SEMANA DE CONGRESOS Y JORNADAS NACIONALES DE PEDIATRÍA 2018
7° CONGRESO ARGENTINO DE NEFROLOGÍA PEDIÁTRICA
23, 24 y 25 de abril de 2018
Sedes: Panamericano Buenos Aires Hotel & Resort Ciudad Autónoma de Buenos Aires

Mesa redonda: SUH: aspectos controvertidos

Coordinador: Dr. Ramón Exeni

Secretaria: Dr. Laura Lombardi

Panelistas

SUH en el menor de 6 meses: alternativas diagnósticas

Dra. Flavia Ramirez

Relevancia del Manejo de la hidratación en el paciente con SUH por STEC

Dra. Andrea Exeni

Tratamiento del SUH por STEC con severo compromiso neurológico: nuevas estrategias

Dra. Marta Adragna

Andrea Exeni

Servicio de Nefrología Infantil

Hospital Universitario Austral

SUH

30% de los paciente con IRA, IRC y/o HTA

2-5% MORTALIDAD

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Cambio de paradigma

Décadas previas: « Es riesgoso y perjudicial administrar fluidos a un paciente en IRA por el riesgo potencial de sobrecarga de volumen »

Actualidad: "Hay un tiempo sensible para poder administrar los fluidos de manera adecuada y efectiva»

Shifting the Paradigm in Hemolytic Uremic Syndrome

David N. Cornfield, MD

PEDIATRICS Volume 137, number 1, January 2016:e20153524

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Causas deshidratación SUH

- 50% nauseas y vómitos
- Diarrea inicialmente acuosa y luego sanguinolenta
- Sensorio que impide tomar
- Aportes de líquidos

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Valorar hidratación

CUADRO 3. ***Evaluacion del estado de hidratación.***

	A. Normohidratado	B. Leve y Moderado	C. Grave
1. *Pregunte por:*			
Sed	Normal.	Más de lo normal.	Excesiva.
Orina	Normal.	Poca cantidad. Oscura.	No orinó por 6 hs.
2. *Observe:*			
Aspecto		Irritado o somnoliento.	Deprimido o comatoso. *
Ojos		Hundidos.	Muy hundidos. Llora sin lágrimas.
Boca y lengua		Secas.	Muy secas, sin saliva.
Respiración		Más rápida de lo normal.	Muy rápida y profunda.
3. *Explore:*			
Elasticidad de la piel	Pliegue se deshace con rapidez.	Pliegue se deshace con lentitud.	Pliegue se deshace muy lentamente: más de 2 segundos.
Fontanela	Normal.	Hundida.	Muy hundida (se palpa y observa).
Pulso	Normal.	Más rápido de lo normal.	Muy rápido, fino o no se palpa.*
Llenado capilar	Menor de 2 seg.	De 3 a 5 segundos.	Mayor de 5 segundos. *
4. *Decida:*	No tiene deshidratación.	Si tiene 2 o más síntomas o signos, tiene deshidratación.	Si tiene uno o más de los signos marcados con * tiene deshidratación grave con shock. Si tiene dos o más de los otros signos pero ninguno marcado con * tiene deshidratación grave sin shock.
5. *Tratamiento:*	Aplique el Plan A para prevenir la deshidratación.	Aplique el Plan B para tratar la deshidratación.	Aplique el Plan C para tratar la deshidratación grave con shock. Inicie tratamiento con rehidratación intravenosa. Para tratar la deshidratación grave sin shock, inicie tratamiento por vía oral y observe la respuesta.

Consenso Nacional

DIARREA AGUDA EN LA INFANCIA.
Actualización sobre criterios
de diagnóstico y tratamiento

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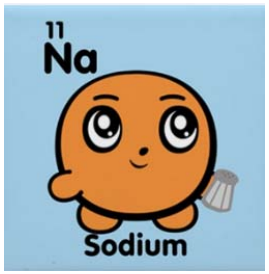
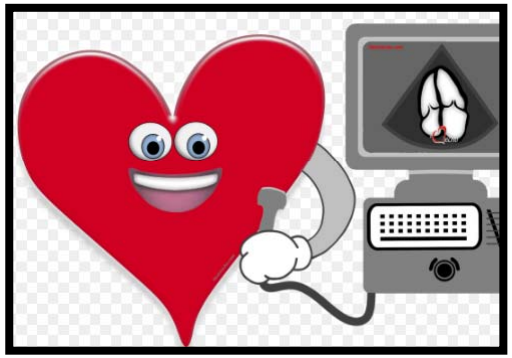
Valorar la hidratación





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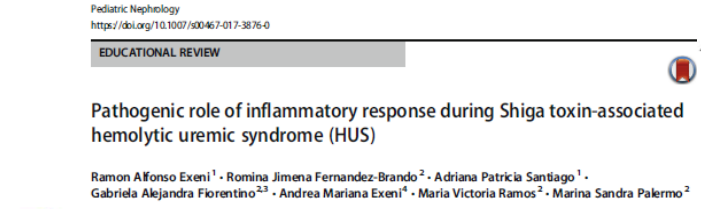
Alteraciones coagulación

- La activación de la coagulación y la alteración de la fibrinólisis ocurre **ANTES** de que se desarrolle el SUH promoviendo la estabilización del trombo

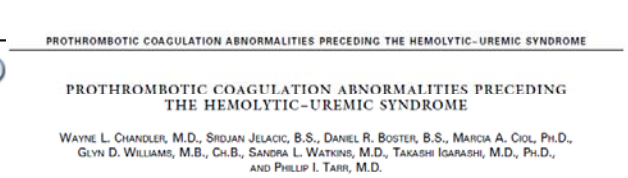
- La shiga toxina promueve la formación de trombos y aumenta la concentración de fibrina y estimula la producción de citoquinas y chemokinas en la célula endotelial


Pediatric Nephrology
https://doi.org/10.1007/s00467-017-3876-0

EDUCATIONAL REVIEW

Pathogenic role of inflammatory response during Shiga toxin-associated hemolytic uremic syndrome (HUS)

Ramon Alfonso Exeni[1] · Romina Jimena Fernandez-Brando[2] · Adriana Patricia Santiago[1] · Gabriela Alejandra Fiorentino[2,3] · Andrea Mariana Exeni[4] · Maria Victoria Ramos[2] · Marina Sandra Palermo[2]


PROTHROMBOTIC COAGULATION ABNORMALITIES PRECEDING THE HEMOLYTIC-UREMIC SYNDROME

PROTHROMBOTIC COAGULATION ABNORMALITIES PRECEDING THE HEMOLYTIC-UREMIC SYNDROME

Wayne L. Chandler, M.D., Srdjan Jelacic, B.S., Daniel R. Boster, B.S., Marcia A. Ciol, Ph.D., Glyn D. Williams, M.B., Ch.B., Sandra L. Watkins, M.D., Takashi Igarashi, M.D., Ph.D., and Phillip I. Tarr, M.D.


frontiers in IMMUNOLOGY

ORIGINAL RESEARCH ARTICLE

Pro-coagulant endothelial dysfunction results from EHEC Shiga toxins and host damage-associated molecular patterns

Chad L. Mayer[1], Caitlin S. L. Parello[1], Benjamin C. Lee[1], Kiyoshi Itagaki[2], Shinichiro Kurosawa[1]* and Deborah J. Stearns-Kurosawa[1]

[1] Department of Pathology and Laboratory Medicine, Boston University School of Medicine, Boston, MA, USA
[2] Department of Surgery, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA

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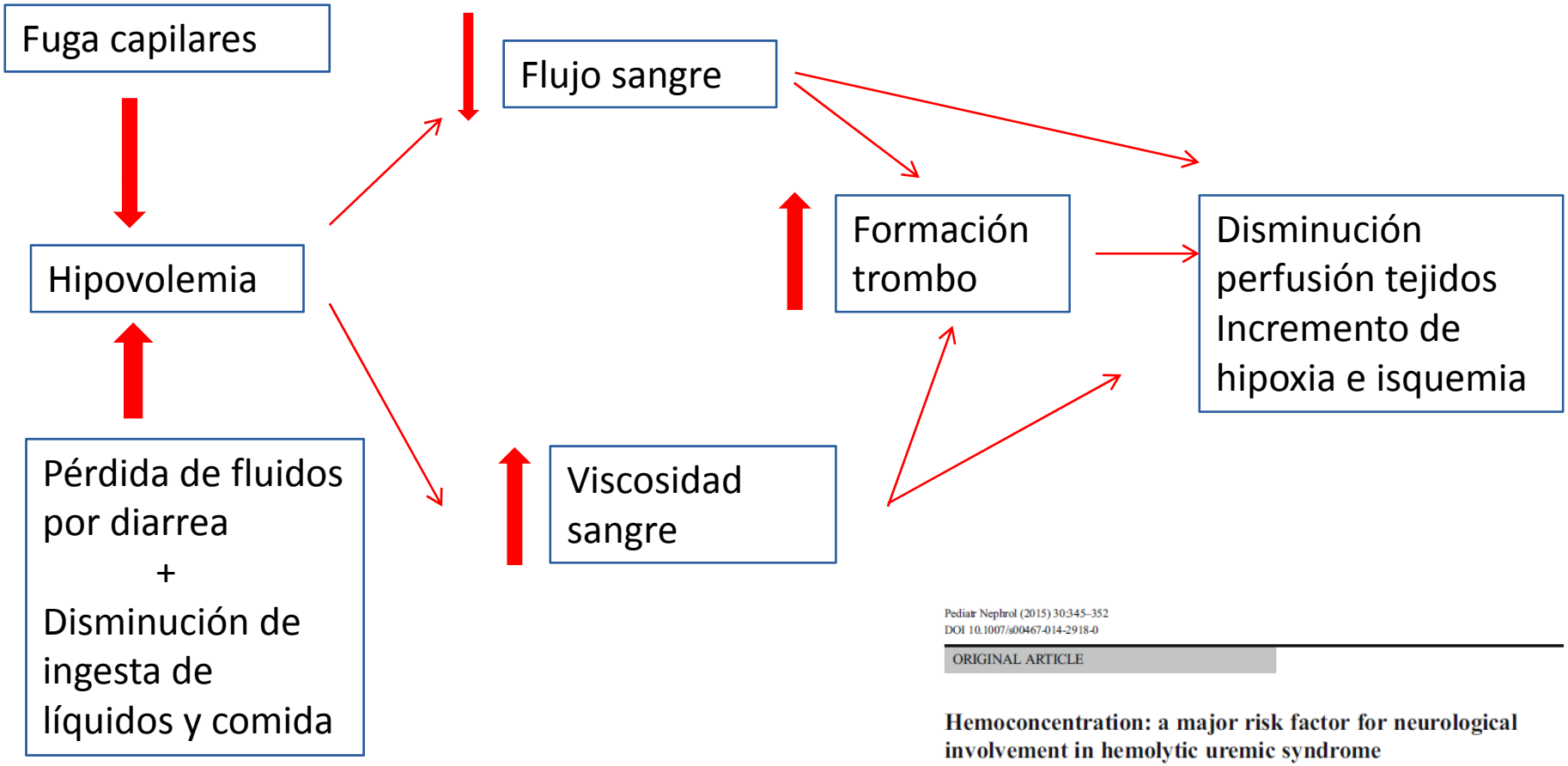
Daño por Hemoconcentración y por hipovolemia



Pediatr Nephrol (2015) 30:345–352
DOI 10.1007/s00467-014-2918-0

ORIGINAL ARTICLE

Hemoconcentration: a major risk factor for neurological involvement in hemolytic uremic syndrome

Gianluigi Ardissino · Valeria Daccò · Sara Testa · Cristina Felice Civitillo · Francesca Tel · Ilaria Possenti · Mirco Belingheri · Pierangela Castorina · Nicolò Bolsa-Ghiringhelli · Silvana Tedeschi · Fabio Paglialonga · Stefania Salardi · Dario Consonni · Elena Zoia · Patrizia Salice · Giovanna Chidini

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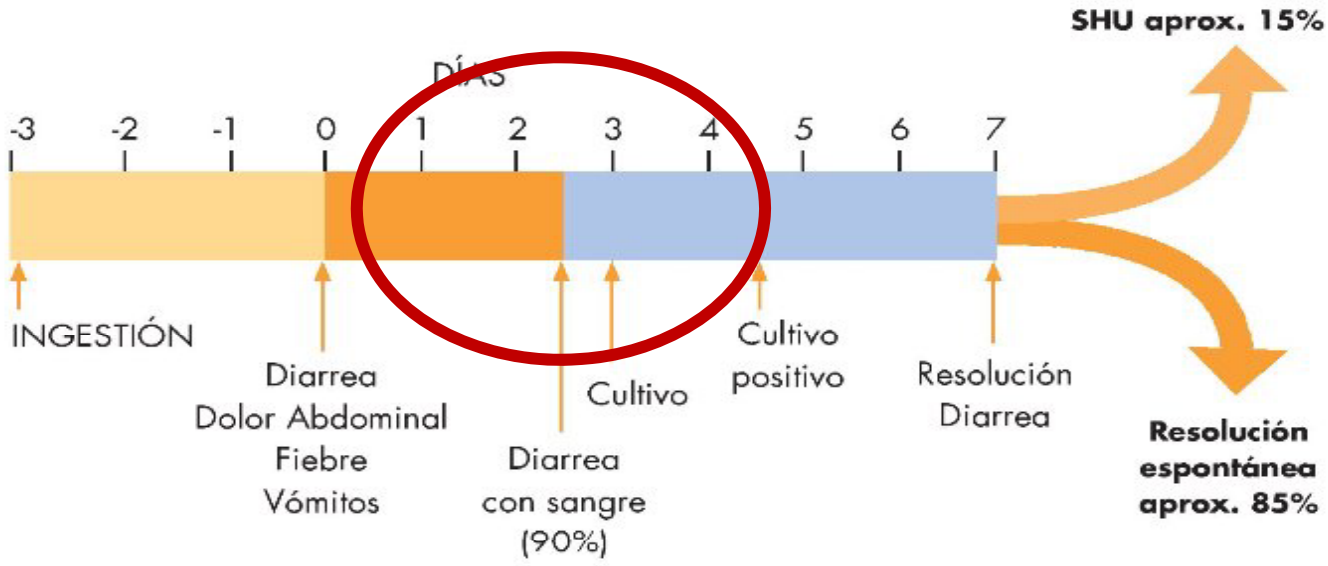
En que momento impacta la hidratación ?

<u>Al 4to DIA DE LA DIARREA</u> en pacientes *que van a desarrollar SUH* ya está la cascada trombótica en curso y la inhibición de la fibrinólisis



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Relative Nephroprotection During *Escherichia* PEDIATRICS Vol. 115 No. 6 June 2005
Association With Intravenous Volume Expansion

Julie A. Ake, MD*‡; Srdjan Jelacic, BS§; Marcia A. Ciol, PhD‡; Sandra L. Watkins, MD‡§;
Karen F. Murray, MD‡§; Dennis L. Christie, MD‡§; Eileen J. Klein, MD, MPH‡§; and Phillip I. Tarr, MD‡§

29 pacientes Oligoanúricos recibieron durante los primeros 4 días **17,1 veces menos líquidos y 21,8 veces menos Na**

Arch Pediatr Adolesc Med. 2011 October ; 165(10): 884–889. doi:10.1001/archpediatrics.2011.152.

Early Volume Expansion During Diarrhea and Relative Nephroprotection During Subsequent Hemolytic Uremic Syndrome

Dr. Christina A. Hickey, MD, Dr. T. James Beattie, MB, CHB, FRCPCH, Dr. Jennifer Cowieson, DPN, Dr. Yosuke Miyashita, MD, MPH, Dr. C. Frederic Strife, MD, Dr. Juliana C. Frem, MD, Dr. Johann M. Peterson, MD, Dr. Lavjay Butani, MD, Dr. Deborah P. Jones, MD, Dr. Peter L. Havens, MD, Dr. Hiren P. Patel, MD, Dr. Craig S. Wong, MD, MPH, Dr. Sharon P. Andreoli, MD, Dr. Robert J. Rothbaum, MD, Dr. Anne M. Beck, MD, and Dr. Phillip I. Tarr, MD

50 pacientes **1,6 veces mayor riesgo de presentar oligoanuria** si no se dieron ***fluidos endovenosos los primeros 4 días de diarrea (aporte de Na y fluidos)***

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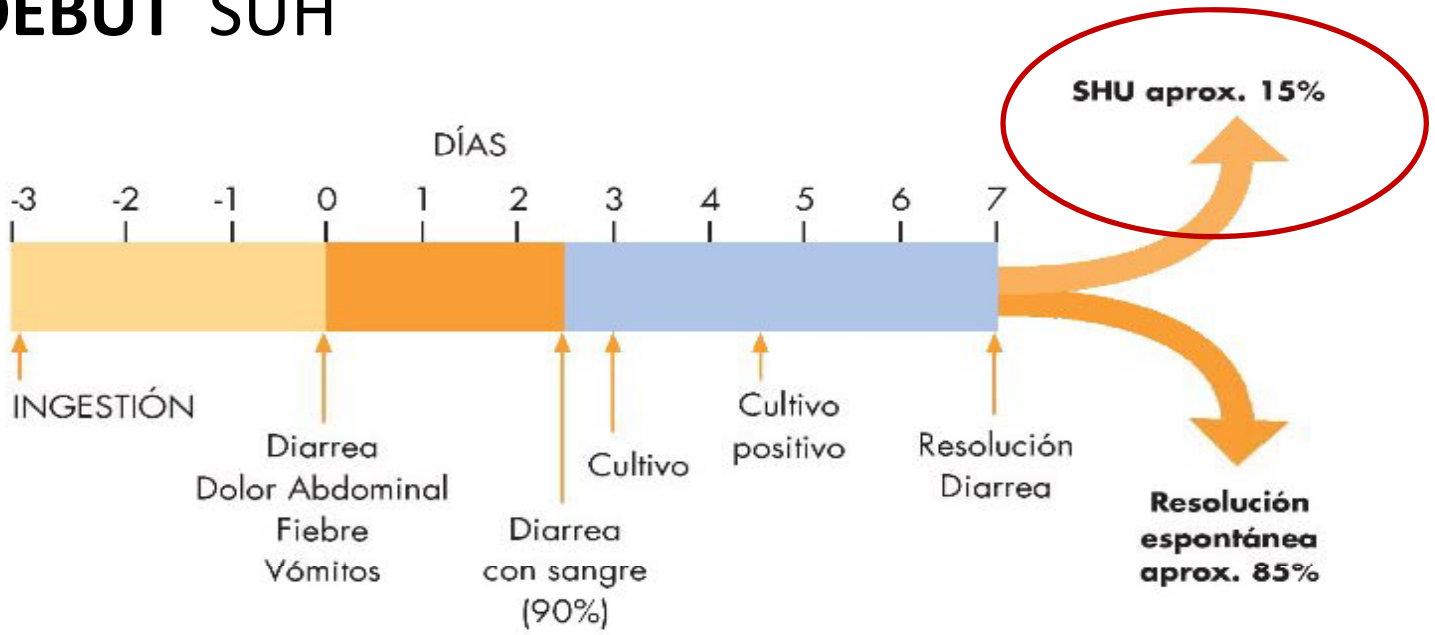
¿En qué otro momento impacta la hidratación ?

DEBUT SUH



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Mayor requerimiento de diálisis

Pediatr Nephrol (2012) 27: 1407–1410
DOI 10.1007/s00467-012-2158-0

BRIEF REPORT

Dehydration at admission increased the need for dialysis in hemolytic uremic syndrome children

Alejandro Balestracci · Sandra Mariel Martin · Ismael Toledo · Caupolican Alvarado · Raquel Eva Wainsztein

137 pac : 86 normohidratados

51 deshidratados (↑Urea ↑hto ↓Na ↓pH ↓bic)

Mayor presencia de vómitos y mayor requerimiento de diálisis en pacientes deshidratados

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Mayor riesgo compromiso neurológico

Pediatr Nephrol (2015) 30:345–352
DOI 10.1007/s00467-014-2918-0

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16/61 pacientes con síntomas neurológicos severos iniciales
17% de mortalidad cuando hay compromiso neurológico (convulsiones, coma, piramidalismo, extrapiramidalismo)

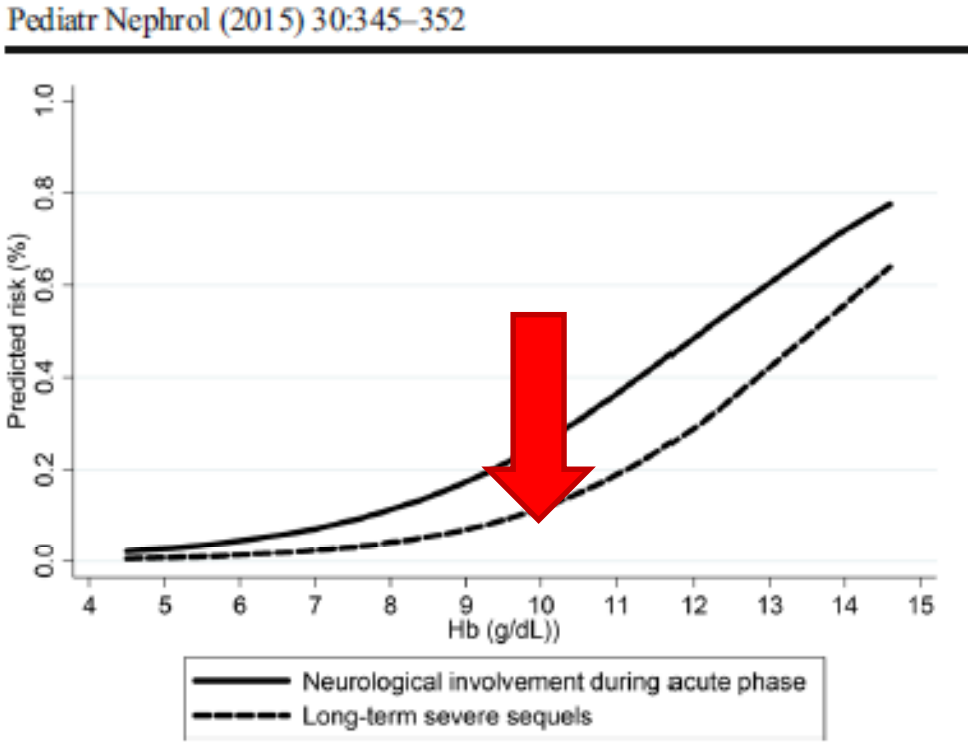

Fig. 1 Predicted probability (risk) of neurological involvement and of long-term severe sequelae in relation with hemoglobin (*Hb*) levels. *Solid line* Risk of acute neurological involvement, *broken line* risk of long-term severe (renal and neurological) sequelae

Mayor riesgo de colitis hemorrágica

Pediatr Nephrol (2012) 27:229–233
DOI 10.1007/s00467-011-1973-z

ORIGINAL ARTICLE

Hemorrhagic colitis in postdiarrheal hemolytic uremic syndrome: retrospective analysis of 54 children

Ricardo C. Rahman · Carlos J. Cobeñas · Ricardo Drut · Oscar R. Amoreo · Javier D. Ruscasso · Ana P. Spizzirri · Angela del C. Suarez · Javier H. Zalba · Celia Ferrari · Marcela C. Gatti

987 Pacientes

54 pacientes (5,5% con colitis hemorrágica)

HT0> 30% significativamente mas frecuente en paciente con ***colitis hemorrágica***

Estos pacientes tuvieron mayor ***mortalidad, anuria*** *mas prolongada y mayor* ***compromiso neurológico***

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Mayor riesgo compromiso renal a largo plazo

originales breves

http://www.revistanefrologia.com

La deshidratación al ingreso es un factor de riesgo para la recuperación incompleta de la función renal en niños con síndrome urémico hemolítico

José M. Ojeda[1], Isolda Kohout[2], Eduardo Cuestas[1]

[1] Área de Pediatría y Neonatología. Hospital Privado, Unidad Académica, Facultad de Ciencias Médicas, Universidad Nacional de Córdoba. Córdoba (Argentina)

[2] Sección de Nefrología Pediátrica. Hospital Privado, Unidad Académica, Facultad de Ciencias Médicas, Universidad Nacional de Córdoba. Córdoba (Argentina)

Nefrologia 2013;33(3):372-6

doi:10.3265/Nefrologia.pre2012.Nov.11648

36 pacientes : 23 con recuperación completa

La **deshidratación > 5%** esta significativamente asociada a la falta de recuperación completa de la función renal a **largo plazo**

Pediatr Nephrol (2015) 30:345–352

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HTO>30% peor pronostico a largo plazo

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JAMA Pediatrics | Original Investigation

Associations Between Hydration Status, Intravenous Fluid Administration, and Outcomes of Patients Infected With Shiga Toxin–Producing *Escherichia coli*

A Systematic Review and Meta-analysis

Silviu Grisaru, MD; Jianling Xie, MD, MPH; Susan Samuel, MD; Lisa Hartling, PhD; Phillip I. Tarr, MD; David Schnadower, MD, MPH; Stephen B. Freedman, MDCM, MSc; for the Alberta Provincial Pediatric Enteric Infection Team

8 REPORTES / 2888 ESTUSI(2 RETROSPECTIVOS /2 PROSPECTIVOS /2 CASOS CONTROL)

2 ARGENTINA
4 EEUU
2 ITALIA

1511 PACIENTES : 57% Requirieron diálisis
18% complicaciones neurológicas
3,7% fallecieron

NINGUNO EVALUO EL RIESGO DE DESARROLLAR SUH LUEGO DE INFECCION POR STEC ACORDE A HIDRATACION

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ADMINISTRACION DE FLUIDOS E.V

- 3 estudios que vinculan a la hidratación con menor requerimiento de diálisis
- 2 estudios vinculan a la hidratación en cualquier momento de la diálisis con menor requerimiento de diálisis y compromiso del SNC
- 2 estudios con hidratación durante los primeros 4 días de la diarrea disminuye riesgo de diálisis
- 2 estudios con hidratación durante los primeros 4 días de la diarrea disminuye el riesgo de compromiso del SNC

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ESTADO DE HIDRATACIÓN

Se consideró Hto de 23% y evaluación clínica de la deshidratación

El hto >23% al debut o al momento de la internación aumenta los riesgos de

4 estudios : insuficiencia renal oligo-anúrica OR, 2.38 [95% CI, 1.30-4.35]

- 5 estudios: requerir diálisis OR, 1.90 [95% CI, 1.25-2.90];
- 3 estudios : compromiso de SNC OR, 2.07 [95% CI, 0.93-4.60]
- 4 estudios : muerte OR, 5.13 [95% CI, 1.50-17.57]

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Associations Between Hydration Status, Intravenous Fluid Administration, and Outcomes of Patients Infected With Shiga Toxin–Producing *Escherichia coli*

A Systematic Review and Meta-analysis

Table 1. Summary of Included Studies

Source	Country	Study Design	STEC or HUS?	Sample Size	Age	Pathogens	Exposures Evaluated	Outcomes
Ake et al,[10] 2005	United States	PC	Both	29	Median (range): 3.1 y (0.8-8.8 y)	*E coli* O157:H7	IVF before HUS onset; IVF in first 4 d of illness	OARF (urine output <0.5 mL/kg/h for ≥24 consecutive h)
Ardissino et al,[12] 2015[a]	Italy	RC	Both	61	Median (IQR): 3.7 y (6 mo to 15 y)	STEC (unspecified)	Hemoconcentration (hemoglobin at disease onset)	Acute: RRT, neurologic complications; chronic: renal sequelae 2 y after disease onset
Ardissino et al,[17] 2016[a]	Italy	RC	Both	76	Median (IQR): 4.5 y (1.5-7.1 y) for control group; 3.5 y (1.6-7.3 y) for volume expansion group	STEC (O26, O157, O103, O111, and O145)	Volume expansion initiated on the day HUS was established or at admission.	Acute: RRT, neurologic complications, length of stay in ICU; chronic: long-term sequelae; death
Balestracci et al,[13] 2012	Argentina	RC	Diarrhea-associated HUS	137	Mean (range): 1.91 y (0.3-11.8 y) for normohydrated group; 1.6 y (0.5-6.4 y) for dehydrated group	Diarrhea-associated HUS (unspecified)	Dehydration at admission (based on clinical assessment)	RRT (yes/no and duration), days of oligoanuria
Hickey et al,[11] 2011	United States and Scotland	PC	Diarrhea-associated HUS	50	Median (range): 4.1 y (1.0-17.2 y)	*E coli* O157:H7 (n = 27); *E coli* O121:H19 (n = 1); diarrhea-associated HUS (unspecified) (n = 22)	IVF during pre-HUS diarrhea phase	Oligoanuria (urine output ≤0.5 mL/kg/h for ≥24 consecutive h)
Mody et al,[19] 2015	United States	PC	Diarrhea-associated HUS	770	Median (range): 3.7 y (2.3 mo to 17.8 y)	*E coli* O157 (n = 512); non-O157 STEC (n = 23); diarrhea-associated HUS (unspecified) (n = 235)	Highest leukocyte count; lowest hematocrit value	RRT, death
Ojeda et al,[24] 2013	Argentina	Case-control	Diarrhea-associated HUS	13 Cases; 23 controls	Mean (SD) [range]: 29.1 y (16 mo) [9.2 mo to 7.3 y]	Diarrhea-associated HUS (unspecified)	Dehydration at admission (based on clinical assessment)	Incomplete recovery of renal function (proteinuria, hypertension, reduced creatinine clearance, or CRF)
Oakes et al,[27] 2006	United States	Case-control	Diarrhea-associated HUS	12 Cases; 340 controls	Median (range): 2.1 y (1.15-8.6 y) for cases; not provided for controls	Diarrhea-associated HUS (unspecified)	Dehydration, oliguria, and lethargy at admission; WBC counts >20 000/μL; HCT value >23%	Death

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Meta-analysis	No. of Studies/ Participants	Estimated OR (95% CI)	I^2, %	Level of Study Limitations	Level of Inconsistency[a]	Overall Assessment[b]
IVF beginning anytime from presentation up to and including the day HUS was diagnosed and association with need for RRT	3/237	0.26 (0.11-0.60)	0	Medium[c]	Consistent	Moderate: significant association between anytime from presentation up to and including the day HUS was diagnosed and need for RRT
IVF beginning anytime from presentation up to and including the day HUS was diagnosed and association with CNS involvement	2/140	0.26 (0.07-0.91)	0	Medium[c]	Consistent	Moderate: significant association between anytime from presentation up to and including the day HUS was diagnosed and CNS involvement
IVF initiated in the first 4 d of STEC illness before HUS developed and association with OARF	2/129	0.16 (0.05-0.51)	0	Medium[c]	Consistent	Moderate: significant association between IVF initiated in the first 4 d of STEC illness before HUS developed and OARF
HCT value >23% and association with OARF	4/452	2.38 (1.30-4.35)	2	Medium[c]	Consistent	Moderate: significant association between HCT value >23% and OARF
HCT value >23% and association with RRT	5/1626	1.90 (1.25-2.90)	17	Medium[c]	Consistent	Moderate: significant association between HCT value >23% and need for RRT
HCT value >23% and association with death	4/1359	5.13 (1.50-17.57)	55	High[d]	Inconsistent	Moderate: significant association between HCT value >23% and death
HCT value >23% and association with death restricted to low risk-of-bias studies[a]	3/997	2.57 (1.15-5.73)	0	Medium[c]	Consistent	Moderate: significant association between HCT value >23% and death

PREDICTORES DE MAL PRONOSTICO EN PACIENTES INFECTADOS CON STEC **QUE PROGRESAN A SUH**

LA FALTA DE ADMINISTRACION DE FLUIDOS ENDOVENOSOS PREVIO AL ESTABLECIMIENTO DEL SUH

HEMATOCRITO MAS ELEVADO AL DEBUT

EVIDENCIA MODERADA

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Relative Nephroprotection During *Escherichia coli* O157:H7 Infections: Association With Intravenous Volume Expansion

Julie A. Ake, MD*‡; Srdjan Jelacic, BS§; Marcia A. Ciol, PhD‡; Sandra L. Watkins, MD‡§; Karen F. Murray, MD‡§; Dennis L. Christie, MD‡§; Eileen J. Klein, MD, MPH‡§; and Phillip I. Tarr, MD‡§

We have encouraged hospitalizing children who are infected with *E coli* O157:H7 and then administering intravenous isotonic fluids[20] for a variety of reasons: mandated contact precautions for hospitalized patients who are infected with *E coli* O157:H7[31] are too stringent to be provided by caregivers at home. Vomiting[4,5] complicates attempts to provide oral rehydration, and oral hypotonic fluids will not expand intravascular volume as well as isotonic fluids that are administered intravenously. Also, we have observed that boluses of intravenous isotonic fluids frequently diminish the discomfort associated with eating or drinking during *E coli* O157:H7 infections.

Our data do not permit us to recommend the optimal salinity of intravenous fluids or the duration of their administration; it is possible that the sustained infusion beyond the first 4 days of illness extended the benefit. Also, we could not examine the influence of fluids taken by mouth, because it was impossible to determine accurately their volumes or sodium contents. In addition, our data do not address whether intravenous volume expansion diminishes the risk for developing HUS among infected children. However, data[11,15] suggest that the differentiation between oligoanuric HUS and nonoligoanuric HUS is at least as consequential as the differentiation between uncomplicated gastrointestinal infection and nonoligoanuric HUS. Finally, our analysis does not consider the costs and risks of hospitalization for children who are not destined to develop HUS, but we believe that there is considerable potential benefit to volume expansion, in aggregate and in individual cases, if this intervention can convert a case of oligoanuric HUS to nonoligoanuric HUS, as suggested by our data.

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Grupo	Eventos	Acum SE 52/2016	Acum SE 52/2017	Semana 52/2017	Cuatrisemana 1-4/2018	Mediana /*Media*	Índice epidémico o Variación %
Envenenamiento por animales ponzoñosos	Env. por animal ponzoñoso - Alacranismo	9037	8524	216	**581**	8983,4	0,95
	Env. por animal ponzoñoso - Araneismo	1029	1304	30	**62**	1148,8	1,14
	Env. por animal ponzoñoso - Ofidismo	878	869	7	**49**	760,2	1,14
Gastroentéricas	Botulismo [1]	32	31	2	**1**		-3,12%
	Botulismo del Lactante [1]	63	54	0	**4**		-14,2%
	Triquinellosis [1]	642	555	7	**16**		-13,5%
	Diarreas	1076443	988066	18880	**41595**	1194014,6	0,83
	Diarreas agudas sanguinolientas	2063	2639	65	**187**	1807,6	1,46
	Fiebre tifoidea y paratifoidea	6	5	0	**1**	7,0	
	Intox. por moluscos	0	2	0	**0**	1,0	
	Síndrome urémico hemolítico (SUH)	Ver informe en el cuerpo del BIV					

Durante el 2017 hasta la SE52, se notificaron al SNVS

Diarrea con sangre 2639

SUH 355 casos (13,45%)

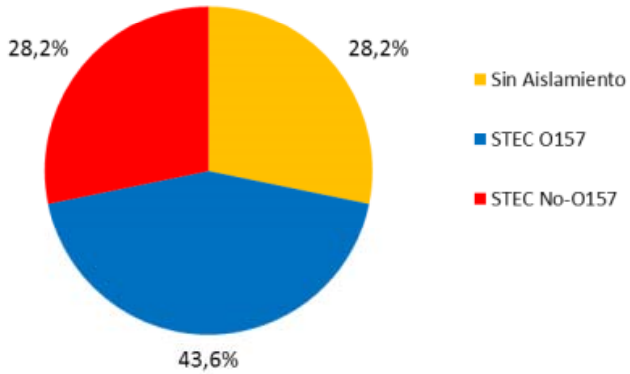
71,8 % 254 pacientes

STEC positivos

Riesgo de SUH con STEC positivo 5-10% (1775 ?)

¿HIDRATACION ENDOVENOSA ?

Gráfico 6: Aslamientos de STEC en caso de SUH notificados.Total País. (N=227).



***Fuente**: Elaboración propia en base a datos del Sistema Nacional de Vigilancia de la Salud (SNVS C2-SIVILA-UCSUH).*

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Given that HUS is a disease whose key feature is hemolysis, it was striking to discover that the more severe cases were associated with little or no anemia and that the more anemic patients experienced milder disease.

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ORIGINAL ARTICLE

Hemoconcentration: a major risk factor for neurological involvement in hemolytic uremic syndrome

Gianluigi Ardissino · Valeria Daccò · Sara Testa · Cristina Felice Civitillo · Francesca Tel · Ilaria Possenti · Mirco Belingheri · Pierangela Castorina · Nicolò Bolsa-Ghiringhelli · Silvana Tedeschi · Fabio Paglialonga · Stefania Salardi · Dario Consonni · Elena Zoia · Patrizia Salice · Giovanna Chidini

HOSPITAL UNIVERSITARIO AUSTRAL

Integrantes del Servicio de Nefrología Infantil

Dra Andrea Exeni

Dra María Paula Rigali

Dra Debora Cisnero

Dra Anabella Colazo

Lic Karina Villareal

Consultor Dr Ramón Exeni

HOSPITAL UNIVERSITARIO AUSTRAL