

## Kennsla læknanema á 5. námsári

# "Vökvameðferð í æð hjá börnum: nýir tímar, nýjar áherslur"

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# Clinical Practice Guideline: Maintenance Intravenous Fluids in Children

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# Introduction

- Maintenance intravenous fluids (IVFs) are used to provide supportive care for children who are acutely ill.
- IVFs are required if sufficient fluids cannot be taken orally for reasons such as
  - gastrointestinal illness, respiratory compromise, neurologic impairment, a perioperative state, or being moribund from an acute or chronic illness
- The goals of maintenance IVF prescription are to
  - preserve a child's extracellular volume while simultaneously minimizing the risk of developing volume depletion, fluid overload, or electrolyte disturbances, such as hyponatremia or hypernatremia.
  - The administered **fluid composition** is key.

# Introduction

- Guidelines for maintenance IVF therapy in children have to date primarily been “opinion-based” and “evidence-based” consensus guidelines for fluid composition and electrolyte monitoring are lacking.
  - Administration of **hypotonic IVFs** has been the standard in pediatrics.
  - Concerns have been raised that this approach results in a high incidence of hyponatremia and that isotonic IVFs could prevent the development of hyponatremia.

# Historical (current) IVF's prescription practices

## Hypotonic maintenance IVF administration

- This practice is based on theoretical calculations from the 1950's, based on the energy expenditure of **healthy** children, with 1 mL of fluid provided for each kilocalorie (kcal) expended.
- The electrolyte concentration of IVFs was estimated to reflect the composition of human and cow's milk. The final composition consisted of 3 mEq of sodium and 2 mEq of potassium per 100 kcal metabolized.

# The Holliday – Segar 4-2-1 Rule

to estimate Maintenance Hourly Fluid (WATER) Requirements

Weight (kg)	Hourly	Daily	Kunna vel
<10 kg	4 mL/kg/hr.	100 mL/kg/day	
10 –20 kg	40 mL + 2 mL/kg for every kg >10 kg	1000 mL + 50 mL/kg/day for every kg >10	
>20 kg	60 mL + 1 mL/kg for every kg >20 kg	1500 mL + 20 mL/kg/day for every kg > 20	

## 4-2-1 rule EXAMPLES

**For a 5 kg infant, Maintenance Hourly Fluid (water) Requirements would be:**

$$4 \times 5 = 20\text{ml/hr.}$$

$$\text{Daily rate: } 20 \times (24\text{hr}) = 480 \text{ ml/day}$$

Electrolytes (maintenance):

- Na<sup>+</sup> = 3-4 mEq/100 Kcal

- K<sup>+</sup> = 1-2 mEq/100 KCal

**For a 15 kg child, Maintenance Hourly Fluid (water) Requirements would be:**

$$4 \times 10 = 40 \text{ ml} + 2 \times 5 = 10 \text{ ml}$$

$$\text{Total: } 40 + 10 = 50\text{ml/hr.}$$

# Hyponatremia and vasopressin (ADH) excess

- **Hyponatremia ( $S\text{-Na} < 135 \text{ mEq/L}$ )** is the most common electrolyte abnormality in hospitalized patients, affecting between 15% and 30% of both children and adults.
- Patients who are acutely ill frequently have disease states associated with vasopressin (ADH) excess (inappropriate antidiuresis (SIAD) or SIAD-like states) which impair free-water excretion.
  - High risk for of hyponatremia, when **hypotonic fluids** are infused.
- Nonosmotic stimuli of ADH release include
  - **pain, nausea, vomiting, stress, a postoperative state, hypovolemia, various medications (morphine), and pulmonary and CNS disorders, including pneumonia and meningitis.**

# Major complication of hypotonic IVF infusion

## Acute hospital-acquired hyponatremia

- The Institute for Safe Medical Practices of both the United States and Canada have released reports on deaths from severe hyponatremia in patients who were hospitalized and received hypotonic IVFs.
- The United Kingdom released a national safety alert reporting 4 deaths and 1 near miss from hospital-acquired hyponatremia.
  - A number of cases of serious brain injury or child death from the administration of hypotonic IVFs reported.



# Major complication of hypotonic IVF infusion

## Acute hospital-acquired hyponatremia

- Occurs primarily in **otherwise healthy children** who are receiving hypotonic IVFs, in many cases after minor surgical procedures
  - Hyponatremic encephalopathy is the most serious complication
    - A medical emergency that can be fatal or lead to irreversible brain injury if inadequately treated.
    - Usually develops acutely in less than 48 hours, leaving little time for the brain to adapt.

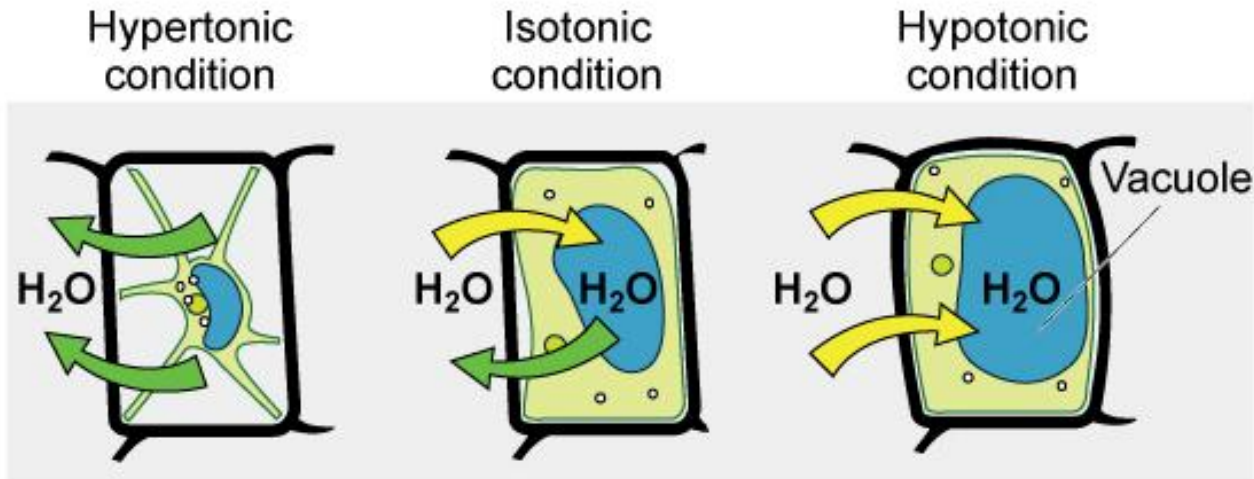
# Composition of available IVF's

IVF	G (%)	Na <sup>+</sup> mmol/L	K <sup>+</sup> mmol/L	Ca <sup>++</sup> mmol/L	Mg <sup>++</sup> mmol/L	Cl <sup>-</sup> mmol/L	Acetate mmol/L	Gluconate mmol/L	Osmo mosm/kg
Ringer Acetate	-	130	4	2	1	110	30	0	277
NaCl (0.9%)	-	154	0	0	0	154	0	0	0
Rehydrex G	2,5	70	0	0	0	45	25	0	280
Plasmalyte G	5	140	5	0	1,5	98	27	27	572
Benelyte G	1	140	4	1	1	118	30	0	351
Na/K/Glucose	5	40	20	0	1,5	45	23	0	400

Vita að Na<sup>+</sup> í isoton vökvum er 130-154 mEq/L

# Tonicity

- Cellular expansion occurs during immersion in hypotonic fluids, free water enters the cell; the converse happens in hypertonic fluid immersion: free water shifts out of the cells, leading to cellular contraction.



*Image credit: OpenStax Biology, modification of work by Mariana Ruiz Villareal*

When isotonic fluids are infused, the cells stay the same size.

# Tonicity and osmolality

Skilja mun á osmolality og tonicity vökva

- The tonicity of IVF is primarily affected by the sodium and potassium concentration.
  - Although glucose affects the osmolarity of IVFs, it is not a significant contributor to the plasma osmotic pressure or tonicity as it is **rapidly metabolized after entering the blood stream**.
  - In the plasma, urea affects osmolality but not tonicity because urea moves freely across cell membranes with no effect on tonicity.
- Osmolality of plasma
  - $2 \times \text{Se-Na}^+$  (mEq/L) + serum glucose (mmol/L) + urea (mmol/L)

# Tonicity and osmolality

- The tonicity of IVF is primarily affected by the sodium and potassium concentration.
- Isotonic solutions
  - Has a Na<sup>+</sup> concentration similar to plasma (135-144 mEq/L) and osmolarity 280-300 mOsm/L.
- Hypertonic solutions
  - Has a Na<sup>+</sup> concentration > plasma (>144 mEq/L) and osmolarity more than 300 mOsm/L
- Hypotonic solution
  - Has a Na<sup>+</sup> concentration < plasma (>135 mEq/L) and osmolarity < 280 mOsm/L.

# Tonicity and osmolality

- What is the tonicity of 0.9% NaCl?
  - Isotonic or hypertonic?

Áhugavert !!!

# Tonicity and osmolality

- Plasma is approximately 93% aqueous and 7% anhydrous (proteins and lipids) with a **sodium concentration in the aqueous phase of plasma of 154 mEq/L** and osmolarity of 308 mOsm/L, similar to that of 0.9% sodium chloride (NaCl).
- Therefore, 0.9% NaCl **is an isotonic solution** and all the other “so called” isotonic solutions are indeed slightly hypotonic.

# Tonicity and osmolality

- Hypertonic solutions can cause severe damage to the vein, including thrombophlebitis and infiltration.
  - IVF's with an osmolarity less than 600 mOsm/liter (perhaps up to 750) can safely be infused via peripheral vein.
  - IVF's with an osmolarity greater than 600 mOsm/liter should be infused through a central venous catheter.



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# Goal of new AAP guideline

To provide evidence-based approach for choosing the tonicity of maintenance IVFs in most patients from 28 days to 18 years of age.

# Key Action Statement

The AAP recommends that patients 28 days to 18 years of age requiring maintenance IVFs should receive isotonic solutions with appropriate potassium chloride (KCl) and dextrose (d-glucose) because they significantly decrease the risk of developing hyponatremia - (evidence quality: A).

# Studies and patients included

17 randomized clinical trials comparing the incidence and risk of hyponatremia in patients receiving **isotonic vs hypotonic maintenance** iv fluids

Studies included 2455 patients

# Studies and patients included

These recommendations do not apply to patients with neurosurgical disorders, congenital or acquired cardiac disease, hepatic disease, cancer, renal dysfunction, diabetes insipidus, voluminous watery diarrhea, or severe burns; neonates who are younger than 28 days old or in the NICU; or adolescents older than 18 years old.

- Please note: at our Children’s Medical Center (Barnaspítali Hringisins) this recommendation applies to the age-group **7 days to 18 years.**

# What does the evidence say?

- When comparing hypotonic and isotonic IVF's
  - Hyponatremia was significantly associated with the use of hypotonic IVF's.
  - Hypernatremia was uncommon, and not more common than with isotonic fluids administration.
  - Hyperchloremic metabolic acidosis was not associated with isotonic IVF's, including 0.9% NaCl.
  - Data for the estimation of fluid overload were lacking.



- Sixteen of these 17 studies revealed that isotonic fluids were superior to hypotonic fluids in preventing hyponatremia.
- The number needed to treat with isotonic fluids to prevent hyponatremia (sodium  $<135$  mEq/L) was 7.5 across all included studies and 27.8 for moderate hyponatremia (sodium  $<130$  mEq/L).

# Study findings

## - hyponatremia

- The relative risk of developing mild and moderate hyponatremia (se-Na < 135 mEq/L and < 130 mEq/L, respectively) was > 2 and > 5, respectively.
- The risk related to hyponatremia persisted regardless of age, medical versus surgical status, and intensive care versus general pediatric ward setting.



# Study findings - hyponatremia

- These data strongly reveal an increased risk of hyponatremia when children receive hypotonic versus isotonic IVFs
- In the clinical trials in which researchers assessed the possible mechanism for this finding, elevated ADH concentration was found to play a role.

# Discussion of study findings - hyponatremia

- Some may argue that mild hyponatremia (plasma sodium 130–134 mEq/L) and moderate hyponatremia (plasma sodium 125–129 mEq/L) may not be clinically significant or constitute harm.
- The true effects of hypotonic IVFs may have been underestimated as many patients were removed from the studies if mild hyponatremia developed.

# Recommendations

- At our Children's Medical Center (Barnaspítali Hringssins) this recommendation applies to the age-group 7 days to 18 years.
- Children age 7 days to 18 years of age requiring maintenance IVFs should receive isotonic solutions with appropriate KCl and d-glucose (dextrose) concentration.
  - Add KCl if: Ongoing K<sup>+</sup> losses (vomiting, diarrhea)
  - **Never add K<sup>+</sup> in patients with acute kidney injury**
  - Bæta við KCl 20-40 mmol/L ef vökvameðferð í >24 klst eða ef Kalium er < 3,5 mmol/L í upphafi meðferðar
- The approach of using hypotonic maintenance IVFs should be abandoned.

# Recommendations - maintenance fluids

Children age **7** days to **18** years of age

- At our Children's Medical Center (Barnaspítali Hringssins)
- Isotonic IVF's with glucose and potassium as indicated
  - Benelyte G1% or plasmalyte G5%
- Hypotonic maintenance IVFs should no longer be used.
  - Rehydrex.
  - Glucose solutions (5%, 10% etc) with NaCl 40 and KCl 20 mEq/L
    - Should however be available for the treatment of certain conditions such as significant hypernatremia.

# Dehydrated patients – reduced intravascular volume

Children age **7** days to **18** years of age

- Isotonic IVF's with glucose and potassium as indicated
  - Benelyte 1% G
  - 0.9% NaCl or Ringer Acetate if hyperglycemia
  - Use 10-20 mL/kg bolus, repeated as needed (**sjá einnig AKI fyrirl**).
- When intravascular volume is restored
  - Use IVF's recommended for maintenance
    - Benelyte G1% or Plasmalyte G5% (never use Glucose 5% with NaCl 40 mEq/L and KCl 20 mEq/L).

# Dehydrated patients – reduced intravascular volume

## Children age 7 days to 18 years of age

- Einkenni þurrks eru margvísleg og sum þeirra koma ekki fram fyrr en vandinn er orðinn alvarlegur/ yfirvofandi lost.
- Alvarleiki þurrks er reiknaður sem mismunur af þyngd barns fyrir veikindi og þyngd barns við komu. Þannig er 10 kg barn sem er búið að léttast um 1 kg með 10% þurrk.
  - Sjá töflu á næstu mynd um mat á þurrki/dehydration

## Þekkja þessa töflu/skyggnu

Purrkur, %	Vægur ( < 3%, < 30 mL/kg)	Miðlungs (3-9%, 30-90 mL/kg)	Alvarlegur ( > 10%, >100 mL/kg)
Meðvitundarstig	Vakandi	Óróleiki	Sljóleiki
Púls	Innan marka	Hækkaður	Hækkaður
Styrkleiki púls	Vel greinanlegur	Daufur	Daufur / ógreinanlegur
Háræðafylling	Innan marka	um 2 sek	>2 sek
Blóðþrýstingur	Innan marka	Innan marka	Innan marka eða lækkaður
Öndunartíðni	Innan marka	Hækkuð	Hækkuð, andar djúpt
Augu	Eðlileg	Sokkin	Sokkin, grætur án tára
Fontanella	Eðlileg	Sokkin	Sokkin
Þvagústkilnaður	Eðlilegur	Minni	Minni eða pissar ekki
Slímhúðir	Rakar	Þurrar	Þurrar
Húðturgor	Eðlilegur	Eðlilegur	Minnkaður

Alltaf að fá þyngd og meta purrk út frá þyngdartapi!

**Dæmi:** 10 kg barn sem er búið að léttast um 1 kg er með 10% purrk.