



**stecSUH**

**EXPANSIÓN TEMPRANA DE VOLUMEN  
MEJORA EL PRONOSTICO  
DE CORTO Y LARGO PLAZO**

**Dr. Pablo Bonany  
Nefrologo Infantil  
Hospital de Niños Ricardo Gutierrez (CABA)**



**Giuseppe Arcimboldo**, ([Milán, 1527](#) - [ibídem, 11 de julio de 1593](#)) [pintor italiano](#),  
Representa el rostro humano a partir de flores, frutas, plantas, animales u objetos; en el  
contexto de las [ilusiones ópticas](#).

## *The hemolytic-uremic syndrome*

*The combination of acute renal failure, thrombocytopenia, and hemolytic associated with distorted erythrocytes ("burr" cells) constitutes the hemolytic-uremic syndrome. These observations of the natural history of 58 affected infants and children represent the largest single group studied. Preliminary serologic studies point to a viral etiology in some cases. During the acute phase, the mortality rate was lowered substantially by the judicious use of transfusions of packed erythrocytes and improvements in the treatment of the acute renal failure. The severity of renal and central nervous system abnormalities appear to influence the frequency of sequelae. It is not clear whether affected children represent the clinical picture of one disease or reflect similar changes induced by diverse disease processes.*

Carlos Gianantonio, M.D.,\* Margarita Vitacco, M. D.,  
Fernando Mendilaharsu, M.D., Arnaldo Ruty, M.D., and  
Javier Mendilaharsu, M.D.

BUENOS AIRES, ARGENTINA

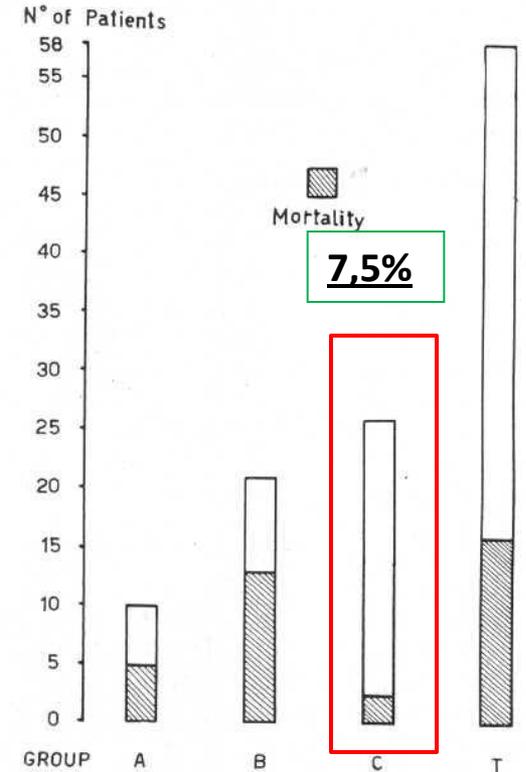
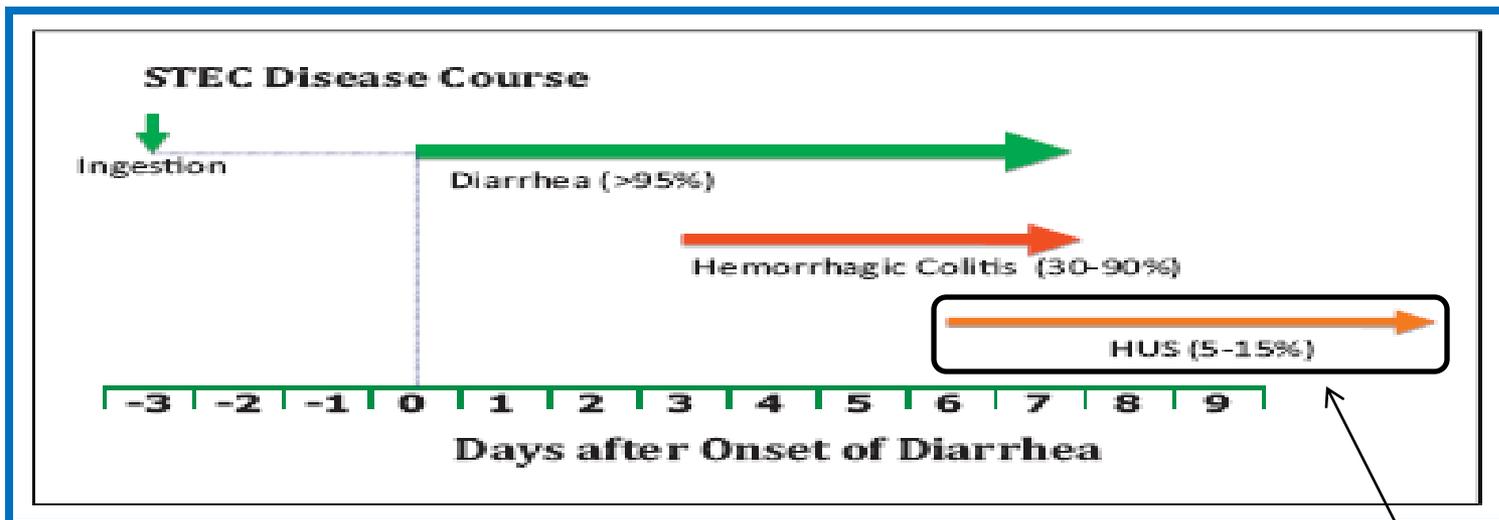


Fig. 2. Mortality rates related to year of admission. *Group A*—1957 to 1960; *Group B*—1960 to 1962; *Group C*—1962 to 1963; *T* = Total group (58 patients).

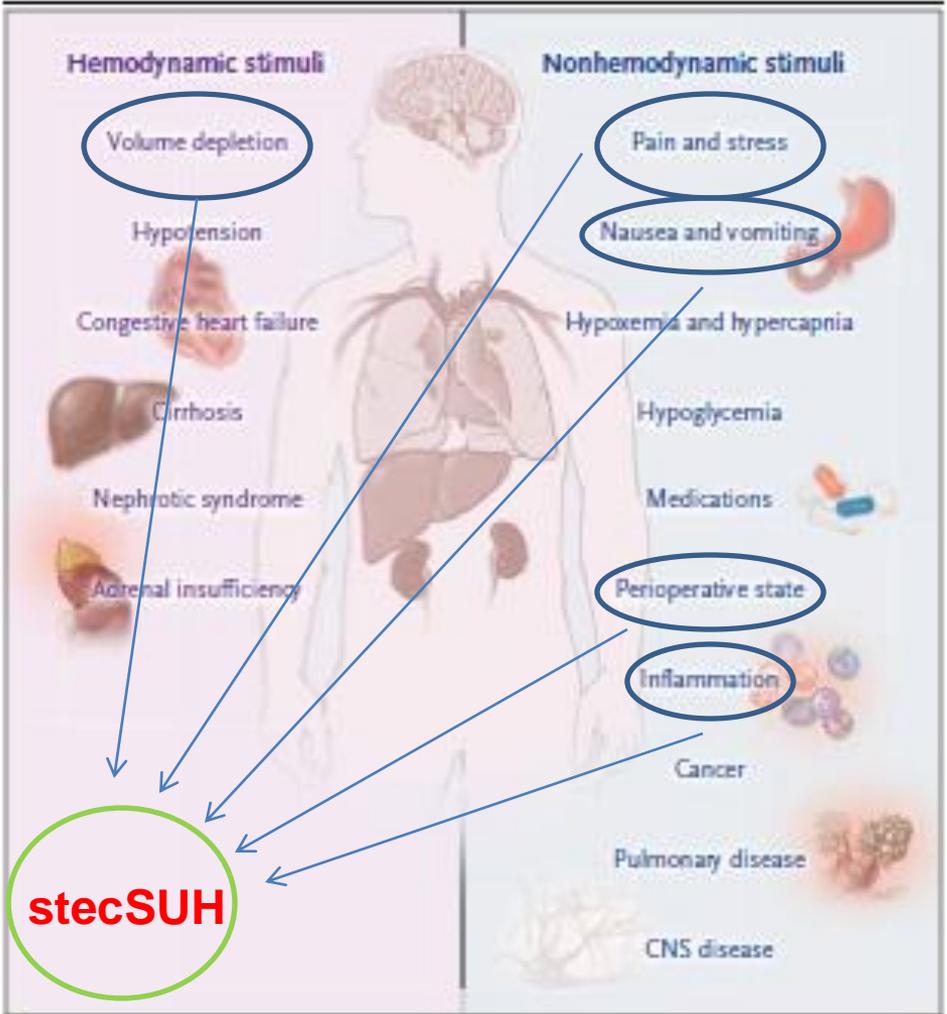


**ZONA DE ACCIÓN**

# Maintenance Intravenous Fluids in Acutely Ill Patients

Michael L. Moritz, M.D., and Juan C. Ayus, M.D.

N ENGL J MED 373;14 NEJM.ORG OCTOBER 1, 2015



Isotonic fluids are the most appropriate maintenance fluid in the vast majority of situations.

Figure 1. Nonosmotic States of Arginine Vasopressin (AVP) Excess.

# 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‡§

From the \*Department of Medicine, Madigan Army Medical Center, Tacoma, Washington; ‡Children's Hospital and Regional Medical Center, Seattle, Washington; and §Department of Pediatrics, University of Washington School of Medicine, Seattle, Washington.



PEDIATRICS Vol. 115 No. 6 June 2005



El volumen y el contenido de sodio de los fluidos intravenosos,

administrado temprano en la enfermedad,

afectan el riesgo de desarrollar síndrome urémico hemolítico oligoanúrico

después de la infección con E coli O157: H7



# METODO:

- ✓ Estudio prospectivo de cohorte.
- ✓ 29 niños con stecSUH confirmado microbiológicamente (*E coli O157:H7*).
- ✓ Periodo: Mayo 1997 a Mayo 2003.



# RESULTADOS



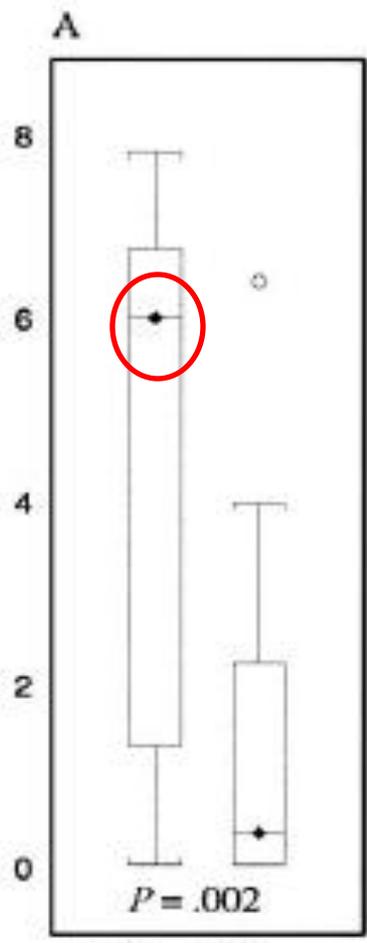
## ✓ Grupo SUH Oligoanúrico ( 16 ptes. )

- ✓ Todos requirieron diálisis,
- ✓ Recuento inicial de GB y Cr mas alto,
- ✓ Recuento de plaquetas mas bajo,
- ✓ Mas días de hospitalización

## ✓ SUH No oligoanúrico (13 ptes)

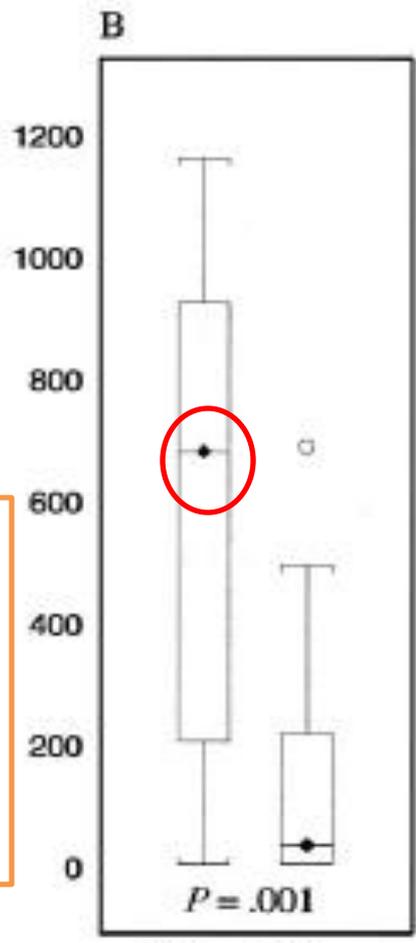
- ✓ Ninguno requirió diálisis.

Total intravenous fluid volumes (L/m<sup>2</sup>/first 4 days of illness)



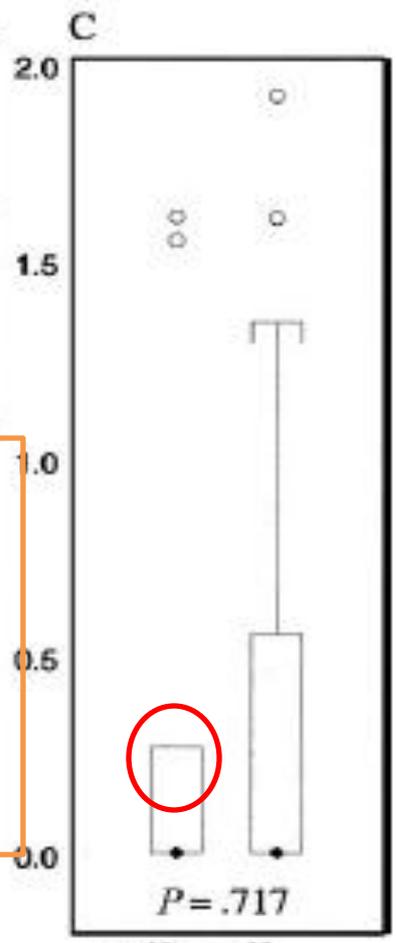
No Oligoanuria  
~~Oligoanuria~~

Total intravenous sodium (mmol/m<sup>2</sup>/first 4 days of illness)



No Oligoanuria  
~~Oligoanuria~~

Total intravenous free water (L/m<sup>2</sup>/first 4 days of illness)



No Oligoanuria  
~~Oligoanuria~~

# Expansión de Volumen

Mejora la perfusión renal  
Mantiene flujo tubular renal

contraresta

Trombosis de pequeños vasos

Hipoperfusión e isquemia

Nefrotoxicidad de Uratos, Hb y Stx

Células tubulares renales  
Monocitos



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

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

## Objetivo:

-Determinar si la intervención pre SUH D+ ayuda a mantener diuresis en la fase de SUH.

## Estudio:

-Prospectivo observacional de cohorte. N= 50 ptes, < 18 años.

## Intervención:

-Infusión de líquidos isotónico IV dentro de los 4 días de iniciada la diarrea.

## Resultados:

-Pctes. oligoanúricos 68%

-84% de oligoanúricos no recibieron líquidos IV



**Table 3. Differences in Total Fluid Volume and Sodium Given Intravenously to the Oligoanuric and Nonoligoanuric Groups**

	Median (Range) [IQR]			<i>U</i>	Effect Size ( <i>r</i> ) <sup>a</sup>	<i>P</i> Value
	All Patients (n=50)	Anuric Patients (n=34)	Nonoligoanuric Patients (n=16)			
<b>Total fluid volume, L/m<sup>2</sup></b>						
During all days before HUS	1.5 (0.0-10.0) [4.3]	1.3 (0.0-9.5) [3.9]	3.8 (0.0-10.7) [6.7]	182	-0.26	.06
During first 4 days of illness	0.05 (0-7.5) [2.8]	0 (0-4.9) [1.7]	1.7 (0-7.5) [3.4]	170	-0.32	.02
<b>Total sodium, mEq/m<sup>2</sup></b>						
During all days before HUS	193 (0-1457) [483]	170 (0-1457) [430]	370 (0-1225) [551]	193	-0.23	.13
During first 4 days of illness	7.8 (0-755) [295]	0 (0-755) [220]	189 (0-483) [362]	185	-0.27	.05

**Table 4. Logistic Models**

Logistic Model	Variable	Odds Ratio (95% Confidence Interval)
First	Age	1.1 (0.9-1.3)
	Antibiotics	2.9 (0.7-11.4)
	Total intravenous fluid given during the first 4 days of illness	6.1 (0.8-46.8)
	Total intravenous sodium given during the first 4 days of illness	1.0 (0.97-1.0)
Second <sup>a</sup>	Antibiotics	3.1 (0.8-11.9)
	Total intravenous fluid given during the first 4 days of illness	1.4 (1.0-2.0)
Final <sup>b</sup>	Total intravenous sodium given during the first 4 days of illness	1.4 (1.0-1.9)

**CONCLUSIÓN:**

- la expansión de volumen es una intervención subutilizado que podría disminuir la frecuencia de insuficiencia renal oligúrica en pacientes de riesgo de SHU

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

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Ismael Toledo · Caupolican Alvarado ·  
Raquel Eva Wainsztein

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1270 Ciudad Autónoma de Buenos Aires, Argentina

## Estudio restrospectivo

### Objetivo:

Determinar si los pacientes SUH D+ que ingresaban deshidratados tenían mas requerimientos de diálisis.

### Metodo:

- Revision de HC de 137 pacientes,
- Dividieron en 2 grupos: normohidratados (n 86) y deshidratados (n 51).

### Resultados:

El grupo “deshidratados” presento mayor tasa de diálisis (70.6 versus 40.7 %,  $p < 0.0007$ ).

Characteristic	Normohydrated	Dehydrated	<i>p</i> value
Creatinine mg/dl	1.65 (0.3–7.5)	2.4 (0.11–11)	0.07 <sup>b</sup>
Need for dialysis	35 (40.7 %)	36 (70.6 %)	0.0007 <sup>a</sup>
Days of oligoanuria	1 (0–28)	5 (0–23)	0.007 <sup>b</sup>
Days of dialysis	8 (2–30)	12 (3–25)	0.005 <sup>b</sup>

# Shifting the Paradigm in Hemolytic Uremic Syndrome

David N. Cornfield, MD

*Divisions of Center for Excellence in Pulmonary Biology,  
Pulmonary, Asthma, and Critical Care Medicine,  
Department of Pediatrics, Stanford University Medical  
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*Pediatrics. 2016;137(1):e20153524*

Los datos son  
los primeros en varias décadas  
que motivan a una  
cambio  
en la práctica clínica estándar.



# Early Volume Expansion and Outcomes of Hemolytic Uremic Syndrome

Gianluigi Ardissino, MD, PhD,<sup>a</sup> Francesca Tel, MD,<sup>a</sup> Ilaria Possenti, MD,<sup>a</sup> Sara Testa, MD,<sup>a</sup> Dario Consonni, MD,<sup>b</sup> Fabio Paglialonga, MD,<sup>a</sup> Stefania Salardi, BS,<sup>c</sup> Nicolò Borsa-Ghiringhelli, MD,<sup>c</sup> Patrizia Salice, MD,<sup>d</sup> Silvana Tedeschi, MD,<sup>c</sup> Pierangela Castorina, MD,<sup>a</sup> Rosaria Maria Colombo, BS,<sup>e</sup> Milena Arghittu, BS,<sup>e</sup> Laura Daprai, BS,<sup>e</sup> Alice Monzani, MD,<sup>f</sup> Rosangela Tozzoli, MD,<sup>g</sup> Maurizio Brigotti, PhD,<sup>h</sup> Erminio Torresani, BS<sup>e</sup>

<sup>a</sup>Center for HUS Control, Prevention and Management, <sup>b</sup>Epidemiology Unit, <sup>c</sup>Laboratory of Medical Genetics, <sup>d</sup>Pediatric Cardiology Unit, and <sup>e</sup>Unit of Microbiology, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; <sup>f</sup>Division of Pediatrics, Department of Health Science, University of Piemonte Orientale, Novara, Italy; <sup>g</sup>Istituto Superiore di Sanità, Roma, Italy; and <sup>h</sup>Università di Bologna, Bologna, Italy



PEDIATRICS Volume 137, number 1, January 2016



## **BACKGROUND:**

- ✓ La Hemoconcentración al inicio se asocia con una enfermedad más grave.
- ✓ El tratamiento ha sido influenciada por el riesgo de sobrecarga de líquidos (FO).
- ✓ Los beneficios de la expansión de volumen después del inicio síndrome urémico hemolítico (SUH) no se han explorado.

# Objetivo:

-Determinar si la EVT puede reducir la severidad del SUH

# Metodo:

- ✓ 38 ptes. steCHUS atendidos entre 2012 and 2014
- ✓ Recibieron infusion IV de solución isotónica (+10% del working weight).
- ✓ Fueron comparados con 38 pacientes históricos del periodo que el tratamiento era la restricción hidrosalina.
- ✓ Se evaluó la evolución a corto y largo plazo (1 años).



# Expansion de Volumen

Infusiones de **solución salina al 0,9%** desde el momento del diagnóstico de SUH hasta alcanzar su peso objetivo :

- ✓ **+7% del WW\***, c/albumina plasmática **>3 g/dL** or ,
- ✓ **+10% de WW\*** c/ albumina plasmática de **<3 g/dL**.

## \*working weight (WW )

•En base a:

- Peso histórico del paciente reportado por cuidador,
- por evaluación clínica.

•**Comienzo EV con diagnóstico de SUH:**

•**Dosis: 10 a 15 mL/kg por hora** (dependiendo del grado de DSH)

•**Matenimiento** con solución glucosada isotónica.



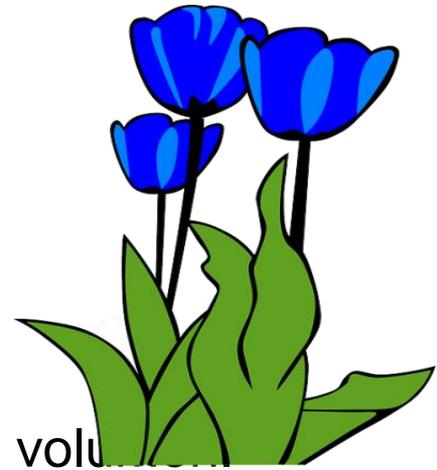
# RESULTADOS

Al momento del diagnostico, **no habia diferencia significativas** entre los grupos en cuanto a

- sexo,
- edad,
- peso,
- dias antes del diagnostico de SUH,
- TA,
- recuento de GB,
- Hb,
- Albumina,
- Acido Urico,
- Recuento plaquetario.

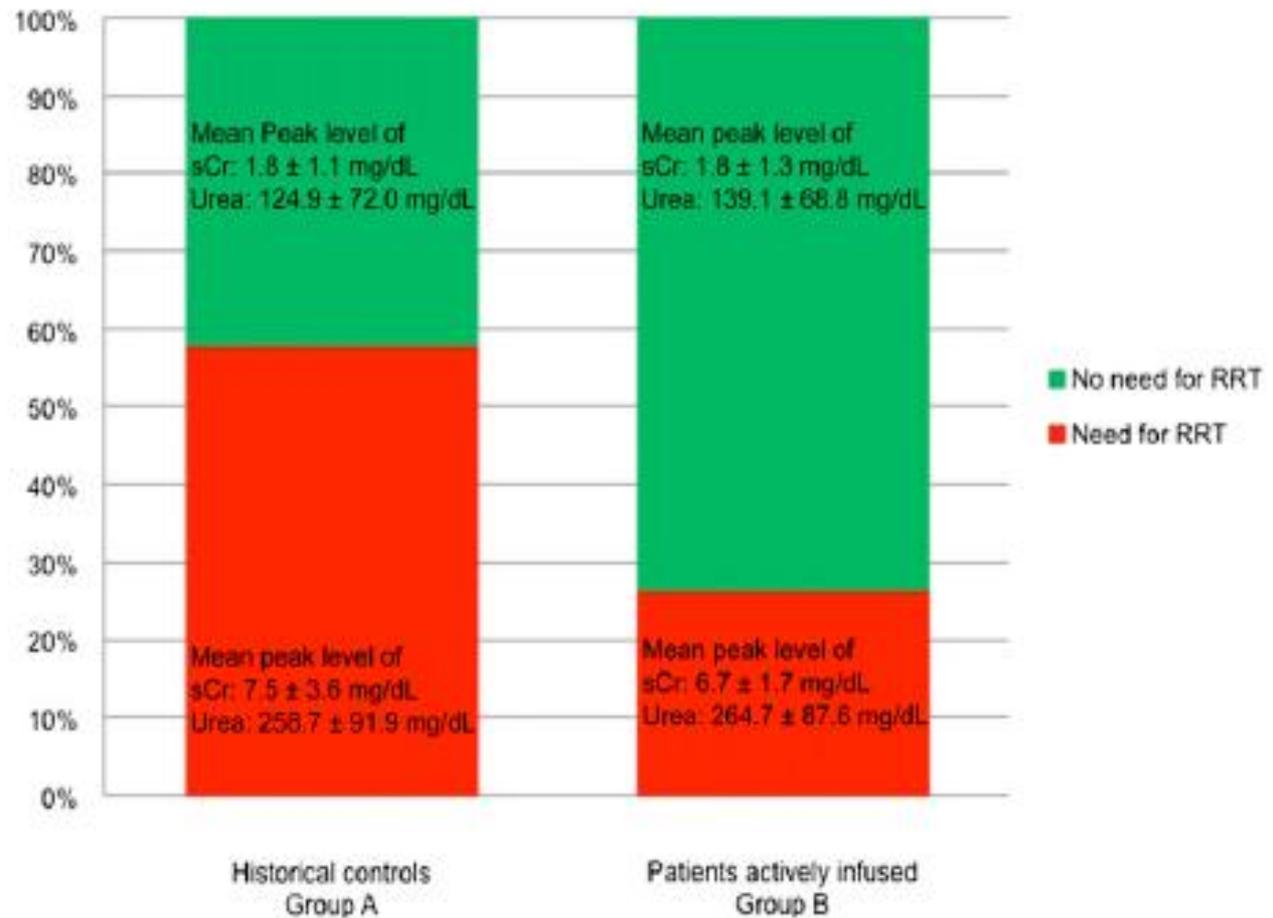


# RESULTADOS



## Pacientes del grupo EVT mostraron

- ✓ **Incremento medio del peso del 12.5% (vs 0%),**  
no registraron casos de sobrecargas cardio-pulmonares de volu
- ✓ **resultado a corto plazo significativamente mejor:**
  - menor tasa de **TRR** (26.3% vs 57.9%,  $P = .01$ )
  - menos días en **UTI** (2.0 vs. 8.5 days,  $P = .02$ ),
  - menos días de **hospitalización** (9.0 vs 12.0 days,  $P = .03$ ).
  - Menor tasa de **compromiso del SNC** (7.9% vs 23.7%,  $P = .06$ ),
- ✓ **Resultados a largo plazo**
  - menor porcentaje de secuela renales y extra-renales (13.2% vs 39.5%,  
 $P = .01$ )



**FIGURE 3**

Rate of need for RRT in historical controls and in patients actively infused and respective peak of sCr in dialyzed and nondialyzed patients.



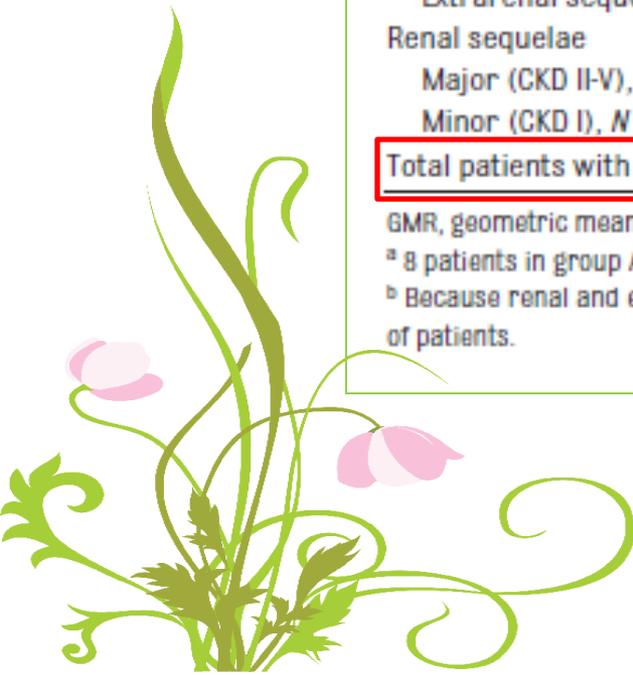
**TABLE 3** Comparison of Short- and Long-Term Outcomes in Patients Addressed to Early FI (Group B) and in Controls (Group A)

	Controls ( <i>N</i> = 38)	Volume Expansion ( <i>N</i> = 38)	RR/GMR (95% CI)	<i>P</i>
<b>Outcomes during acute phase</b>				
Death, <i>N</i> (%)	2 (5.2)	0 (0)	NA	.49
CNS involvement, <i>N</i> (%)	9 (23.7)	3 (7.9)	0.33 (0.10–1.14)	.06
Need for RRT, <i>N</i> (%)	22 (57.9)	10 (26.3)	0.45 (0.25–0.83)	.01
Days of hospitalization, median (IQR)	12 (7–18)	9 (7–12)	0.75 (0.59–0.96)	.02
Days in PICU, median (IQR) <sup>a</sup>	8.5 (3.5–15.5)	2 (1–4.5)	0.31 (0.12–0.82)	.02
<b>Long-term outcomes</b>				
Extrarenal sequelae, <i>N</i> (%)	1 (2.6)	1 (2.6)	NA	.99
<b>Renal sequelae</b>				
Major (CKD II-V), <i>N</i> (%)	1 (2.6)	0 (0)	NA	.49
Minor (CKD I), <i>N</i> (%)	12 (34.3)	5 (13.2)	0.38 (0.15–0.98)	.03
<b>Total patients with long-term sequelae, <i>N</i> (%)<sup>b</sup></b>	<b>15 (39.5)</b>	<b>5 (13.2)</b>	<b>0.33 (0.13–0.83)</b>	<b>.01</b>

GMR, geometric mean ratio; NA, not applicable.

<sup>a</sup> 8 patients in group A and 8 patients in group B.

<sup>b</sup> Because renal and extrarenal sequelae are not mutually exclusive, the total of long-term sequelae exceeds the number of patients.



# Limitacion:



## ✓ **Estudio retrospectivo**

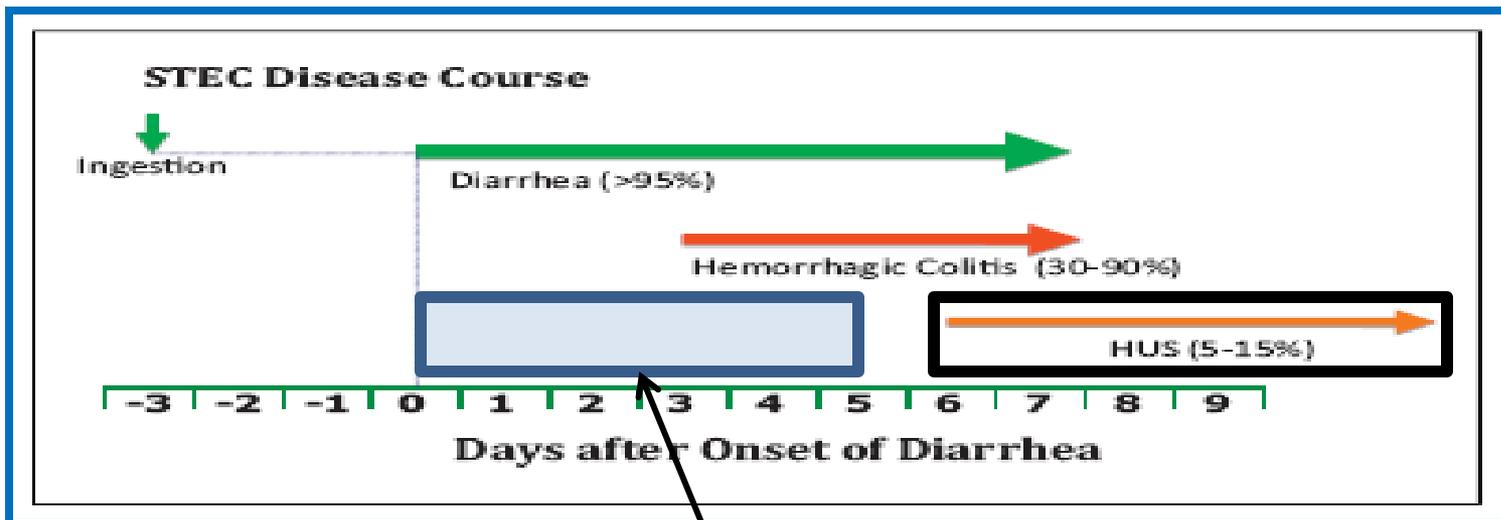
Poco ético para llevar a cabo un ensayo clínico aleatorizado, ya que los pacientes infundidos evolucionan mucho mejor.



**stecSUH = restricción de volumen**



stecSUH = expansión de volumen



ZONA DE ACCIÓN AMPLIADA

# ALGORITMO DIAGNOSTICO Y TERAPEUTICO

DIARREA c/ Sangre

- Diarrea que se convierte en sanguinolenta después de 1-3 días.
- No hay fiebre
- Dolor abdominal que empeora con defecación.
- Más de 5 deposiciones en las últimas 24 horas.
- No hay, pocos o moderados leucocitos fecales
- La diarrea sanguinolenta, persiste durante la primera 8 horas en el hospital.
- No hay bandemia relativa en el diferencial de células blancas.

1gPo2

Cult/Stx/WPS

**INTERNACION POR 48hs**

+  
**EV**

+  
**MANTENIMIENTO C/ SC. ISOTONICA**

**REDUCE**

- **MORBILIDAD DE stecSUH**
- **DOLOR ABDOMINAL**
- **CONTAGIO INTERPERSONAL**





# CRITERIOS DE ALTA



-COPROCULTIVO STEC (-)

-> 4 DIAS DESDE INICIO DE DIARREA

-MARCADORES DE TROMBOSIS/DAÑO ENDOTELIAL (-)

-LABORATORIO SUH (-)

(Hto, formas de hemolisis, LDH, Rto. plaq U, Cr, HPTG)

## Acute Bloody Diarrhea: A Medical Emergency for Patients of All Ages

Lori R. Holtz\*

Marguerite A. Neill†

Phillip I. Tarr\*

GASTROENTEROLOGY 2009;136:1887-1898



## Treatment of Shiga Toxin–Producing *Escherichia coli* Infections

T. Keefe Davis, MD<sup>a</sup>, Ryan McKee, MD<sup>b</sup>,  
David Schnadower, MD, MPH<sup>b</sup>, Phillip I. Tarr, MD<sup>c,\*</sup>

Infect Dis Clin N Am 27 (2013) 577–597

## Shiga Toxin/Verocytotoxin–Producing *Escherichia coli* Infections: Practical Clinical Perspectives

T. KEEFE DAVIS,<sup>1</sup> NICOLE C. A. J. VAN DE KAR,<sup>2</sup> and PHILLIP I. TARR<sup>3</sup>

<sup>1</sup>Division of Nephrology, Department of Pediatrics, Washington University School of Medicine, St. Louis, MO 63110; <sup>2</sup>Division of Nephrology, Department of Pediatrics, Radboud University Medical Centre, Nijmegen, The Netherlands; <sup>3</sup>Division of Gastroenterology, Hepatology, and Nutrition, Department of Pediatrics, and Department of Molecular Microbiology, Washington University School of Medicine, St. Louis, MO 63110

**Citation:** Davis TK, Van De Kar NCAJ, Tarr PI. 2014. Shiga toxin/verocytotoxin-producing *Escherichia coli* infections: practical clinical perspectives. *Microbiol Spectrum* 2(4):EHEC-0025-2014. doi:10.1128/microbiolspec.EHEC-0025-2014.

PACIENTE	EDAD	SEXO	COPROCULT	DIAS DE DIARREA	DIARREA SANGUINO.
1	2	F	E Coli O157:h7	4	SI
2	5	F	E Coli O157:h7	4	SI
3	2	M	E Coli O157:h7	6	SI

Colaboración: Dra. Luz Mery Rivera Parra

# INGRESO

PCTE	PESO	RD	Cr	U	Na	Au	Hto	PLAQ.	LDH
1	13,2	ANUR. 6 hs	1,09	108	134	8,6	27	52000	1841
2	18,4	ANUR. 8 hs	0,7	55	134	6,6	21	46000	993
3	11,1	ANUR. 12 hs	1,34	144	134	11,4	25	47000	1296

Colaboración: Dra. Luz Mery Rivera Parra

# 24 horas

PCTE	PESO	RD	Cr	U	Na	Hto	PLAQ.	LDH
1	14,8 (+12%)	2,5	0,68	87	138	24	67000	1928
2	18,8 (+2%)	2	0,5	35	135	26	53000	1354
3	11,3 (+1,8%)	2,6	0,81	105	136	30	49000	867

Colaboración: Dra. Luz Mery Rivera Parra

# 48 horas

PCTE	PESO	RD	Cr	U	Na	Hto	PLAQ.	LDH
1	14,7	2	0,55	43	139	26	59000	1660
2	18,3	3	0,58	39	137	24	87000	1377
3	11,7	2,5	0,48	32	140	32	98000	830

Colaboración: Dra. Luz Mery Rivera Parra

# Por su atención...





Gianluigi Ardissino

15 de febrero de 2016, 3:41 Para:

"buen365 ."

Thanks for appreciating our work.

The described approach has really changed the outcome of HUS a lot.

Yes, in your example if what is reported by parents is reasonable according to the clinical conditions (including the determination of the child's stroke volume),

I would infuse the child with saline solution as needed to reach a body weight of 11 kg within the next 24 hours.

The earlier's the better.

This specific child will be infused 3 L during the first 24 hours (150-200 cc/hour for the first 12 hours followed by 50-100 cc/hour for the following 12 hours).

If anuric the total amount might have to be reduced as soon as you realize that the patient's diuresis is inadequate.

If you need more details, please do not hesitate to contact me.

Best regards.

Gianluigi Ardissino

Centro per la Cura e lo Studio della Sindrome Emolitico-Uremica (Center for HUS

Control, Prevention and Management) Fondazione IRCCS Ca' Granda Ospedale

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