

Prime Giornate Pediatriche  
dell'Ospedale del Bambino "P. Barila" di Parma

Tra Diabetologia e Pediatria  
preventiva e sociale



# La Disidratazione Acuta

***Giuliano Lombardi***

Direttore U.O.C. di Pediatria Medica e  
Unità di Gastroenterologia ed Endoscopia Digestiva Pediatrica  
Ospedale Regionale "Spirito Santo"  
Pescara



[giuliano.lombardi@ausl.pe.it](mailto:giuliano.lombardi@ausl.pe.it)



# Background [1]

## OMEOSTASI

Mantenimento del volume e della composizione dei liquidi corporei, garantita sia attraverso la regolazione dell'introduzione di liquidi (controllo della sete) sia attraverso la regolazione dell'eliminazione di liquidi e soluti.

# Background [2]

- ❑ L'acqua rappresenta il più importante componente dell'organismo umano;
- ❑ Nei primi mesi di vita rappresenta il 78% del peso corporeo, si riduce rapidamente fino ad avvicinarsi al valore proprio dell'età adulta, pari al 60% del peso corporeo dopo il primo anno;
- ❑ È contenuta quasi completamente nella massa magra.

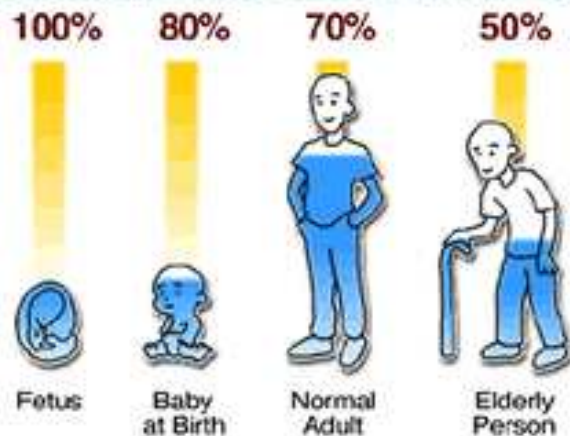


# Age-related fluids distribution

Tabella 1 - Contenuto e distribuzione dei fluidi corporei (FC) secondo l'età

	Prematuro	Neonato	1° anno	3 anni	9 anni	Adulto
Peso (kg)	1,5	3	10	15	30	70
Area superficie corporea (m <sup>2</sup> )	0,15	0,2	0,5	0,6	1	1,7
Peso Liquidi Corpo in %	80	78	65	60	60	60
<u>FEX Extracellulari (%)</u>	50	45	25	20	20	20
FICC Intracellulari (%)	30	33	40	40	40	40

## Percent of Water in the Human Body



# Daily water requirements

Tabella 2 - Fabbisogno idrico giornaliero

Bambini <10 Kg	100 ml/Kg/24 ore
Bambini 11-20 Kg	1.000 ml + 50 ml/Kg/ die per ogni Kg sopra a 10 Kg
Bambini >20 Kg	1.500 ml + 20 ml/Kg/ die per ogni Kg sopra a 20 Kg
Adulti	2.000-2.400 ml/die

## ... and losses

Tabella 3 - Perdita idrica giornaliera in rapporto all'età (ml/kg/die)

Componente	0-6 mesi	6 m/5 anni	5-10 anni	Adolescente
Insensibile	40	30	20	10
Urinario	60	60	50	40
Fecale	20	10	-	-
<b>Totale</b>	<b>120</b>	<b>100</b>	<b>70</b>	<b>50</b>

# Causes of dehydration

Tabella 4 - Cause di disidratazione

## **Ridotta assunzione di liquidi:**

- adipsia, alterazioni dello stato di coscienza, lesioni delle prime vie digestive, mancanza di liquidi disponibili.

## **Aumento delle perdite gastrointestinali:**

- diarrea, vomito.

## **Aumento delle perdite urinarie:**

- diabete insipido e mellito, farmaci (es. diuretici), insufficienza surrenalica, malattie renali con sindrome da perdita di sali, ecc.

## **Aumento delle perdite cutanee:**

- infiammazioni cutanee, ipertermia, sudorazione eccessiva, ustioni.

## **Aumento delle perdite dall'apparato respiratorio:**

- iperventilazione; ridotta umidità dei gas inspirati.

## **Perdite interne per sequestro:**

- “terzo spazio” addominale o toracico (ascite, ARDS, chilotorace, ecc.)
- ipoprotidemie (sindrome nefrosica, ustioni).

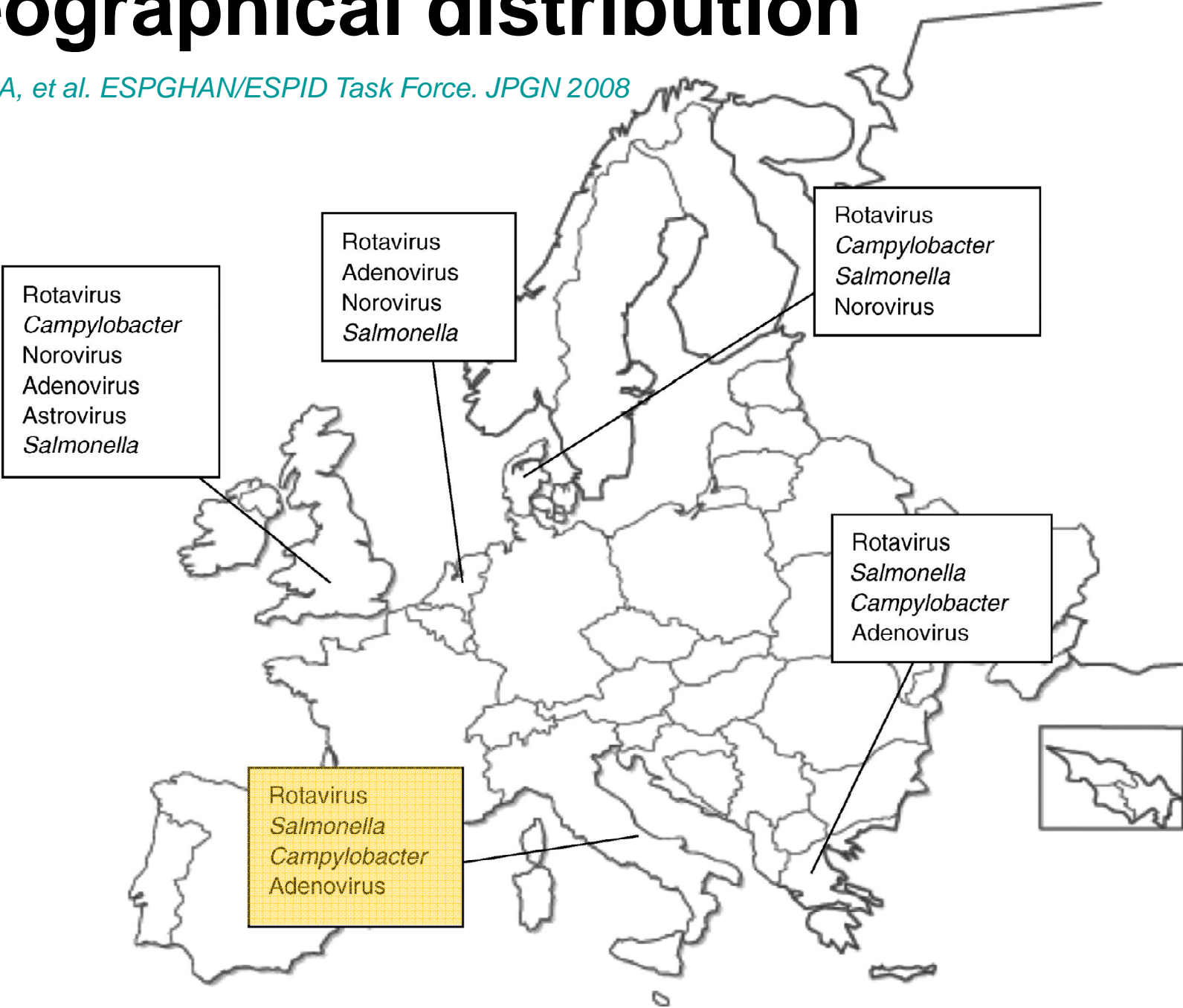
# Infectious causes

Pathogen	Frequency, %
Rotavirus	10–35
Norovirus	2–20
<i>Campylobacter</i>	4–13
Adenovirus	2–10
<i>Salmonella</i>	5–8
EPEC	1–4.5
<i>Yersinia</i>	0.4–3
<i>Giardia</i>	0.9–3
<i>Cryptosporidium</i>	0–3
EAggEC	0–2
<i>Shigella</i>	0.3–1.4
STEC	0–3
ETEC	0–0.5
<i>Entamoeba</i>	0–4
No agent detected	45–60

EPEC = enteropathogenic *Escherichia coli*; EAggEC = enteroaggregative *E coli*; STEC = Shiga toxin-producing *E coli*; ETEC = enterotoxigenic strains of *E coli*.

# Geographical distribution

Guarino A, et al. ESPGHAN/ESPID Task Force. JPGN 2008



# Who is at risk of dehydration ?



- ✓ **Bambini < 1 anno (in particolare < 6 mesi)**
- ✓ **Lattanti nati LBW**
- ✓ **Più di 5 evacuazioni nelle precedenti 24 ore**
- ✓ **Più di 2 episodi di vomito precedenti nelle 24 ore**
- ✓ **Rifiuto reidratazione orale**
- ✓ **Interruzione dell' allattamento al seno in corso di sintomi**
- ✓ **Bambini con segni di malnutrizione**

# Symptoms and degree of dehydration



Tabella 5 – Sintomatologia e grado di disidratazione

Sintomatologia	Disidratazione Lieve	Disidratazione Moderata	Disidratazione Grave
perdita peso	<5 % (3%*)	<10 % (6%*)	>10-15 % (9%*)
aspetto generale	attento, agitato	agitato o letargico, irritabile	ipotonico, freddo, cianosi, sonnolento fino al coma
sete	modesta	moderata	intensa
colore cute	pallida	grigia	marezzata
turgore cute	normale	diminuito	nullo
mucose	asciutte	secche	secche, aride
occhi	normali	infossati	infossati e alonati
lacrimazione	presente	assente	assente
SNC	normale	irritabile	letargico
fontanella bregmatica	normale	depressa	molto depressa
respiro	normale	profondo	rapido e profondo
polso	normale	rapido	tachicardia, piccolo, debole
t. circolo	< 2 sec.	2-3 sec.	> 3- 4 sec
p. arteriosa	normale	bassa in ortostatismo	diminuita
vena giugulare est.	visibile supino	non visibile a meno di compressione	non visibile nemmeno dopo compressione
urina	lieve calo	scura e oliguria	anuria o <0,5 ml/Kg/die
perdita stimata ml/kg	30-50	60-90	100 o più

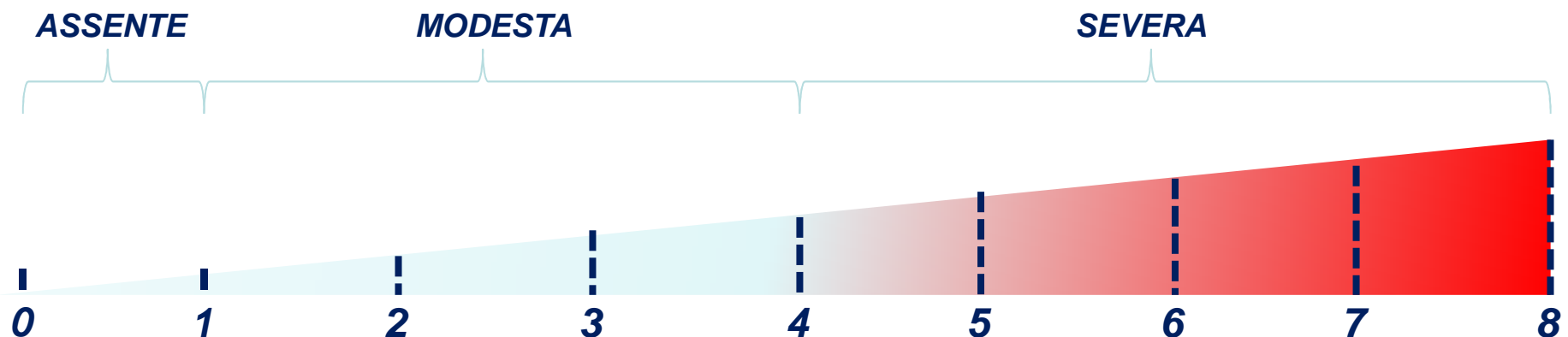
\* Perdita in peso nel bambino dopo il primo anno di vita

# Clinical Dehydration Scale for Children

*Bailey B. Arch Pediatr 2010*



Characteristics	0	1	2
<b>General appearance</b>	Normal	Thirsty, restless, or lethargic but irritable when touched*	Drowsy, limp, cold, or sweaty; comatose† or not
<b>Eyes</b>	Normal	Slightly sunken	Very sunken
<b>Mucous membranes (tongue)</b>	Moist	Sticky	Dry
<b>Tears</b>	Tears	Decreased	Absent



# Clinical Criteria for Dehydration <sup>1</sup>

Bailey B. Arch Pediatr 2010

Presence of clinical sign	LR+ to rule-in $\geq 5\%$ dehydration (95% CI) <sup>c</sup>
Prolonged capillary refill	4.1 (1.7 to 9.8)
Abnormal skin turgor	2.5 (1.5 to 4.2)
Absent tears	2.3 (0.9 to 5.8)
Abnormal respiratory pattern	2.0 (1.5 to 2.7)
Poor overall appearance	1.9 (0.97 to 3.8)

*(Steiner 2004 [1b])*



At least 2 of the 4 following signs:

- capillary refill time
- dry mucous membranes
- absence of tears
- abnormal overall appearance

6.1 (3.8 to 9.8)  
*(Gorelick 1997 [3a])*

# Clinical Criteria for Dehydration <sup>2</sup>

Absence of clinical sign	LR- to rule-out $\geq 5\%$ dehydration (95% CI) <sup>c</sup>	
Abnormally low urine output	0.27	(0.14 to 0.51)
Dry mucous membranes	0.41	(0.21 to 0.79)
Poor overall appearance	0.46	(0.34 to 0.61)
Sunken eyes	0.49	(0.38 to 0.63)
Absent tears	0.54	(0.26 to 1.13)
Prolonged capillary refill	0.57	(0.39 to 0.82)

*(Steiner 2004 [1b])*

# Which dehydration ?

Tabella 10 – Sintomatologia e tipi di disidratazione

Sintomatologia	Isotonica	Ipotonica	Ipertonica
	Na > 130 e < 150	Na < 130 mEq/L	Na > 150 mEq/L
Cute	grigia, secca	grigia, umida	grigia, pastosa
turgore	scarso	molto scarso	normale
temperatura	fredda	fredda	fredda
mucose	secche	leggermente umide	molto secche
occhi	infossati, molli	infossati, molli	infossati
fontanella	depressa	depressa	depressa
polso	rapido	rapido	leggermente rapido
coscienza	letargico	coma	irritabilità
Pressione art.	↓↓	↓↓↓	↓
Volume extracellulare	↓↓	↓↓↓	↓
Volume intracellulare	↓ o N	N o ↑	↓↓

**Osmolarità sierica:** 280 – 295 mOsm/KgH<sub>2</sub>O

# Electrolytes

Tabella 7 - Fabbisogno ionico giornaliero (mEq/kg/die): lattanti e bambini

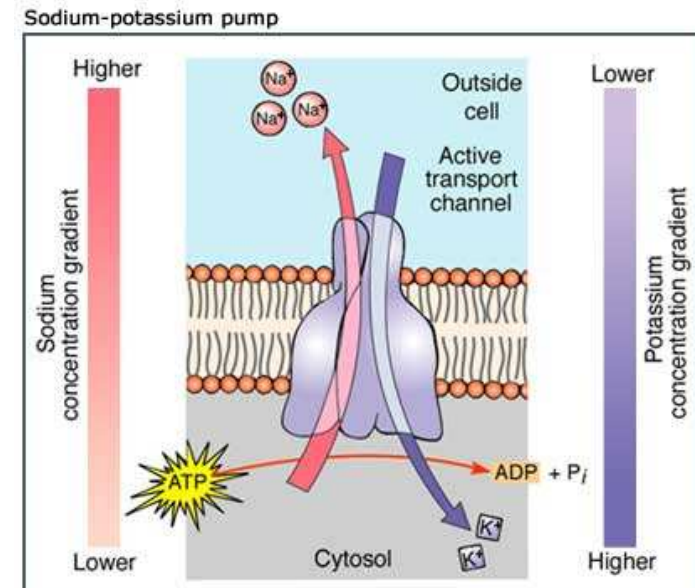
Ioni sierici	Peso del paziente in kg		
	<5 Kg	5-20 Kg	> 20 Kg
Na	3	3	3
K	2	2	1,5-2
Ca	1,5	1	0,8
Mg	0,25	0,25	0,25
P	0,5	0,5	0,5

**Tabella 8 - Valori normali dello ionogramma in rapporto all'età**

		mEq/l	mmol/l
Na	neonati	135-155	135-155
	Lattanti	133-142	133-142
	Bambini	133-142	133-142
	Altre età	135-145	135-145
Ca	neonati	4,5-5,5	2,25-2,75
	Lattanti	4-5,6	2-2,8
	Bambini	3,9-5,7	1,95-2,85
	Altre età	4,4-5,5	2,20-2,75
K	neonati	4-5	4-5
	Lattanti	4,8-5,5	4,8-5,5
	Bambini	3,9-4,9	3,9-4,9
	Altre età	3,8-4,8	3,8-4,8
Cl	neonati	103-120	103-120
	Lattanti	100	100
	Bambini	98-108	98-108
	Altre età	101-105	101-105
P	neonati	2,61-4,30	1,45-2,3
	2 giorni-2 mesi	3,95-4,10	2,1-2,27
	2-5mesi	3,38-4,30	1,8-2,38
	1 anno	3,15-3,50	1,75-1,9
	2-12anni	1,75-2,23	0,9-1,29
Bicarbonati	Neonati	17-25	17-25
	Lattanti	20-25	20-25
	Bambini	19-28	19-28

# Ionogram

Principali cationi corporei (meq/L)			Principali anioni corporei (meq/L)		
	extra	intra		extra	intra
Na <sup>+</sup>	141	10	Cl <sup>-</sup>	103	4
K <sup>+</sup>	4	140	HCO <sub>3</sub> <sup>-</sup>	24	10
Ca <sup>2+</sup>	5	10 <sup>-4</sup>	Proteine <sup>-</sup>	16	36
Mg <sup>2+</sup>	2	3	HPO <sub>4</sub> <sup>2-</sup> / SO <sub>4</sub> <sup>2-</sup>	10	130
H <sup>+</sup>	4x10 <sup>-5</sup>	4x10 <sup>-5</sup>			
<b>Tot</b>	<b>153</b>	<b>180</b>	<b>Tot</b>	<b>153</b>	<b>180</b>



Gap anionico: v.n. = 8/16 mEq/l\*

\* Il Gap anionico è uguale alla differenza fra i mEq/l del catione sodio e la somma dei mEq/l dei due anioni bicarbonato e cloro

Gap = Na<sup>+</sup> - (HCO<sub>3</sub><sup>-</sup> + Cl<sup>-</sup>). Il valore normale è 12 (range 8-16)

# QUANDO RICOVERARE ?

2008



ESPGHAN

ESPID

2011

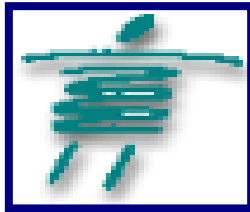


- Shock
- Severe dehydration (>9% of body weight)
- Neurological abnormalities (lethargy, seizures etc.)
- Intractable or bilious vomiting
- ORS treatment failure
- Suspected surgical condition
- Caregivers cannot provide adequate care at home and or there are social or logistical concerns

- The child is severely dehydrated
- The child has intractable vomiting
- The child is unable to maintain hydration orally due to vomiting or diarrhea losses
- Caregivers cannot provide adequate care at home and/or there are social or logistical concerns

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2008



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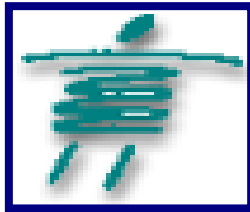


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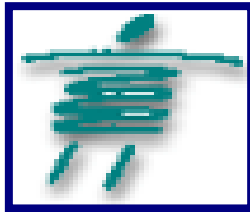


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# Accertamenti diagnostici

- emocromo con formula + indici di flogosi;  
(grado di ispissatio sanguinis e rischio infezione)
- elettroliti sierici e glicemia;
- equilibrio acido-basico;
- azotemia e creatininemia;
- esame chimico-fisico delle urine;  
(peso specifico e quantità urine emesse)
- monitoraggio peso corporeo, diuresi ed eventuali perdite con vomito e diarrea.

# DISIDRATAZIONE

LIEVE

ORS

Age of Child	Try to drink at least:	How?	How much? How long?
4 years or younger	5 to 10 ml every 5 min, or 30 to 60 ml in 30 min, or 60 to 120 ml in 1 hour	Frequent small sips from a bottle, cup, spoon, or syringe	<ul style="list-style-type: none"><li>• Continue for at least 3 to 4 hours or longer to reach a total ORS intake of at least 240 ml for younger children and at least 480 ml for older children.</li><li>• If stools are still very frequent and watery, continue drinking commercial ORS.</li><li>• Otherwise, continue as desired with usual diet with or without additional commercial ORS.</li></ul>
5 years or older	10 to 20 ml every 5 min, or 60 to 120 ml in 30 min, or 120 to 240 ml in 1 hour	If no vomiting, less frequent larger sips are fine	

# WHO and ESPGHAN Recommendation

	OMS 1984	ESPGAN 1989/97
<i>Reidratazione orale</i>		
Glucosio mmol/l	110	74-111
Na mEq/l	90	60
K mEq/l	20	20
Cl mEq/l	80	>25
HCO <sub>3</sub> o Citrato mEq/l	30	20
mOsm/l	330	200-250
Kcal/l	80	52-80
aroma	no	no
probiotici	no	no

**TABLE 3. Composition of commercial oral rehydration solutions (ORS) and commonly consumed beverages**

Solution	Carbohydrate (gm/L)	Sodium (mmol/L)	Potassium (mmol/L)	Chloride (mmol/L)	Base* (mmol/L)	Osmolarity (mOsm/L)
<b>ORS</b>						
World Health Organization (WHO) (2002)	13.5	75	20	65	30	245
WHO (1975)	20	90	20	80	30	311
European Society of Paediatric Gastroenterology, Hepatology and Nutrition	16	60	20	60	30	240
Enfalyte <sup>†</sup>	30	50	25	45	34	200
Pedialyte <sup>§</sup>	25	45	20	35	30	250
Rehydralyte <sup>¶</sup>	25	75	20	65	30	305
CeraLyte <sup>**</sup>	40	50–90	20	NA <sup>††</sup>	30	220
<b>Commonly used beverages (not appropriate for diarrhea treatment)</b>						
Apple juice <sup>§§</sup>	120	0.4	44	45	N/A	730
Coca-Cola <sup>¶¶</sup> Classic	112	1.6	N/A	N/A	13.4	650

\* Actual or potential bicarbonate (e.g., lactate, citrate, or acetate).

† Mead-Johnson Laboratories, Princeton, New Jersey. Additional information is available at <http://www.meadjohnson.com/products/cons-infant/enfalyte.html>.

§ Ross Laboratories (Abbott Laboratories), Columbus, Ohio. Data regarding Flavored and Freezer Pop Pedialyte are identical. Additional information is available at <http://www.pedialyte.com>.

¶ Ross Laboratories (Abbott Laboratories), Columbus, Ohio. Additional information is available at [http://rpdcon40.ross.com/pn/PediatricProducts.NSF/web\\_Ross.com\\_XML\\_PediatricNutrition/96A5745B1183947385256A80007546E5?OpenDocument](http://rpdcon40.ross.com/pn/PediatricProducts.NSF/web_Ross.com_XML_PediatricNutrition/96A5745B1183947385256A80007546E5?OpenDocument).

\*\* Cera Products, L.L.C., Jessup, Maryland. Additional information is available at <http://www.ceralyte.com/index.htm>.

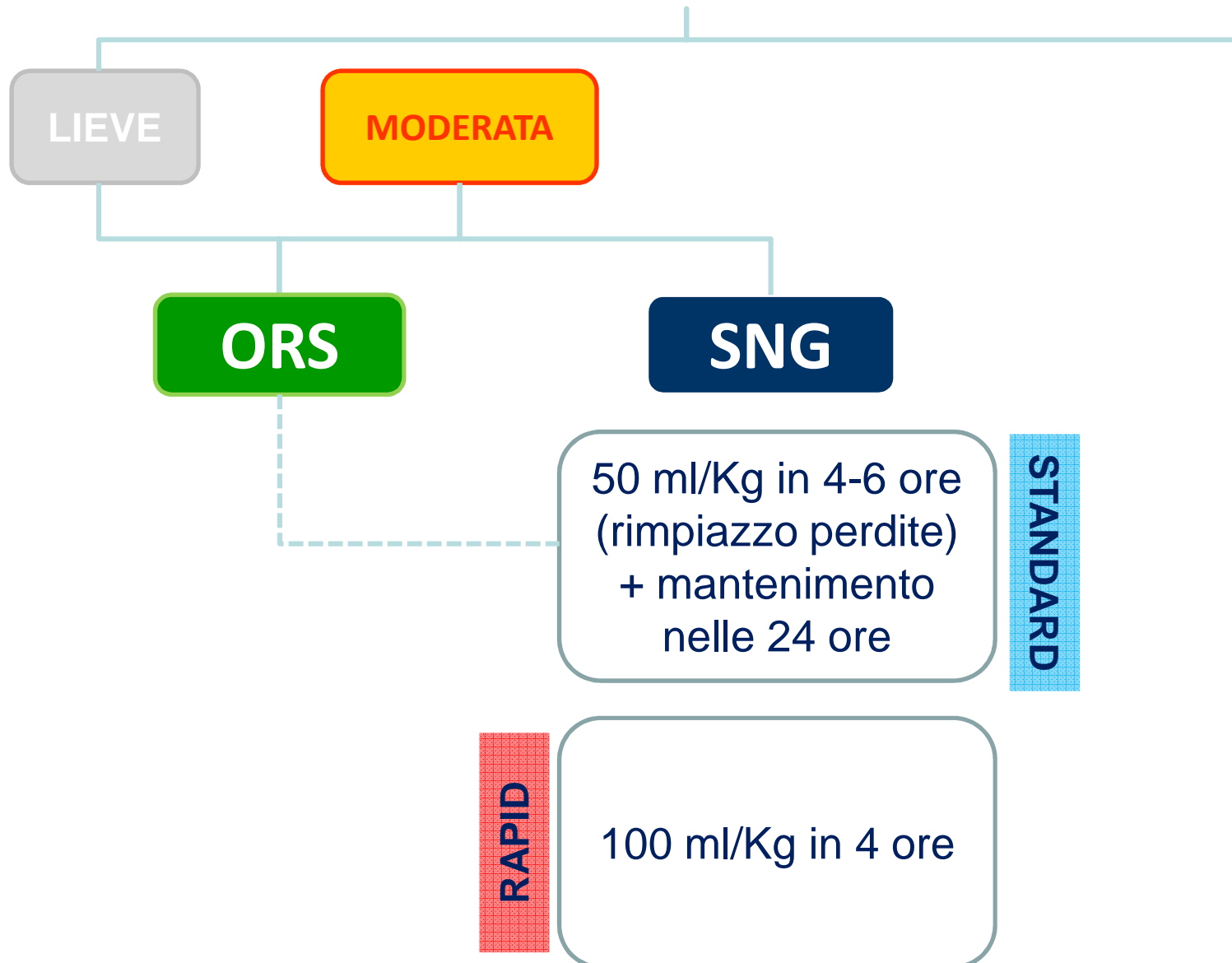
†† Not applicable.

§§ Meeting U.S. Department of Agriculture minimum requirements.

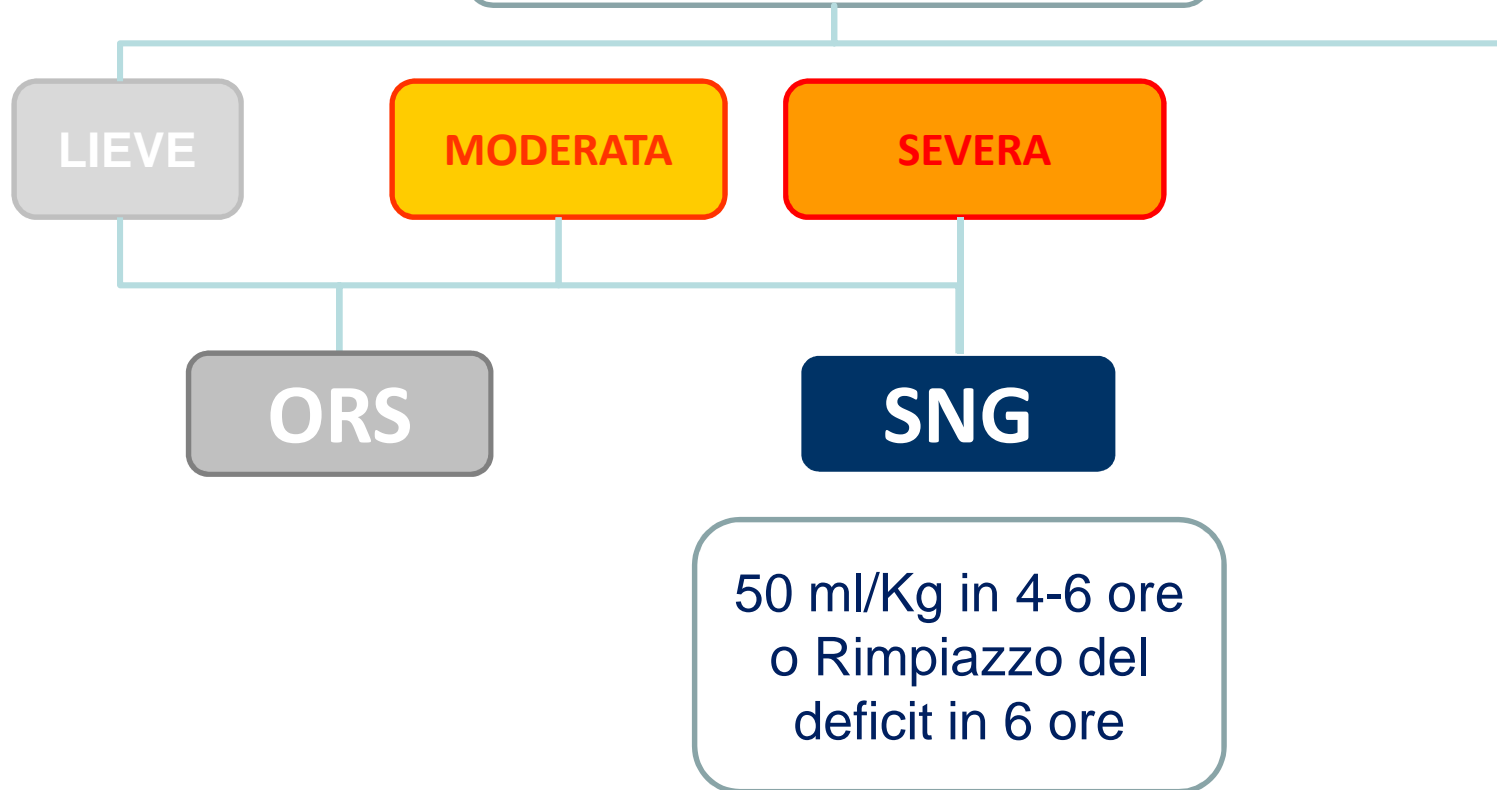
¶¶ Coca-Cola Corporation, Atlanta, Georgia. Figures do not include electrolytes that might be present in local water used for bottling. Base = phosphate.

	90 <sup>®</sup>	DICODRAL 60* <sup>®</sup>	30 <sup>®</sup>	FLORIDRAL	GES 60 <sup>®</sup>	IDRAVITA <sup>®</sup>	REIDRAX <sup>®</sup>
<i>Reidratazione orale</i>							
Glucosio mmol/l	111	90	111	83	108	120	75
Na mEq/l	90	60	30	60	60	60	60
K mEq/l	20	20	20	20	20	20	20
Cl mEq/l	80	37	40	37	50	50	60
HCO <sub>3</sub> o Citrato mEq/l	30	— 14 citr.	10	14 citrato	14 citrato	10 citrato	10 citrato
mOsm/l	331	211	211	214	270	230	225
Kcal/l	80	80	80	80	80	80	60.8
aroma	no	banana	no	banana	no	banana	no
probiotici	No	no	no	LGG 5x10 <sup>9</sup> u.f.c.	no	no	no

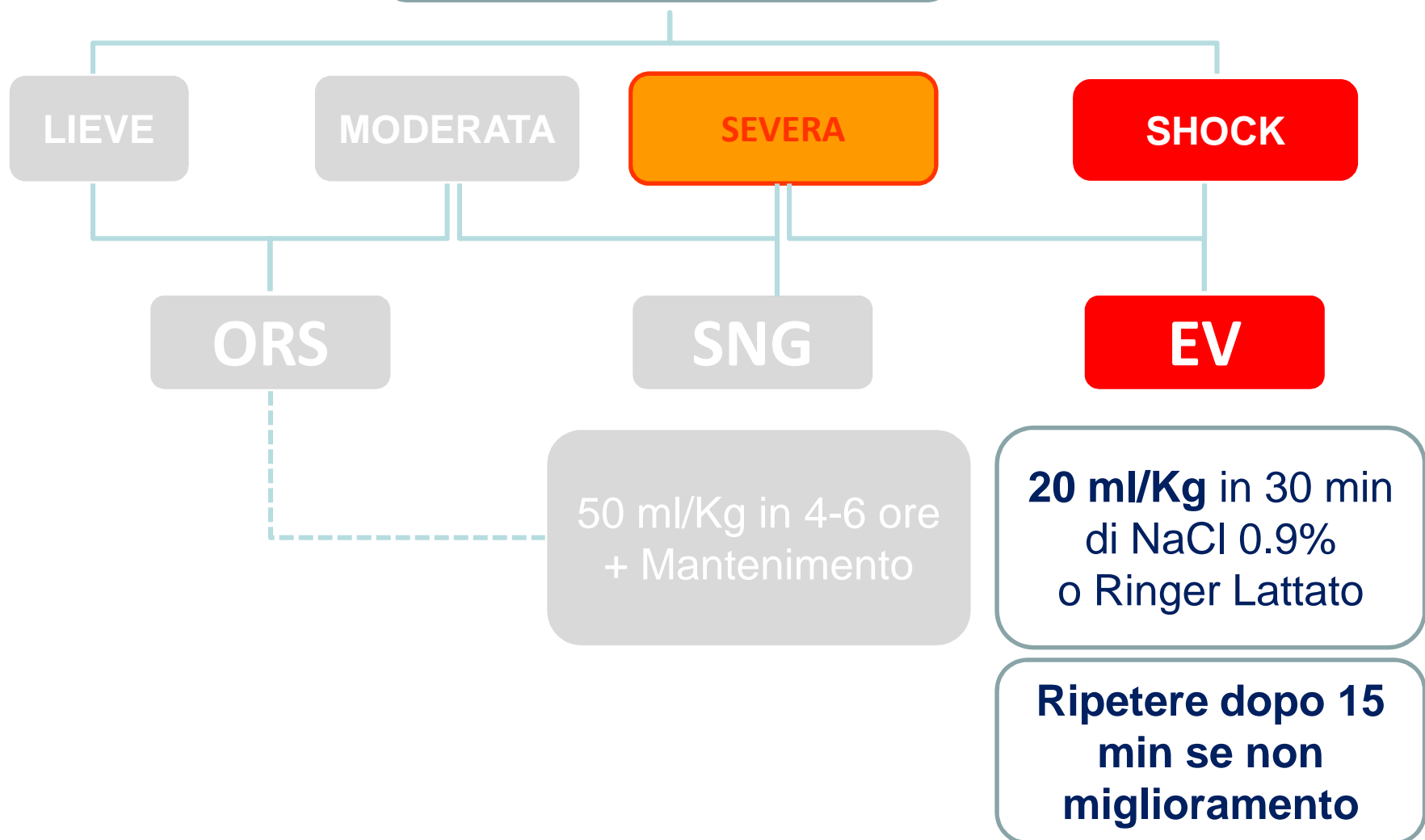
# DISIDRATAZIONE



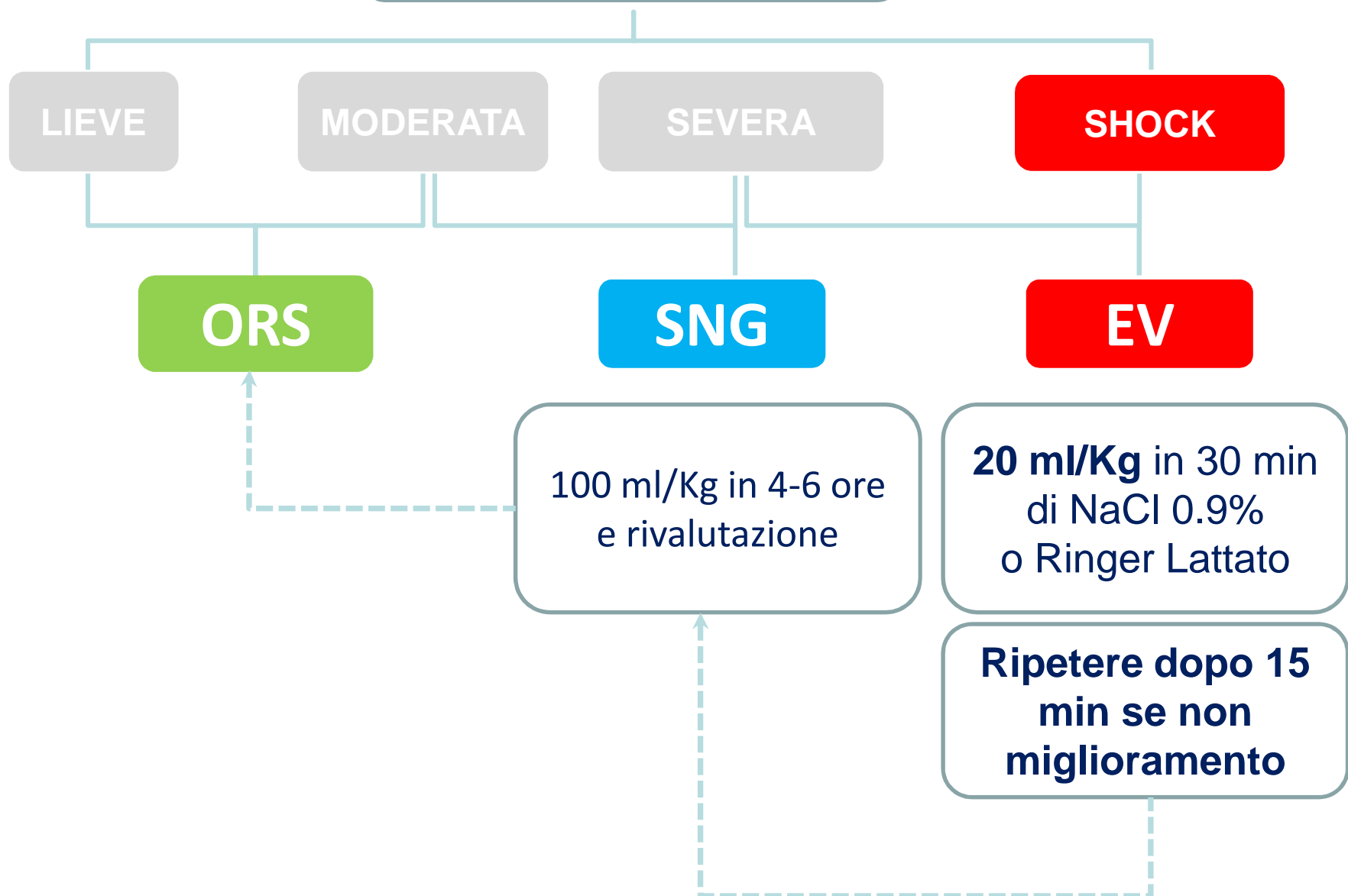
# ***DISIDRATAZIONE***

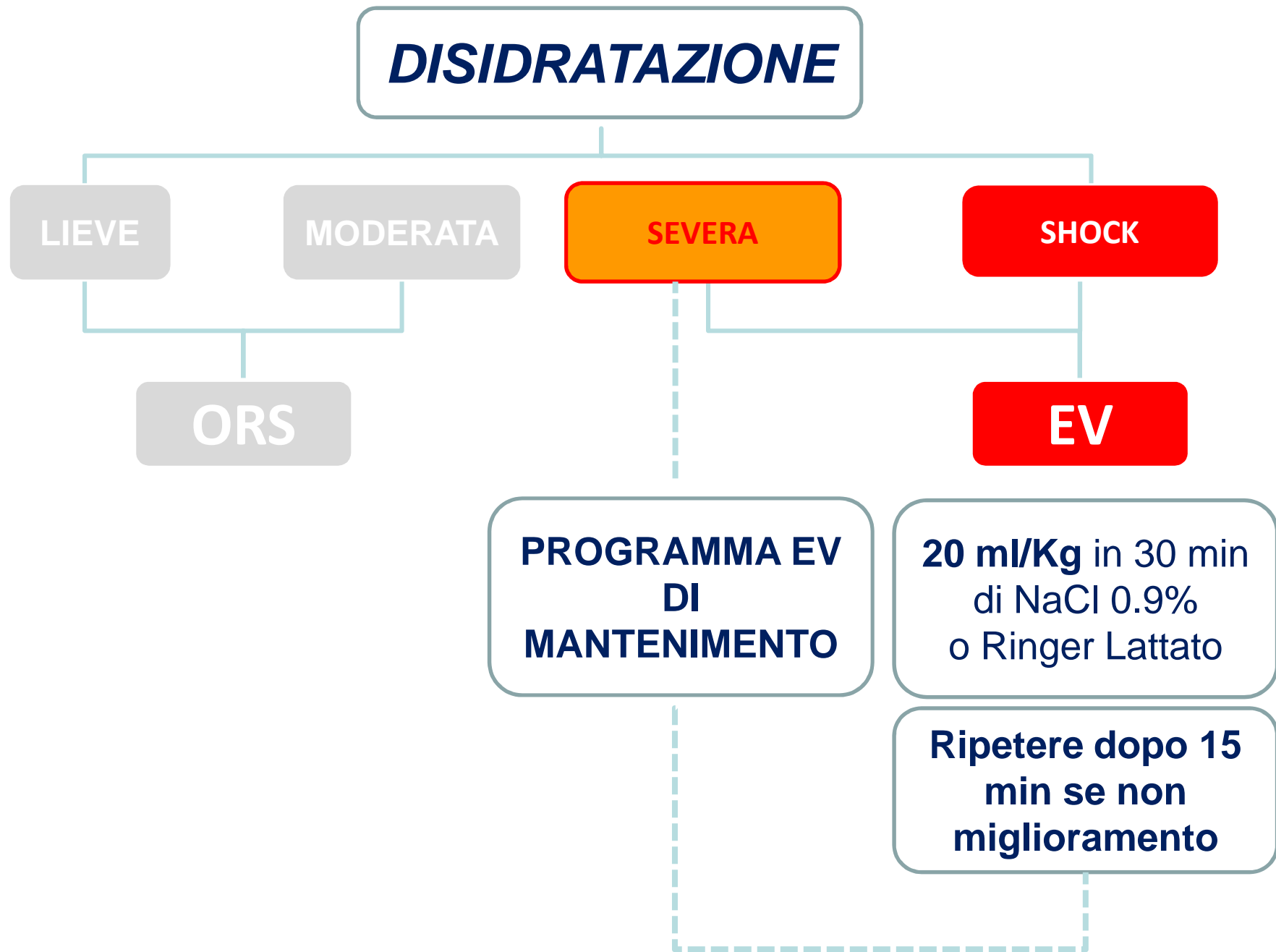


# DISIDRATAZIONE



# DISIDRATAZIONE





# REIDRATAZIONE EV

**MANTENIMENTO**

**RIMPIAZZO  
PERDITE  
PREGRESSE**

**RIMPIAZZO  
PERDITE  
SUBENTRANTI**

<b>WEIGHT (Kg)</b>	<b>VOLUME PER DAY</b>
0 -10 Kg	100 ml /Kg
10 – 20 Kg	1000 ml + 50 ml/Kg for each Kg >10
> 20 Kg	1500 ml + 20 ml/Kg for each Kg >20

# REIDRATAZIONE EV



**RIMPIAZZO  
PERDITE  
PREGRESSE**

**50 ml/Kg**

nei pazienti con disidratazione lieve moderata in terapia con ORS

**100 ml/Kg**

nei pazienti con disidratazione severa in terapia EV

# REIDRATAZIONE EV



**RIMPIAZZO  
PERDITE  
SUBSTRANTI**

**10 ml/Kg**

per ogni evacuazione o vomito

# REIDRATAZIONE EV



Un bambino di **15 Kg** moderatamente disidratato che ha presentato 3 evacuazioni di feci liquide e 2 episodi di vomito



2050 ml/24 ore

**METÀ NELLE  
PRIME 6-8 ORE**

# Disidratazione Ipernatremica

## CARATTERISTICHE CLINICHE

- ❑ Più comune <6 mesi
- ❑ Cute e sottocute di aspetto soffice e pastoso
- ❑ Tachipnea
- ❑ Assenza dei tipici segni di disidratazione (rischio!!!)
- ❑ Segni e sintomi neurologici:
  - ✓ Sonnolenza o irritabilità
  - ✓ Ipertono ed iperreflessia
  - ✓ Convulsioni → Coma

# Disidratazione Ipernatremica

## CORREZIONE DELLE FORME SECONDARIE A GEA

OS

Soluzione ipotonica  
reidratante orale

*Harris 2005 - Australian Guidelines*

EV

Soluzione NaCl 0.9%  
+/- Glucosata 5% (0.45%)

*NICE 2009 - British Guidelines*

- ❖ Reidratare **LENTAMENTE** (OS > 12 ore e EV 48 ore)
- ❖ Monitorare frequentemente il Na<sup>+</sup> (ogni 4 ore)
- ❖ Ridurre la [Na<sup>+</sup>] non più di 0,5 mmol /ora



# Discharge Criteria

It is recommended that for children receiving care in a hospital setting, **prompt discharge (goal of 23 hours or less)** be considered when the following levels of recovery are reached:

- Sufficient rehydration achieved as indicated by weight gain and/or clinical status;
- IV or NG fluids not required;
- Oral intake equals or exceeds losses;
- Adequate family teaching has occurred; and
- Medical follow up is available via telephone or office visit

# Rationale for Early Feeding in Childhood Gastroenteritis

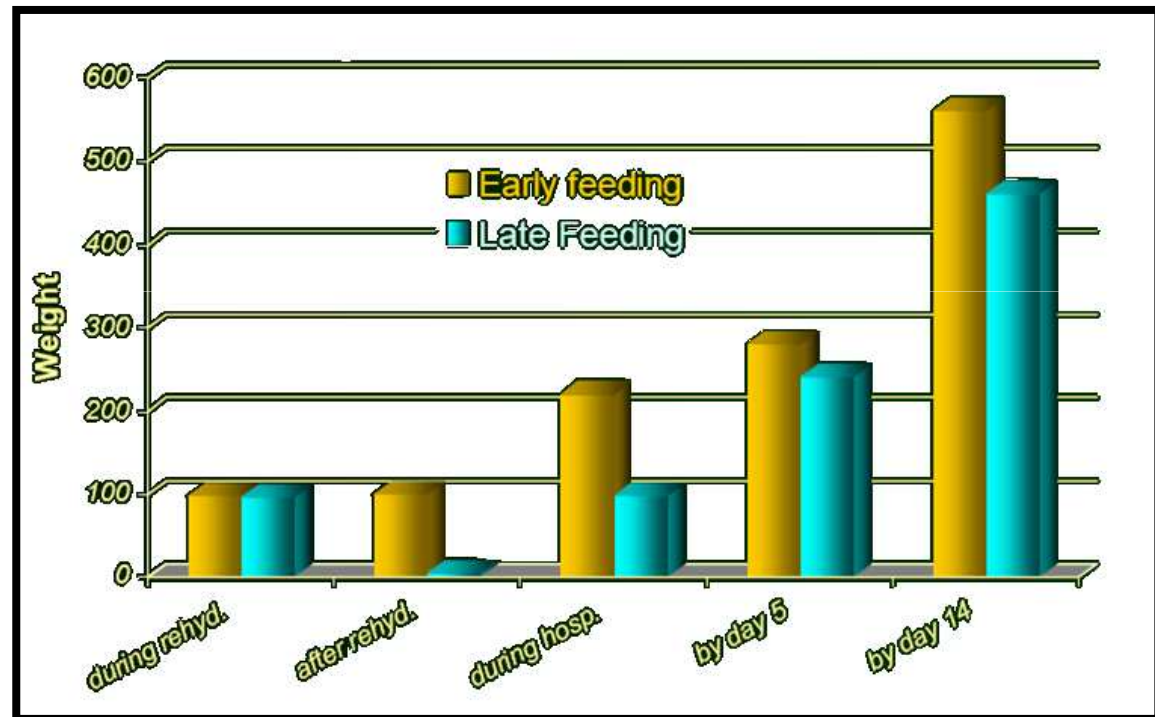
B. K. Sandhu, for the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) Working Group on Acute Diarrhoea

**230 patients**

- **group A** (early-feeding): 134 patients
- **group B** (late-feeding): 96 patients

**Mean age: 13 months**

**Mean duration of diarrhea: 3.2 days**



*Net weight gain during hospitalization was significantly higher in group A compared with group B ( $p = 0.001$ ).*

# Why Early Feeding?

- ✓ Full feeding appropriate for age is well tolerated with no adverse effects, and the practice of withholding food for 24 or more hours is inappropriate.

*Sandhu BK. J Pediatr Gastroenterol Nutr 2001; 33 Suppl12:S36-9*

- ✓ Early feeding decreases changes in intestinal permeability caused by infection, reduces illness duration, and improves nutritional outcomes.

*King CK, Glass R, Bresee JS, Duggan C. MMWR Recomm Rep 2003; 21; 52: 1-16*

- ✓ The old concept of "Bowel Rest" has no scientific validity and it can serve to aggravate and increase the risks of the disease.

*Valois S, Costa-Ribeiro H, Mattos Â, et al. Nutr J 2005; 4: 23*

# DIETARY THERAPY



**INFANTS**



**CHILDREN**

*Breastfed infants*

*Lactose-free formulas*

*Diluted formulas*

# DIETARY THERAPY



## INFANTS

- ❖ **Breastfed infants should continue nursing on demand.**
- ❖ **Formula-fed infants should continue their usual formula immediately upon rehydration in amounts sufficient to satisfy energy and nutrient requirements.**
- ❖ **Lactose-free or lactose-reduced formulas usually are unnecessary.**

# Lactose-free formulas

**A meta-analysis of clinical trials indicates no advantage of lactose-free formulas over lactose-containing formulas for the majority of infants, although certain infants with malnutrition or severe dehydration recover more quickly when given lactose-free formula.**

*Brown KH, Peerson J, Fontaine O. Pediatrics 1994; 93: 17-27*

**If diarrhoea increased on the reintroduction of milk, checking of stool pH and/or reducing substances was recommended. The lactose content was to be reduced only if the stool pH is less than 6 and more than 0.5% reducing substances are present, suggesting lactose intolerance.**

*Szajewska H, et al. J Pediatr Gastroenterol Nutr 2000; 30 Suppl 5: 522-7*

# Diluted formulas

**Controlled clinical trials have demonstrated that this practice is unnecessary and is associated with prolonged symptoms and delayed nutritional recovery.**

*Santosham M, Foster S, Reid R, et al. Pediatrics 1985; 76: 292-8*  
*Brown KH, Gastanaduy AS, Saavedra JM, et al. J Pediatr 1988; 112:191-200*

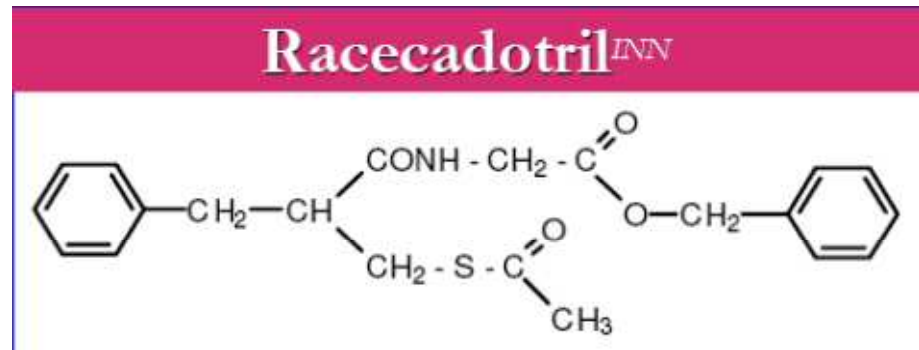
# DIETARY THERAPY

## CHILDREN



- Children receiving semisolid or solid foods should continue to receive their usual diet during episodes of diarrhea.
- Foods *high in simple sugars* (substantial amounts of carbonated soft drinks, juice, gelatin desserts, and highly sugared liquids) should be avoided because the osmotic load might worsen diarrhea.
- Certain guidelines have recommended avoiding fatty foods, but maintaining adequate calories without fat is difficult, and fat might have a beneficial effect of reducing intestinal motility.

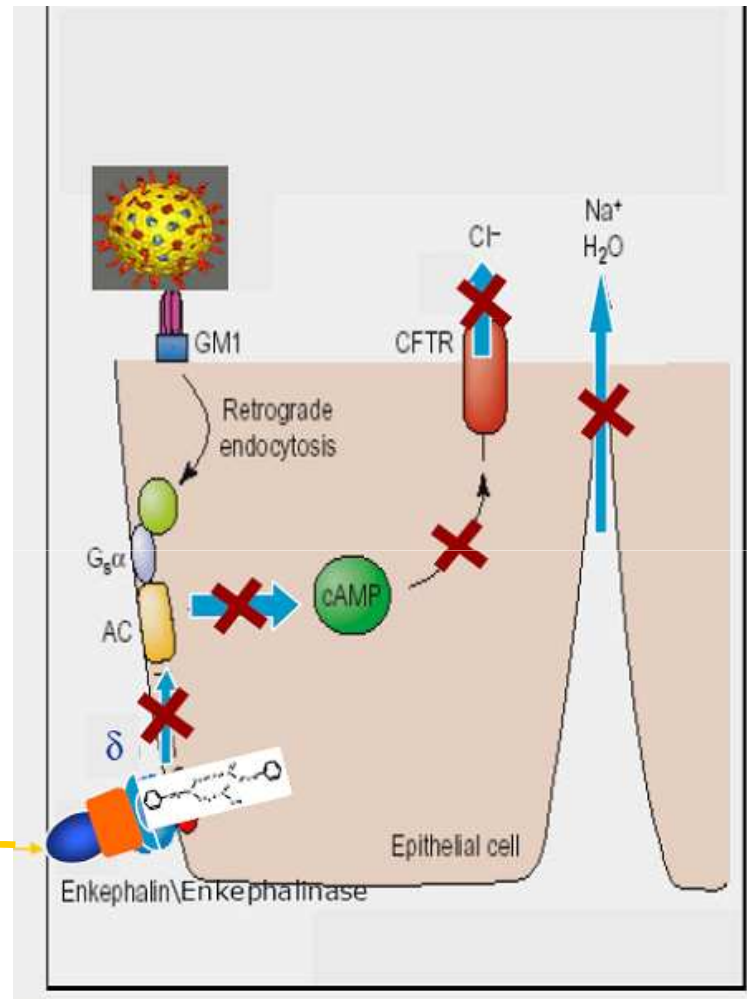
# RACECADOTRIL



**Racecadotril (acetorphan) is an antisecretory drug that exerts its antidiarrhoeal effects by inhibiting intestinal enkephalinase; this prevents the breakdown of endogenous opioids (enkephalins) in the gastrointestinal tract and reduces the secretion of water and electrolytes into the gut without interfering with motility.**

# RACECADOTRIL

The antisecretory mechanism involves activation of  $\delta$  receptors leading to reduced secretion of water and electrolytes through reduction in intracellular cAMP.



submucosal and myenteric neurons



## Systematic review: racecadotril in the treatment of acute diarrhoea in children

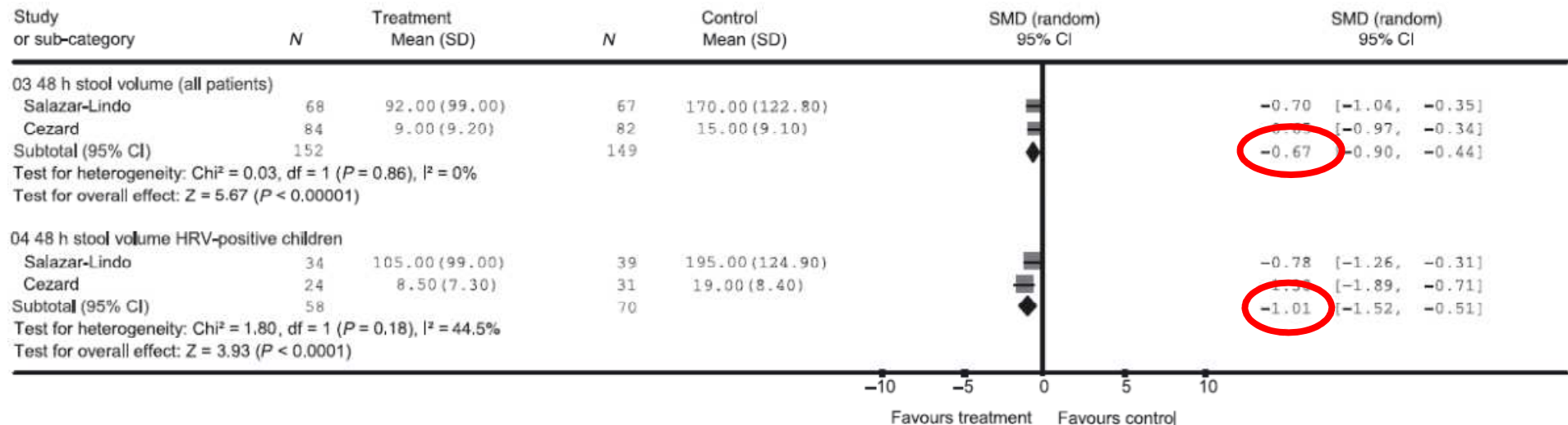
H. SZAJEWSKA, M. RUSZCZYŃSKI, A. CHMIELEWSKA & J. WIECZOREK

**Three RCTs involving 471 participants aged 3 months to 4 years (238 in the experimental group and 233 in the control group) met the inclusion criteria**

- Salazar-Lindo E, Santisteban-Ponce J, Chea-Woo E, et al. *Racecadotril in the treatment of acute watery diarrhea in children*. N Engl J Med 2000; 343: 463–7.
- Cézard JP, Duhamel JF, Meyer M, et al. *Efficacy and tolerability of racecadotril in acute diarrhea in children*. Gastroenterology 2001; 120: 799–805.
- Cojocaru B, Bocquet N, Timsit S, et al. *Effect of racecadotril in the management of acute diarrhea in infants and children*. Arch Pediatr 2002; 9: 774–9.

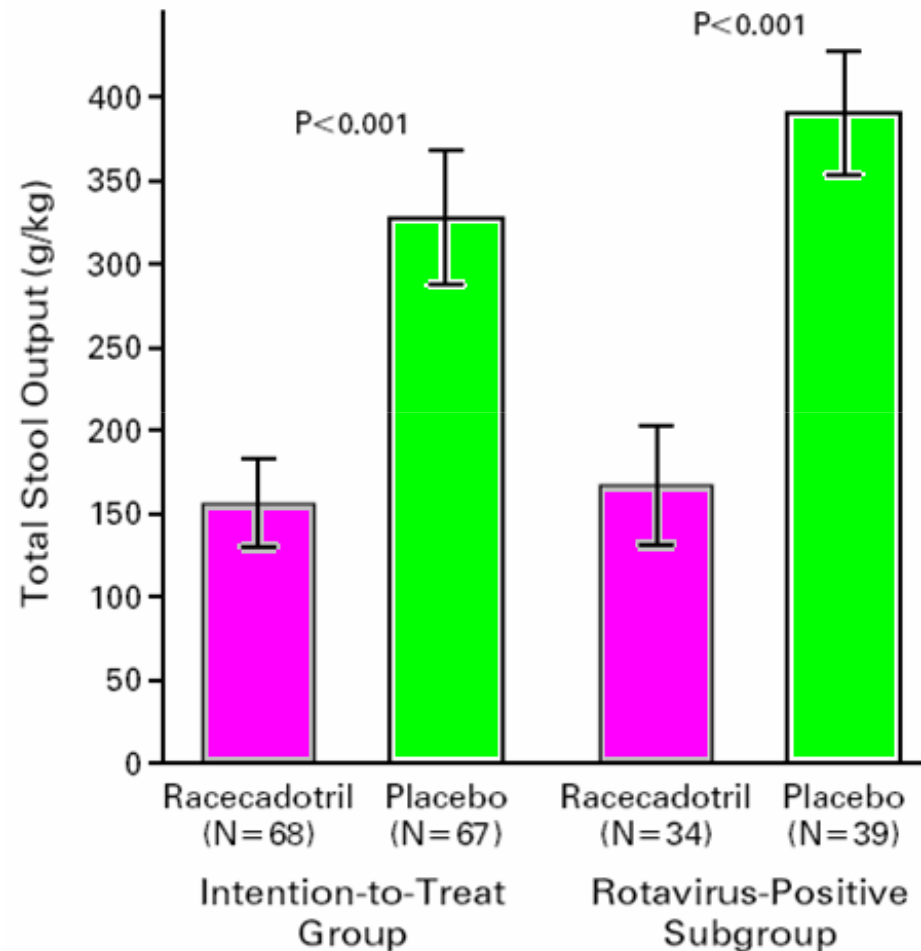
# Effect of racecadotril compared with control on stool volume at 48 h

Review: Racecadotril  
 Comparison: 01 Racecadotril versus control  
 Outcome: 01 Stool volume



# Total stool output

The mean total stool output at 5 days was lower in the racecadotril group than in the placebo group ( $157 \pm 27$  g per kilogram in the racecadotril group and  $331 \pm 39$  g per kilogram in the placebo group, relative risk reduction 53%,  $p < 0.001$ ). The same effect was found in rotavirus-positive boys ( $174 \pm 36$  g per kilogram in the racecadotril group and  $397 \pm 37$  g per kilogram in the placebo group,  $p < 0.001$ ).



# Duration of diarrhoea

The duration of diarrhoea was significantly reduced in the three trials reporting this outcome.

*Salazar-Lindo E, et al.  
N Engl J Med 2000*



The median duration of diarrhoea was significantly reduced in the racecadotril group compared with controls, both in the rotavirus-positive boys (28 h vs. 72 h,  $p < 0.001$ ) and in the rotavirus negative boys 28 h vs. 52 h,  $p < 0.001$ ).

*Cézard JP, et al.  
Gastroenterology 2001*



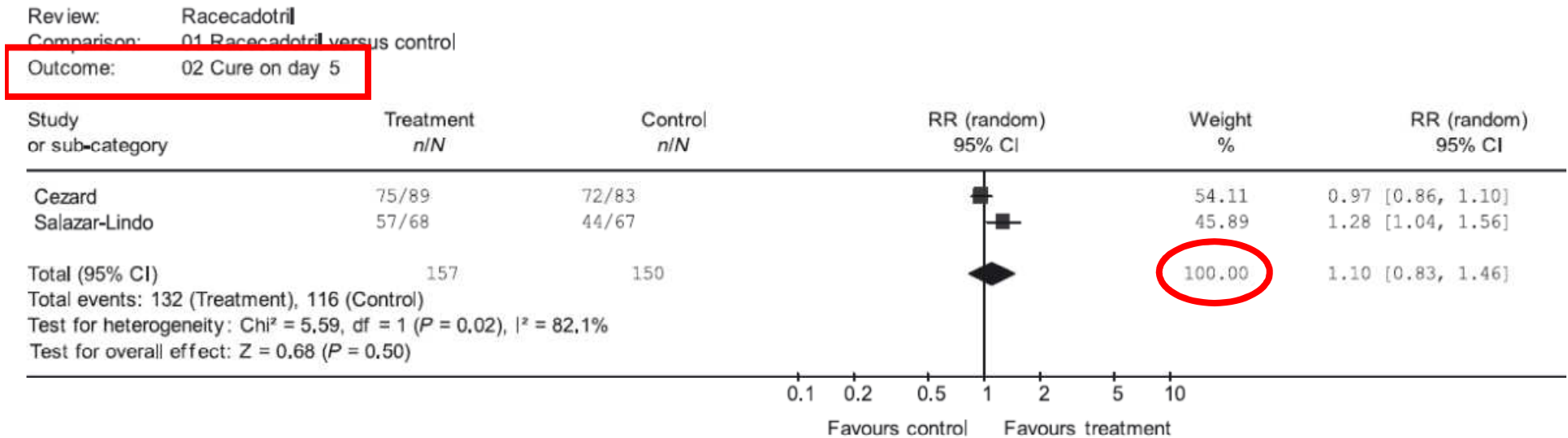
50% of rotavirus-positive patients had recovered after 6.9 and 36 hours in the racecadotril (n=32) and placebo (n=35) groups, respectively ( $p = 0.02$ ).

*Cojocaru B, et al.  
Arch Pediatr 2002*



The duration of diarrhoea was significantly reduced in those treated with racecadotril compared with controls who received no intervention (n = 164,  $97.2 \pm 36$  h vs.  $138 \pm 42$ ).

# Effect of racecadotril compared with placebo on cure on day 5



**The pooled results showed no significant difference between the racecadotril group and the control group.**

# Systematic review: racecadotril in the treatment of acute diarrhoea in children

## ADVERSE EFFECTS

- ❖ Reported adverse effects in the racecadotril group were mild **hypokalemia, ileus, mild fever** and **vomiting**.
- ❖ Some other reported adverse effects of racecadotril (e.g. **nausea, thirst, vertigo, constipation, headache** and hypersensitivity to racecadotril).

# Systematic review: racecadotril in the treatment of acute diarrhoea in children

## LIMITATIONS

- ✓ Only a limited number of trials were available for this review.
- ✓ The methodological quality varied (e.g. inadequate blinding in one of the trials).
- ✓ Two studies received pharmaceutical company sponsorship; the source of funding is not clear in one trial.

# RACECADOTRIL IN THE TREATMENT OF ACUTE DIARRHOEA IN CHILDREN

## CONCLUSIONS AND FUTURE RESEARCH

In conclusion, in three relatively small RCTs with some methodological problems, racecadotril was effective in reducing the volume and frequency of stool output and in reducing the duration of diarrhoea (particularly in children with rotavirus). However, more data are needed. The safety of racecadotril, as well as the cost-effectiveness of this therapy, needs to be defined. Further investigations comparing racecadotril with other treatment options (e.g. smectite and probiotics) would be worthwhile. As two trials were company funded, independent trials are needed.

# FUNCTIONAL FOODS



**PROBIOTICS**



**PREBIOTICS**

# PROBIOTICS

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Perhaps the most studied potentially beneficial effect of probiotics is mild to moderate infectious diarrhea.

*Michail S, Sylvester F, Fuchs G, et al. J Pediatr Gastroenterol Nutr 2006; 43: 550–7*

Results have been summarized in several meta-analyses, all of which found an overall reduction in the duration of diarrhea by about 1 day.

*Szajewska H, Mrukowicz JZ. J Pediatr Gastroenterol Nutr 2001;33 suppl 2: S17-25*

*Allen SJ, et al. Cochrane Database Syst Rev 2004;CD003048*

The probiotic agent showing consistent benefit was Lactobacillus GG.

*Szajewska H, Mrukowicz JZ. J Pediatr Gastroenterol Nutr 2001;33 suppl 2:S17-25*

However, in children with more severe diarrhea, there was no demonstrable benefit.

*Costa-Ribeiro H, et al. J Pediatr Gastroenterol Nutr 2003;36:112-5*

*Salazar-Lindo E, et al. BMC Pediatr 2004;4:18*

# PREBIOTICS

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The oligosaccharides contained in human milk have been called the prototypic prebiotic because they foster growth of lactobacilli and bifidobacteria in the colon of breastfed neonates.

*Dai D, Walker WA. Adv Pediatr 1999; 46: 353-82*

Data have linked higher intakes of breast milk oligosaccharides with a lowered incidence of acute diarrhea.

*Morrow A, Ruiz-Palacios G, Altaye M, et al. Ped Res 2003; 53: 167A*

Two randomized trials of prebiotic supplemented infant cereal did not demonstrate a reduced incidence of diarrheal disease among infants and children living in an urban economically depressed area.

*Duggan C, Penny ME, Hibberd P, et al. Am J Clin Nutr 2003; 77: 937-42*

Gracie