunken fontanelle)

- Patients with SIADH will have normal or increased volume status, because their sodium level is low due to excess water retention.
ED Assessment: History

- After establishing the ABCs (airway, breathing, circulation), the next most important determination for a patient with DI is whether they are due for a desmopressin dose

- Almost all patients with DI are on scheduled dosing of desmopressin and parents or the patient themselves should be able to report when their last dose was taken, and whether their last dose is wearing off (resulting in excessive urine output, i.e. “breakthrough urination”)

- Assessing the presence of vomiting, diarrhea, mental status change, or fever will help determine whether the patient may need to be admitted
ED Assessment: Measure and chart intake and output

- For a patient with DI, measurement of their intake and output is just as important as other classic vital signs.

- Unlike other pediatric patients, urine output is not a good assessment of hydration status for patients with DI. Instead, their urine output is almost entirely dependent on the amount of desmopressin in their system.

- A urine output of > 4 mL/kg/hr is almost always an indication that they require a dose of desmopressin urgently.

- A diaper scale is located in the dirty utility room in the ED. Zero the scale with a dry diaper first.
Known DI Management

• Unlike most other pediatric patients, those that have DI may have a difficult time tolerating the relatively large water and sodium load that comes with a normal saline (NS) bolus.

• If they have recently taken a dose of desmopressin, the NS bolus may cause a rapid drop in their sodium.

• If they are due for a dose of desmopressin, the NS bolus may cause a marked increase in their urine output, and their sodium may rise suddenly.

• For these reasons, NS boluses should be used cautiously in patients with DI, and only when they have clear evidence of intravascular volume depletion causing poor perfusion.
known DI: Management

- Chronic hypernatremia (present at least 24 hours) should be corrected slowly to prevent rapid shifts in body water causing cerebral edema.

- Retrospective studies have shown that for those with chronic hypernatremia, a maximum change in the sodium of 10-12 mEq/L per 24 hours is the fastest safe rate of correction.

- For this reason, a change in sodium of more than 0.5 mEq/L/hr (i.e. > 2 point decrease in 4 hours) in a patient with chronic hypernatremia should prompt a discussion regarding a change in the fluid management.
Dysnatremia Approval & Citation

Approved by the CSW Dysnatremia team for October 29, 2018 go live

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Please cite as:
This pathway was developed through local consensus based on published evidence and expert opinion as part of Clinical Standard Work at Seattle Children’s. Pathway teams include representatives from Medical, Subspecialty, and/or Surgical Services, Nursing, Pharmacy, Clinical Effectiveness, and other services as appropriate.

When possible, we used the GRADE method of rating evidence quality. Evidence is first assessed as to whether it is from randomized trial or cohort studies. The rating is then adjusted in the following manner (from: Guyatt G et al. J Clin Epidemiol. 2011;4:383-94.):

- Quality ratings are downgraded if studies:
  - Have serious limitations
  - Have inconsistent results
  - If evidence does not directly address clinical questions
  - If estimates are imprecise OR
  - If it is felt that there is substantial publication bias

- Quality ratings are upgraded if it is felt that:
  - The effect size is large
  - If studies are designed in a way that confounding would likely underreport the magnitude of the effect OR
  - If a dose-response gradient is evident

Guideline – Recommendation is from a published guideline that used methodology deemed acceptable by the team.

Expert Opinion – Our expert opinion is based on available evidence that does not meet GRADE criteria (for example, case-control studies).

**Quality of Evidence:**
- ☑️☑️☑️ High quality
- ☑️☑️☑️ Moderate quality
- ☑️☑️ Low quality
- ☑️ΟΟ Very low quality

Guideline
Expert Opinion
Summary of Version Changes

- **Version 1.0 (10/29/2018):** Go live
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Medicine is an ever-changing science. As new research and clinical experience broaden our knowledge, changes in treatment and drug therapy are required.

The authors have checked with sources believed to be reliable in their efforts to provide information that is complete and generally in accord with the standards accepted at the time of publication.

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Readers should confirm the information contained herein with other sources and are encouraged to consult with their health care provider before making any health care decision.
Search Methods

Literature searches were conducted in two phases and executed by Jackie Morton, Medical Librarian. The initial search in November 2017, targeted synthesized literature on the topics of dysnatremia, diabetes insipidus and sodium blood levels. The search was executed in Ovid Medline, Cochrane Database of Systematic Reviews, Embase, National Guideline Clearinghouse and TRIP. The search was limited to items published in English, from 2007 to date. The second search, in January 2018, was conducted in Medline and Embase to retrieve both synthesized and primary studies. The topics searched were diabetes insipidus and neurosurgical procedures, hyponatremia and Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH). The search was limited to items published in English, from 1998 to date. The team added one citation containing primary research cited by a recent protocol. Results were exported to RefWorks for system de-duplication, then to Excel for the screening process.

Flow diagram adapted from Moher D et al. BMJ 2009;339:bmj.b2535


