

# Intravenous Fluids in the Hospitalized Child

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July 11<sup>th</sup> ,2018

Special thanks to **Kyle Rehder, MD**, Associate Professor of Pediatric Critical Care at Duke for sharing some of his slides.

# Objectives

- Review the history of current practice in IVF management.
- Discuss the physiology of maintenance IVF therapy.
- Detail the risks of maintenance IVF therapy with hypotonic fluids.
- Describe the physiology and benefits of oral rehydration therapy.

# History of Intravenous Fluid Therapy

“Probably the proper use of water and electrolyte solutions is responsible for saving more lives of seriously ill patients than is the use of any other group of substances.”

-Daniel C. Darrow, M.D.

& Edward L. Pratt, M.D.

May 27, 1950

*JAMA*. 143; 1950: 365.

# History of intravenous fluid therapy

- 1831 pandemic of cholera spread across Europe
- O'Shaughnessy observed:
  1. Cholera serum has "lost a large proportion of its water"
  2. "It has also lost a great proportion of its neutral saline ingredients."
  3. High salt and water content of excrement
- Subsequently proposed "injecting into the veins such substances as an examination of the blood...would show to be most capable of restoring it to the arterial qualities."



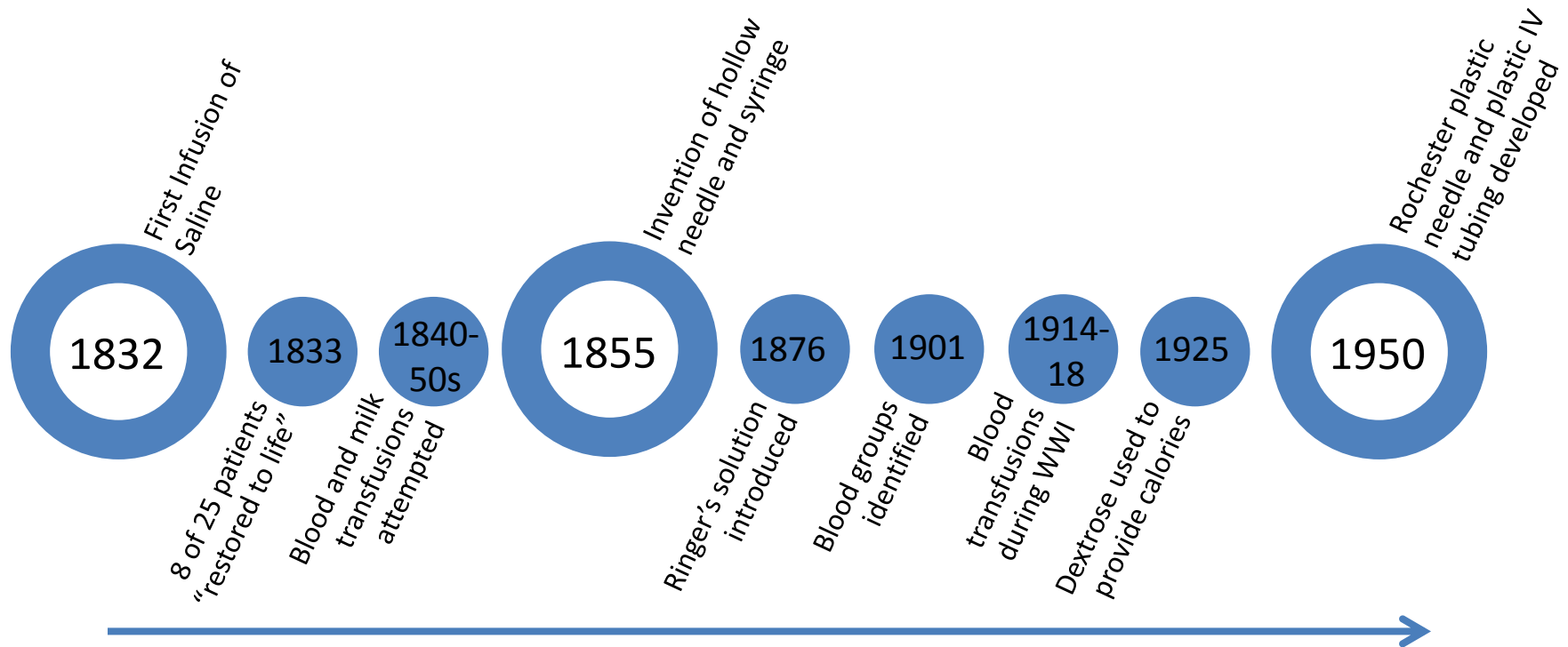
Dr. William Brooke  
O'Shaughnessy

O'Shaughnessy WB. Experiments on the blood in cholera. *Lancet*. 1831; 17:490.

O'Shaughnessy WB. Proposal of a new method of treating The Blue Epidemic of Cholera.

*Lancet*. 1831;18: 366-371.

# Important milestones in intravenous fluid therapy



Barsoum N, Kleeman C. Now and then, the history of parenteral fluid administration. *American Journal of Nephrology*. 2002;22:284-89.

Millam D. The history of intravenous therapy. *Journal of Intravenous Nursing*. 1996;19:5-14.

# Resuscitation Fluids

- Isotonic fluids for resuscitation:
  - Normal Saline (0.9% NaCl)
  - Lactated Ringers aka Hartmann's Solution (130 mEq Na, 109 mEq Cl, 28 mEq lactate, 4 mEq potassium, 3 mEq of calcium)
- 20 ml/kg is typical starting bolus
  - 5-10 ml/kg if concerned about cardiac function
- May repeat several times if perfusion not restored with initial bolus

# Maintenance fluids in the 1950s

- Fluid needs stem from metabolism
- Pathways of water and electrolytes losses:
  - Skin and lungs (insensible heat losses and sweat)
  - Urine (renal load of solutes from protein metabolism)
  - GI tract (stool water is negligible in fasting)
- Give dextrose to decrease protein catabolism and ketosis.

# Amount of water for renal solute

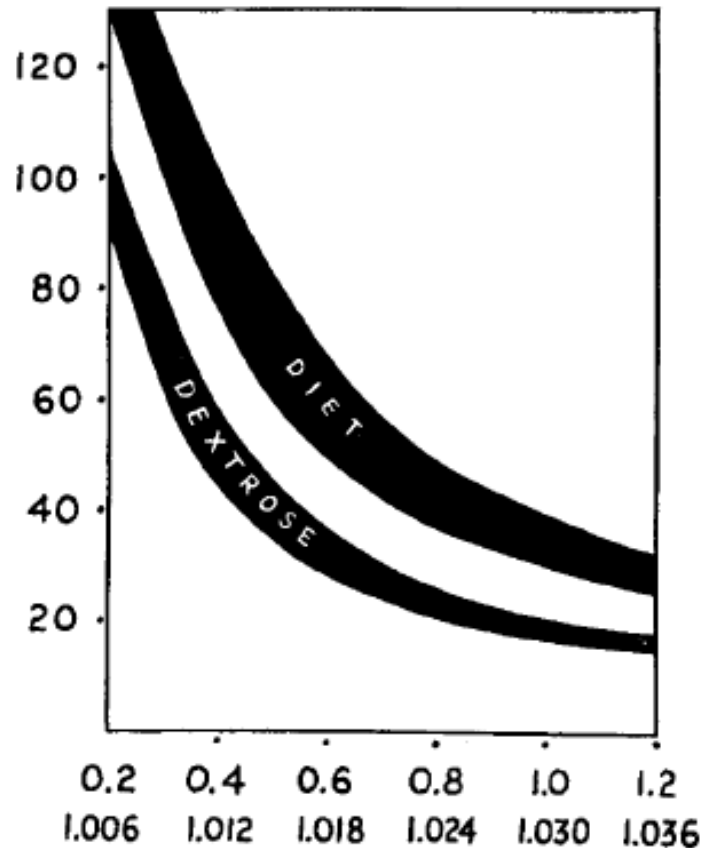
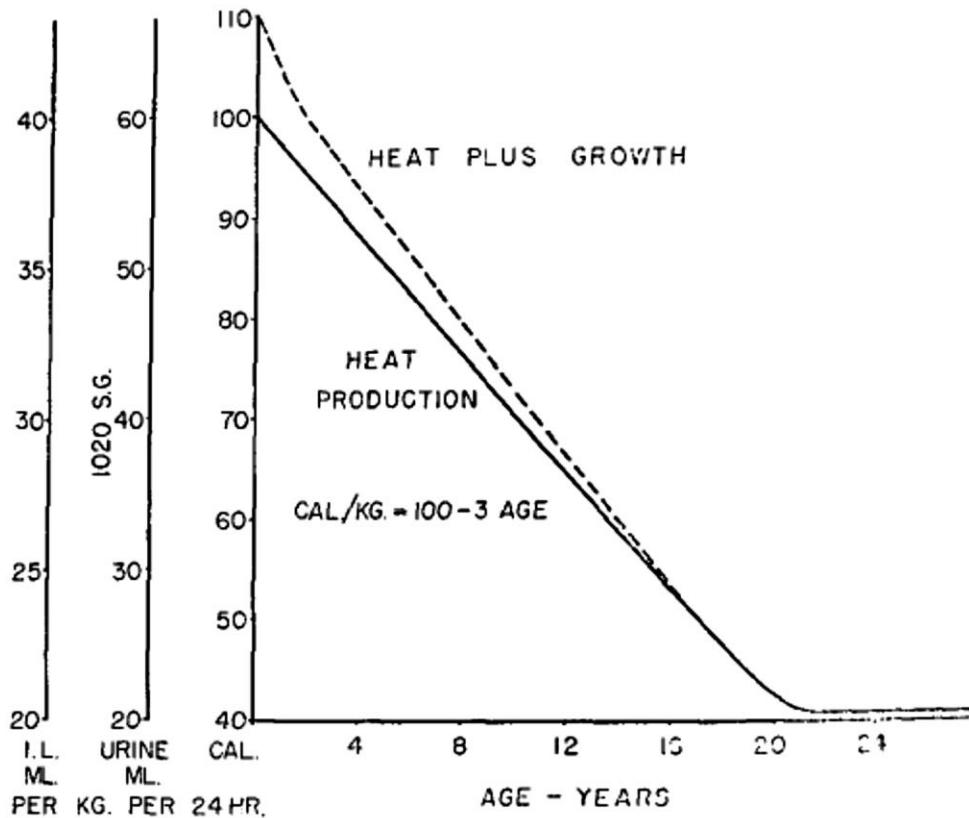


Fig. 4.—The urinary volume required to excrete the solids presented to the kidneys for excretion by the metabolism of 100 calories. The ordinate scale represents milliliters of water per hundred calories; the upper abscissa scale represents osmoles per liter, and the lower, specific gravity.

Darrow DC, Pratt EL. Fluid Therapy: relation to tissue composition and the expenditure of water and electrolyte. *JAMA*. 1950;143:365-373.



# Average Caloric Expenditure



For every 100 kcal burned, the body needs 100 ml water to replace insensible losses and create urine with SG of 1.020.

FIG. 1. Idealized diagram relating the average daily heat production per kilogram of body weight at varying ages to the loss of water *via* skin and lungs (IL) and to the average urinary water requirement on diets usual for each age.

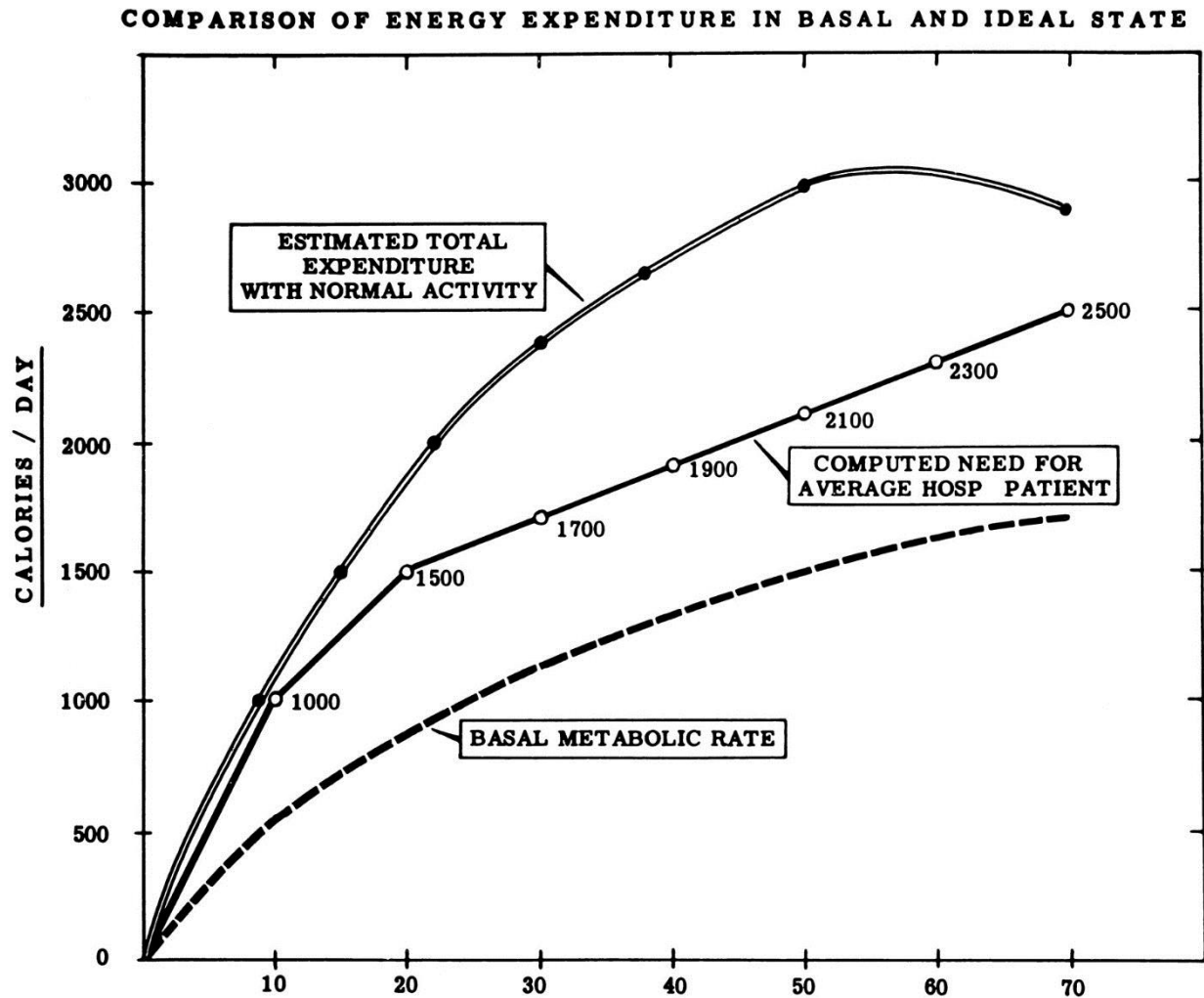
Wallace WM. Quantitative requirements of the infant and child for water and electrolyte under varying conditions. *American Journal of Clinical Pathology*. 1953;23: 1133-1141.

# Approximating caloric expenditure

- $\text{Calories/kg} = 100 - 3 \times \text{age in years}$
- Body surface area ( $1500 \text{ cal/m}^2/\text{day}$ )
- Caloric expenditure method
- Holliday-Segar

“High precision in parenteral therapy is impossible and unnecessary. Even with complex measurements of balance the clinician is always a day late in setting requirements” –William M. Wallace, M.D.

# Basal metabolic rate, normal activity and average hospitalized patient



Holliday MA, Segar WE. The maintenance need for water in parenteral fluid therapy. *Pediatrics*. 1957;19:823-32.

# Holliday-Segar Method

Weight	ml/kg/day	ml/kg/hr
First 10 kg	100	4
Second 10 kg	50	2
Each additional kg	20	1
e.g. 25 kg	$1000+500+100$ $=1600$ ml/day	$40+20+5 =$ 65 ml/hr (1560 ml/day)

*Quantities obtained for various weights are similar to other methods.*

# What to put in the water?

- Goal: *prevent catabolism and hypoglycemia.*
- Minimal catabolism achieved by giving 4-5 g of dextrose per 100 calories metabolized.
- D5W has 5 g dextrose per 100 ml water.
- D5W can be safely given through a PIV.

# What about electrolytes?

Regimen	mEq/100 cal		
	Na	Cl	K
Human Milk	1.0	1.2	2.0
Cow's Milk	3.5	4.5	6.0
Recommended	3.0	2.0	2.0
Recommended (Darrow)	3.0	2.0	3.0
Recommended Adult (Welt)	3.0	3.0	1.0

Recommend adding 3 ml of molar sodium lactate and 1 ml of 2 molar potassium chloride to every 100 ml of D5W to obtain maintenance fluid.

# D5 ¼ NS for infants and D5 ½ NS for older children and adults?

- The sodium concentration should NOT differ:
  - Na needs are 3 mEq/100 *kcal*s, not 3 mEq/kg.
  - Na needs are not linear; they are curvilinear like water.
  - Therefore, the ratio of Na to water should remain constant.
- Normal Saline (0.9% NaCl) has 154 mEq/L of NaCl.
  - 0.2NS has 30.8 mEq/L
  - 0.2% NaCl has 34 mEq/L
  - ¼ NS has 38.5 mEq/L
- *Therefore, D5 0.2 NS with 20 mEq of KCl per liter is an appropriate maintenance fluid for **all** people.*

# Typical Daily Intakes of Water and Sodium

Age	Daily intakes		Sodium Concentration (mmol/L)
	Water(ml/kg)	Sodium(mmol/kg)	
Newborn	150	3	20
1 year	100	2.5	25
5 years	75	2	27
12 years	50	1	20

Coultard MG. Will changing maintenance intravenous fluid from 0.18% to 0.45% saline do more harm than good? *Arch Dis Child*. 2008;93:335-340.



So why don't we use D5 0.2 NS  
for all hospitalized patients?

# Problems with Holliday-Segar Method

1. Calculations based on ***healthy*** kids
2. Sick kids may have different needs
3. Fails to account for non-osmotic triggers of anti-diuretic hormone (ADH) release

# PEDIATRICS®

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## IDIOPATHIC HYPONATREMIA IN AN INFANT WITH DIFFUSE CEREBRAL DAMAGE

Wallace W. McCrory and Duncan Macaulay

*Pediatrics* 1957;20:23

- Case report of hyponatremic infant after CNS injury
- 1<sup>st</sup> published report of SIADH

# ADH elevated in hospitalized children

- ADH may be ***appropriately*** elevated with:
  - Dehydrated patients
  - Sepsis
  - Post-surgical patients
  - Mechanically ventilated children
  - In presence of hypotension
  - Stress

# Retrospective studies of IVF

Year	Study	Population	Findings
2001	Retrospective Review	23 hospitalized kids with hypoNa	<ul style="list-style-type: none"> <li>All on hypotonic fluids</li> <li>16/23 receiving IVF at &gt; 150% maintenance rate</li> </ul>
2003	Lit Review	Iatrogenic hypoNa in kids	<ul style="list-style-type: none"> <li>&gt;50 reports of morbidity, 26 deaths</li> <li>Post-op patients at high risk</li> </ul>
2004	Case Control	40 kids developing hypoNa in hospital	<ul style="list-style-type: none"> <li>HypoNa cases received 3x more free-water</li> <li>HypoNa likely led to 1 seizure and 1 death</li> </ul>
2010	Retrospective Review	124 kids with gastroenteritis	<ul style="list-style-type: none"> <li>19% of children with nl Na developed hypoNa; all on hypotonic IVF</li> <li>Fluid rate not predictive of hypoNa</li> </ul>

Halberthal, et. al. *BMJ* 2001  
 Hoorn, et. al. *Pediatrics* 2004

Moritz, et. al. *Pediatrics* 2003  
 Hanna, et. al. *Ped Neph* 2010

# Flaws with retrospective studies

- Complications due to “egregious errors in management, not from conventional fluid therapy.”
  - Inappropriate use of hypotonic fluids to replace deficits (the 2 x MIVF phenomenon)
  - Hypotonic fluids for surgical patients
  - Lack of fluid restriction in SIADH
- “the amount of fluid infused was not only significantly higher in this in-hospital [hyponatremia] group but also **well above that recommended by the standard formula for maintenance fluid administration.**”

Holliday MA, Segar WE. Reducing errors in fluid therapy management. *Pediatrics*. 2003;111:424-25.

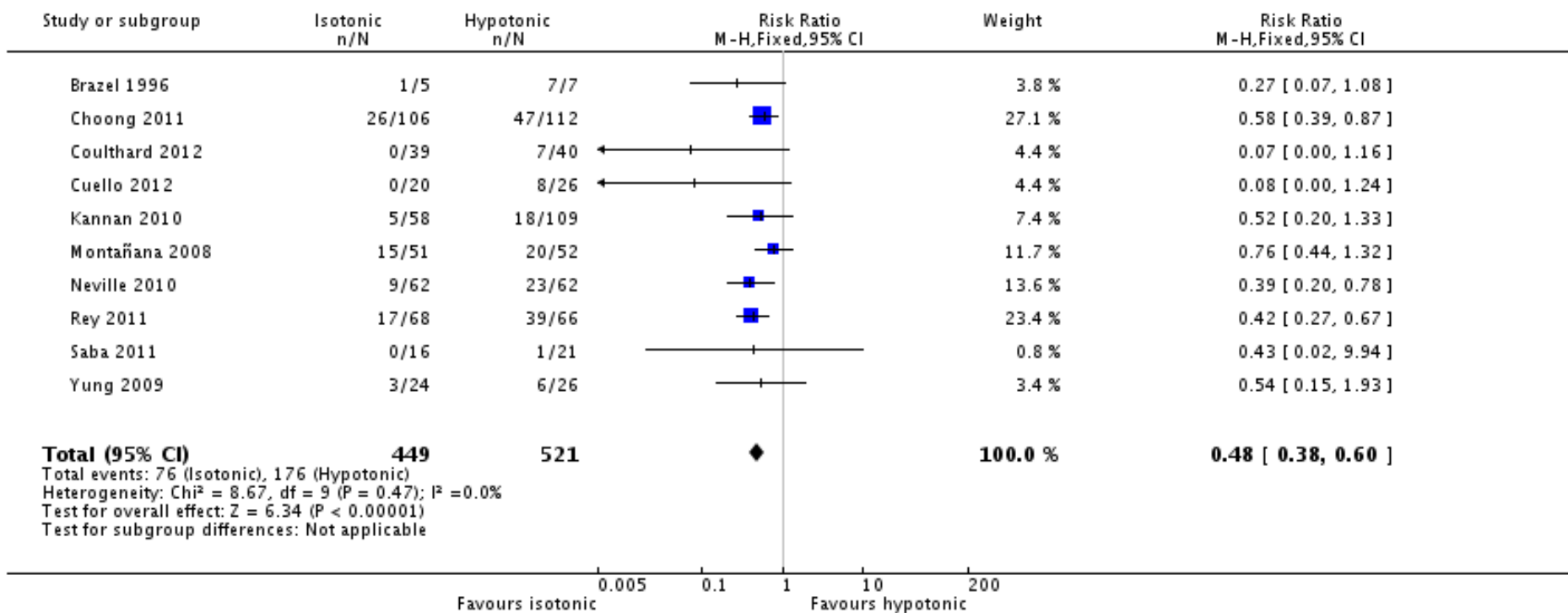
Hoorn EJ, et al. Acute hyponatremia related to intravenous fluid administration in hospitalized children: an observational study. *Pediatrics*. 2004; 113: 1279-84.

# RCTs of isotonic vs. hypotonic fluids

	Study	Condition	Follow-up, h	Hypotonic			Isotonic		
				N	Age, y	Solution	N	Age, y	Solution
1	Brazel 1996	Surgical	≥72	7	Adolescent	0.3% S and 3% D; 0.18% S and 4% D	5	Adolescent	Hartman's solution
2	Yung 2009a	Surgical and medical	≥12	15	4.7 (1.4–8.9)	0.18% S and 4% D	13	5.3 (0.9–12)	0.9% S
	Yung 2009b	Surgical and medical	≥12	11	3.7 (1.5–14.7)	0.18% S and 4% D	11	15.4 (10.8–15.9)	0.9% S
3	Kannan 2010	Medical	≥24	56	4.0 (1.1–6.0)	0.18% S and 5% D at full rate	58	3.0 (1.0–7.0)	0.9% S and 5% D at full rate
		align	≥24	53	3.0 (0.8–5.5)	0.18% S and 5% D at 2/3 rate			
4	Neville 2010a	Surgical	≥8	31	9.9 (2.0–15.0)	0.45% S and 5% D at half rate	31	9.4 (1.0–14.9)	0.9% S and 5% D at half rate
	Neville 2010b	Surgical	≥8	31	9.1 (0.9–14.9)	0.45% S and 2.5% D at full rate	31	8.4 (0.6–14.9)	0.9% S and 2.5% D at full rate
5	Choong 2011	Surgical	≥24	130	9.2 ± 5.7	0.45% S and 5% D	128	9.2 ± 5.5	0.9% S and 5% D
6	Rey 2011	Surgical and medical	≥12	62	4.7 (1.7–9.9)	30–50 mmol/L NaCl and 20 mmol/L KCl	63	4.9 (2.0–10.6)	136 mmol/L NaCl and 20 mmol/L KCl
7	Saba 2011	Surgical and medical	≥8	21	8.9 (1.7–16.5)	0.45% S and 5% D	16	8.2 (2.8–14.3)	0.9% S and 5% D
8	Coulthard 2012	Surgical	≥16	41	11.5 (6.0–14.1)	0.45% S and 5% D	41	11.3 (4.3–13.9)	Hartmann's and 5% D

# Systematic Review Favors Isotonic IVF

Review: Isotonic versus hypotonic solutions for maintenance intravenous fluid administration in children  
 Comparison: 1 Isotonic versus hypotonic  
 Outcome: 1 Hyponatraemia





# Flaws with prospective RCTs

- Small numbers of patients
- Some had poor follow-up
- Physicians not blinded
- Inability to detect differences in morbidity
- Some studies done on selected groups of patients known to have high ADH levels (e.g. surgical patients)
- Some studies used hypotonic fluids to replace deficits.
- One study allowed patients with baseline hyponatremia to be randomized to hypotonic fluids.

# Problems with isotonic fluid

- Does not treat SIADH (fluid restriction more appropriate)
- Does not treat hyponatremia which may be caused by fluid retention.
- May lead to metabolic acidosis with gastroenteritis.
- It's a lot of salt!

Average 70 kg male:

2500 ml NS/day

=385 meq NaCl/day

=3.7 tsp of table salt per day

~9000 mg sodium per day!

# Non-ICU, non-surgical patients?

- Recent RCT from Hospital for Sick Children (Toronto)
  - 110 non-surgical floor patients randomized to D5NS vs. D5 ½ NS for MIVF
  - **No difference in mean [serum Na] at 24 or 48 hours**
    - 2 cases of hyponatremia in hypotonic group (none in isotonic group)
    - 2 cases of edema in isotonic group (none in hypotonic group)
    - 1 case hypernatremia in each group
    - 2 groups were equal for hypertension and weight gain
- 2012 study of U.S. residents: 78% routinely prescribed hypotonic fluids.

# What to do?

# Err on the side of safety

Hyponatremia	Hypernatremia
Headache Confusion / Lethargy Seizures Cerebral Edema Coma Death	Weakness Peripheral Edema Seizures Death
Symptomatic: Na <130	Symptomatic: Na >160

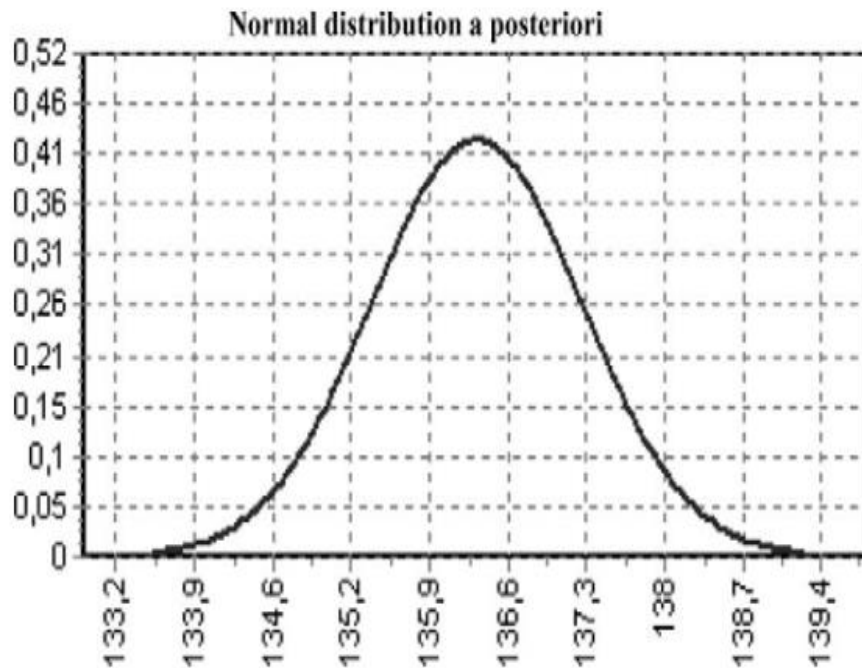
- Encephalopathy in 50% of kids at Na 125

## ZERO studies:

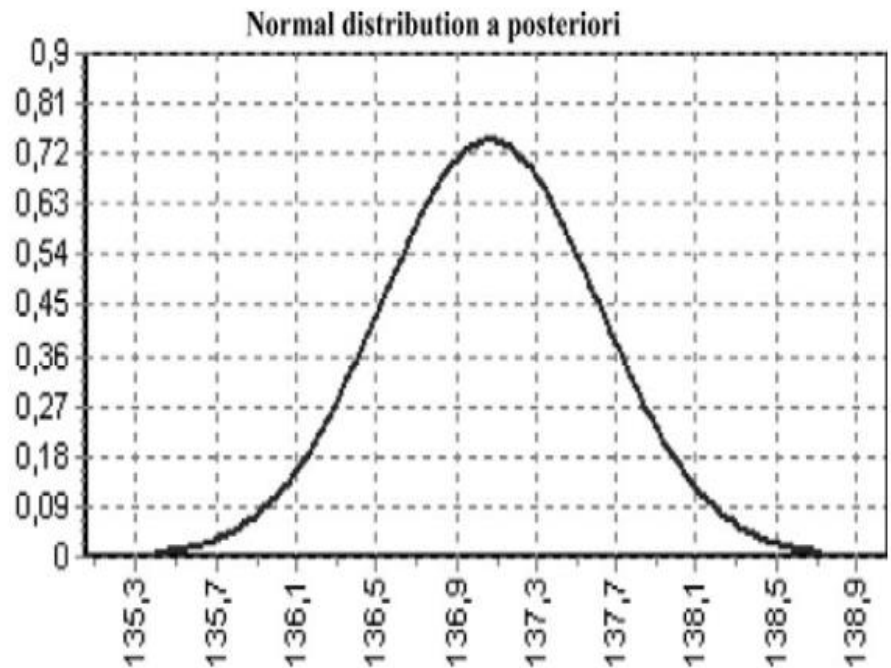
- **demonstrate risk of hyperNa with isotonic fluids**
- **support hypotonic over isotonic IVF**

# Avoid the danger zone

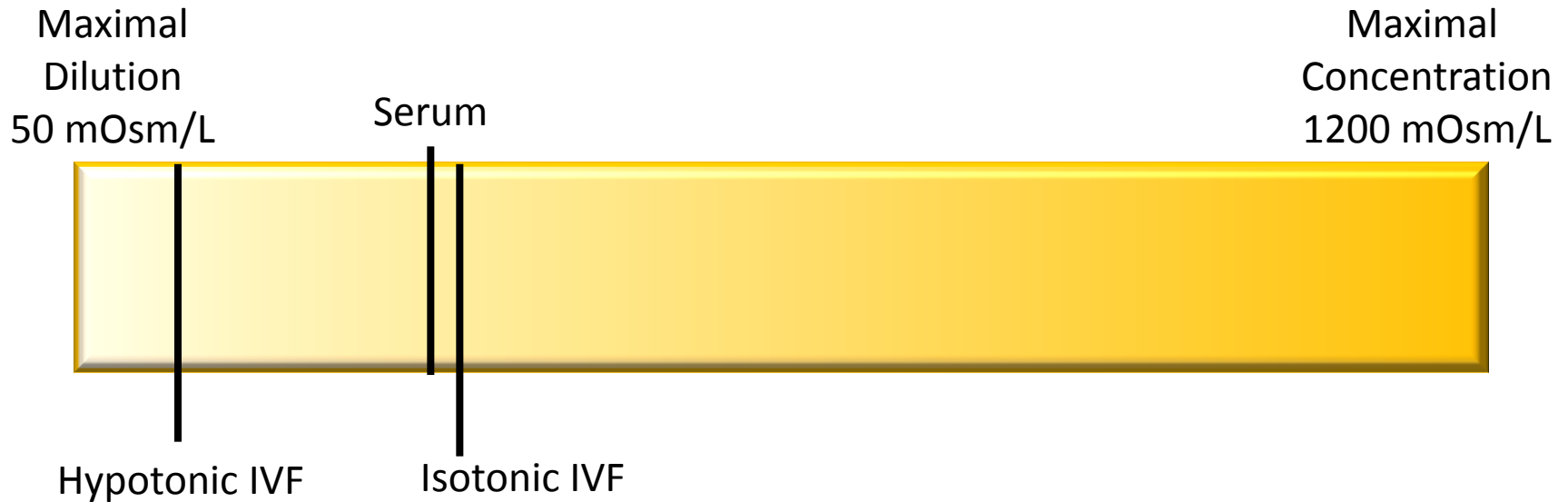
— Hypotonic



— Isotonic



# The kidney can handle the salt



- The kidney is better at excreting excess solute rather than excess free water

# Summary

- Hypotonic maintenance fluids cause more derangements in serum sodium levels than isotonic fluids
- This is particularly true when ADH levels are elevated
- In children with normal kidneys, isotonic solutions are safe because hyponatremic children retain sodium and normonatremic children excrete sodium.



# What about hypernatremia?

Example:

**10** kg patient

Na: **165** mEq/L

FW deficit:

**165-140** x 1000 x 0.6 x **10** kg

140

=1071 ml over 48 hours

~22 *ml/hr*

Y-in D5W at 22 *ml/hr* or give D5 ½ NS at 62 *ml/hr*

***You have to do the math!***

# Duke is not immune...

- SRS reports identify multiple case of iatrogenic hyponatremia:
  - Post-op and non post-op patients
  - Prolonged use of hypotonic fluids
  - Lack of safeguards

# Ordering fluids:

## Order Sets

### ▼ Pediatric Common Intravenous Fluids Manage My Version ▼

#### IV Fluids

Collapse

##### ▼ Bolus

- NS bolus 10 mL/kg over 1 hour STAT  
10 mL/kg (Dosing Weight), Intravenous, STAT
- NS bolus 20 mL/kg over 1 hour STAT  
20 mL/kg (Dosing Weight), Intravenous, STAT
- NS bolus  
Intravenous
- LR bolus  
Intravenous

##### ▼ Common Maintenance IV Fluids

- D5-1/2 NS  
Intravenous, Continuous
- D5-1/2 NS + KCL 10 mEq/L  
Intravenous, Continuous
- D5-1/2 NS + KCL 20 mEq/L  
Intravenous, Continuous
- D5-NS  
Intravenous, Continuous
- D5-NS + KCL 10 mEq/L  
Intravenous, Continuous
- D5-NS + KCL 20 mEq/L  
Intravenous, Continuous

##### > Other Dextrose IV Fluids

Click for more

##### > Other IV Fluids

Click for more

##### ▼ Pediatric Custom IV Fluid Builder

- pediatric iv fluid builder

##### > Replacement Fluids

Click for more

#### 🔍 Additional SmartSet Orders (Type to search)

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# What if we skip IVF altogether?

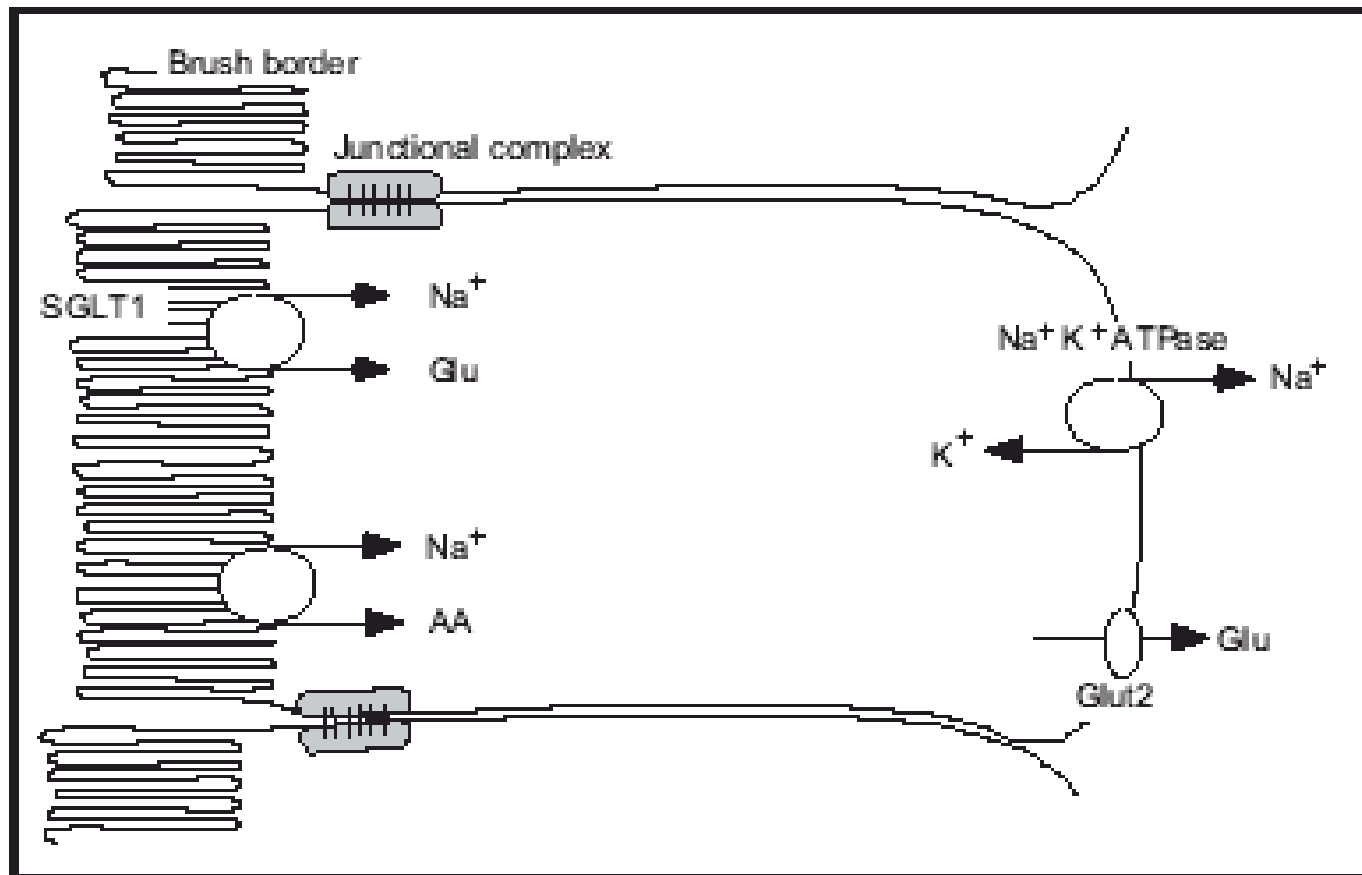
Let's talk about oral  
rehydration...

# Why use oral rehydration?

- Diarrhea is responsible for **12% of deaths worldwide** in children <5 yo.
  - 1.8 million children/year die of diarrheal illnesses.
  - Almost **50% due to dehydration** (mostly in children < 1 yo).
  - Technology not available for safe IV hydration in many places.
- IVF are dangerous!

# Physiology of Absorption

FIGURE. Solute-coupled sodium absorption



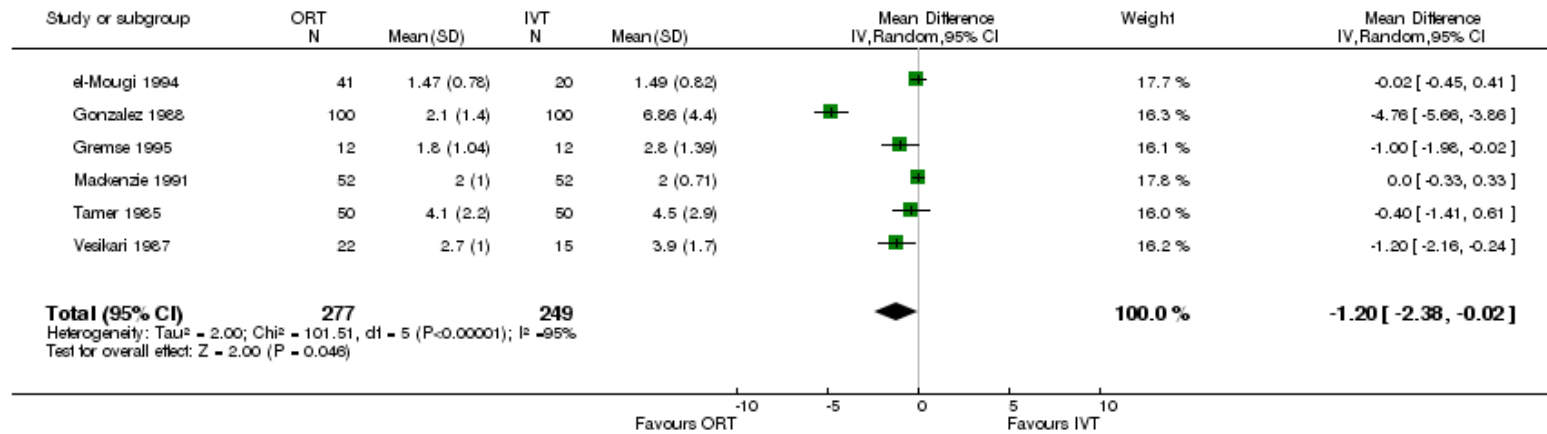
# Physiology take-home points

-  so  cellularly
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# Oral versus intravenous rehydration for treating dehydration due to gastroenteritis in children

## Length of Stay

Review: Oral versus intravenous rehydration for treating dehydration due to gastroenteritis in children  
 Comparison: 1 Oral rehydration therapy (any solution) versus intravenous therapy  
 Outcome: 4 Length of hospital stay (days)

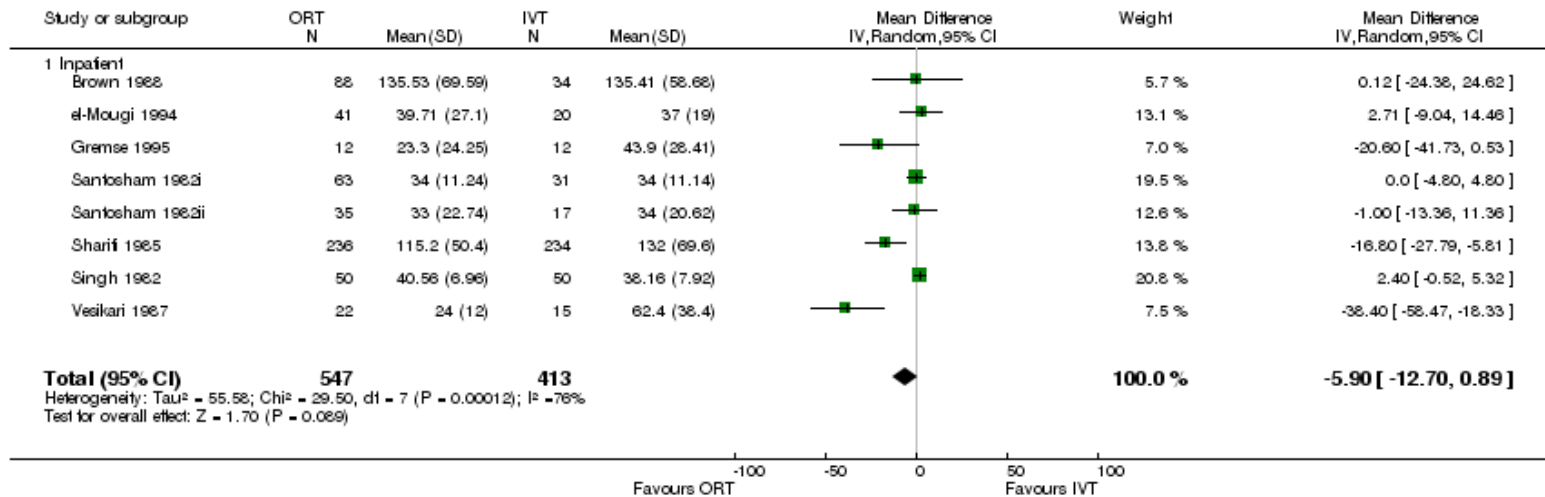




# Oral versus intravenous rehydration for treating dehydration due to gastroenteritis in children

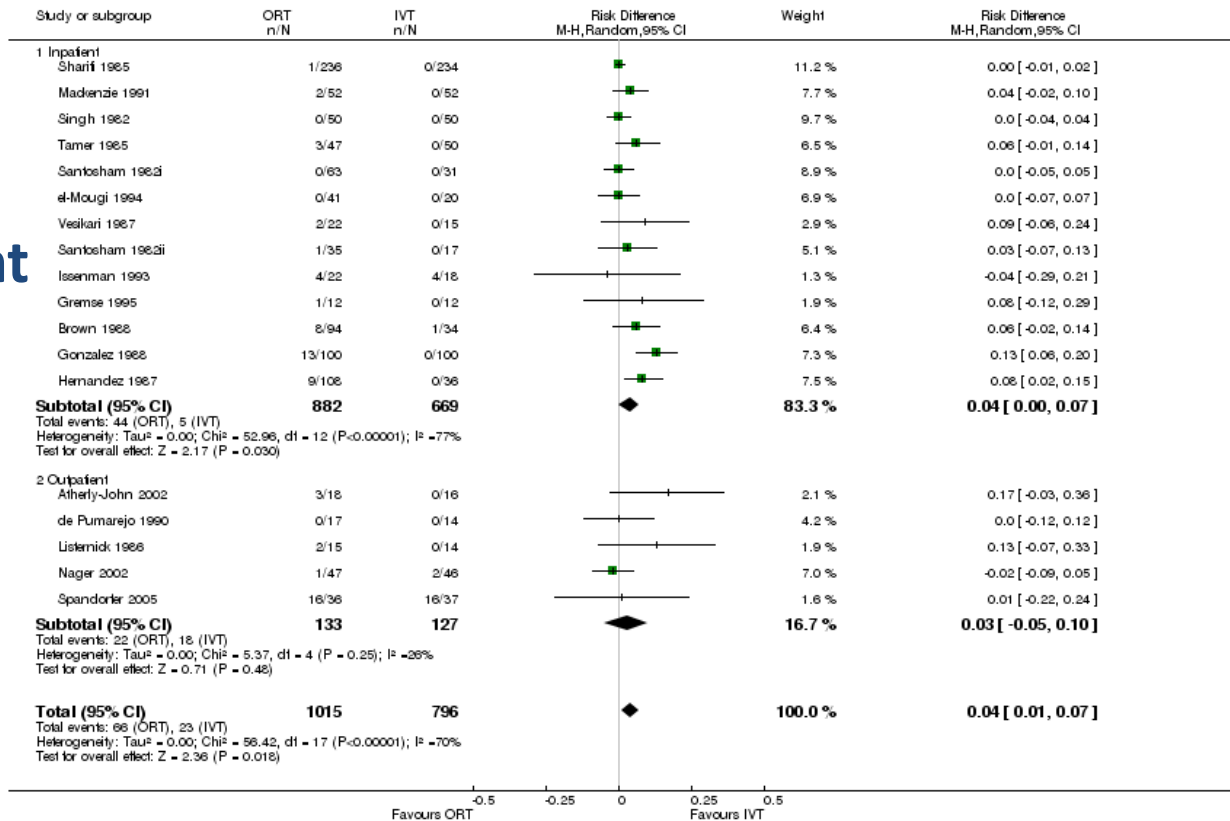
## Duration of Diarrhea

Review: Oral versus intravenous rehydration for treating dehydration due to gastroenteritis in children  
 Comparison: 1 Oral rehydration therapy (any solution) versus intravenous therapy  
 Outcome: 7 Duration of diarrhea (h) (by inpatient/outpatient)



# Oral versus intravenous rehydration for treating dehydration due to gastroenteritis in children

Review: Oral versus intravenous rehydration for treating dehydration due to gastroenteritis in children  
 Comparison: 1 Oral rehydration therapy (any solution) versus intravenous therapy  
 Outcome: 1 Failure to rehydrate (by inpatient/outpatient)



Treatment Failure

Need to treat 25 children with ORT to get one treatment failure

# The Fluid Used Matters

<i>Solution</i>	<i>CHO (g/dL)</i>	<i>Na (mEq/L)</i>	<i>K (mEq/L)</i>	<i>mOsm</i>
<i>Pedialyte</i>	2.5	45	20	250
<i>Rehydralyte</i>	2.5	75 (1/2 NS)	20	310
<i>WHO</i>	2	90	20	310
<i>Gatorade</i>	5.9	21	2.5	377
<i>Apple juice</i>	12	0.4	26	700
<i>Gingerale</i>	9	3.5	.1	565
<i>Coke</i>	11	4	.1	656

# Oral Rehydration

**TABLE 2: Summary of treatment based on degree of dehydration**

Degree of dehydration	Rehydration therapy	Replacement of losses	Nutrition
Minimal or no dehydration	Not applicable	<10 kg body weight: 60–120 mL oral rehydration solution (ORS) for each diarrheal stool or vomiting episode >10 kg body weight: 120–240 mL ORS for each diarrheal stool or vomiting episode	Continue breastfeeding, or resume age-appropriate normal diet after initial hydration, including adequate caloric intake for maintenance*
Mild to moderate dehydration	ORS, 50–100 mL/kg body weight over 3–4 hours	Same	Same
Severe dehydration	Lactated Ringer's solution or normal saline in 20 mL/kg body weight intravenous amounts until perfusion and mental status improve; then administer 100 mL/kg body weight ORS over 4 hours or 5% dextrose ½ normal saline intravenously at twice maintenance fluid rates	Same; if unable to drink, administer through nasogastric tube or administer 5% dextrose ¼ normal saline with 20 mEq/L potassium chloride intravenously	Same

\* Overly restricted diets should be avoided during acute diarrheal episodes. Breastfed infants should continue to nurse ad libitum even during acute rehydration. Infants too weak to eat can be given breast milk or formula through a nasogastric tube. Lactose-containing formulas are usually well-tolerated. If lactose malabsorption appears clinically substantial, lactose-free formulas can be used. Complex carbohydrates, fresh fruits, lean meats, yogurt, and vegetables are all recommended. Carbonated drinks or commercial juices with a high concentration of simple carbohydrates should be avoided.

King CK, Glass R, Bresee JS, Duggan C. Managing acute gastroenteritis among young children. *MMWR*. November 21, 2003/52 (RR16):1-16.

# What about pre-op patients?

- Practice guidelines from ASA:
  - Clears (including ORS) until 2 hours prior to anesthesia or sedation.
- Equivalent/higher gastric volumes in strict NPO patients
- More anxiety requiring more sedation in strict NPO patients
- Better post-op recovery in patients given ORS pre-op

Anesthesiology. 2017 Mar;126(3):376-393.

Journal of Anesthesia. 26(1):20-7, 2012 Feb.

Anesth Prog. 2004;51(2):46-51.

Cochrane Database Syst Rev. 2014;(8):CD009161.

# Final Thoughts

- Think about the fluids you are ordering:
  - No one fluid works for everyone.
- Isotonic maintenance fluids are safer for many hospitalized children, especially perioperative patients.
- Monitor serum [Na] in patients on IVF.
- *Never* resuscitate with hypotonic fluids.
- Oral rehydration works!
- Oral rehydration can be given safely until 2 hours prior to anesthesia or sedation.

# Questions

