1° CONGRESO ARGENTINO DE MEDICINA INTERNA PEDIÁTRICA

2° Jornadas Nacionales de Kinesiología en Medicina Interna Pediátrica

2° Jornadas Nacionales de Farmacia Pediátrica Hospitalaria

3° Jornadas Nacionales de Enfermería en Medicina Interna Pediátrica.

5° Encuentro Nacional de Epidemiología Pediátrica

2, 3 y 4 de noviembre de 2016

Por un niño sano en un mundo mejor

"Medicina Interna Pediátrica: la atención centrada en el paciente"

Mesa Redonda

Falla renal aguda como diagnóstico inicial y como complicación en internación por otra causa.

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Nefrólogo Pediátra
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diegoripeau@gmail.com

Objetivos:

- Descripción de caso clínico
- Qué entendemos como “fallo renal”?
- Diagnósticos diferenciales y estudios
- Sostén y tratamiento

Caso clínico:

- Varón de 14 años de edad.

  Peso 75 Kg, Talla 1,70m

- Antecedentes de Epilepsia Generalizada Primaria, en tratamiento con levetiracetam hace 2 años.
- Luxación de articulación escápulo-humeral hace 15 días. Uso intermitente de AINEs. Poliuria (?).

Caso clínico:

- Consulta a guardia por episodio tónico clónico generalizado de 5-10 minutos de duración, seguida de estado post-ictal con vómitos abundantes.

- Se realiza expansión con solución fisiológica e impregnación con Levetiracetam.

Caso clínico:

	Ingreso	Día 1	Día 2	Día 3
Hto (%)	47,3	37,3	38	37
Urea (mg/dl)	35	55	77,5	91,2
Creatinina (mg/dl)	1,38	3,41	6,10	6,62
CPK (U/l)	223	3256	1683	1891
Iono (mEq/L)	135/3,8/99	134/4,2/105	137/4,2/103	137/4,4/102
Bicarbonato (mEq/L)	17,4	16,9	15,9	18,1

Orina completa: δ1010, pH7,5, Prot ++, Hb +++

Sedimento: leuco 4-6/cpo, hemat 0-1/cpo

Diagnósticos Diferenciales

Rabdomiólisis

Nefritis Intersticial

Prerrenal/ NTA

Hipoxia/ NTA

Glomerulonefritis…

Injuria Renal Aguda

Rabdomiólisis

Nefritis Intersticial

Prerrenal/ NTA

Hipoxia/ NTA

Glomerulonefritis

¿Cómo se define la Injuria Renal Aguda?

Definición:

Insuficiencia Renal Aguda

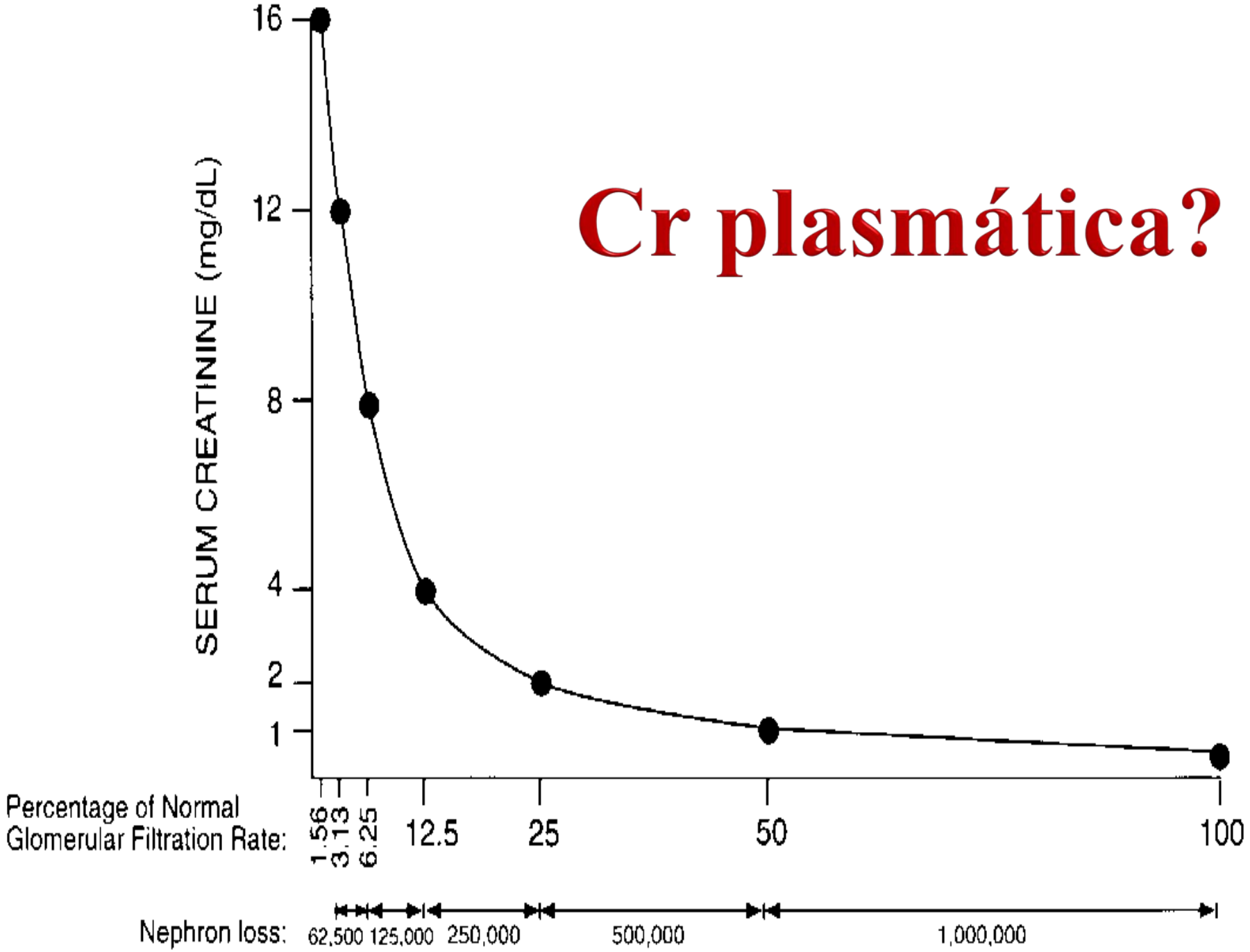
Injuria Renal Aguda

Definición:

Aumento reversible de las concentraciones plasmáticas de creatinina y de los productos de deshecho nitrogenados junto con la incapacidad del riñón de regular los fluídos y la homeostasis de los electrolitos adecuadamente.

- Prevalencia 1-25%
  (8% en internación gral, 35% UTIP)
- Mortalidad 15-60%

Uchino JAMA 2005, 294:813-818



Cr plasmática?

Pediatr Nephrol (2008) 23:2151–2157
DOI 10.1007/s00467-007-0470-x

EDUCATIONAL FEATURE

Biomarkers for the early detection of acute kidney injury

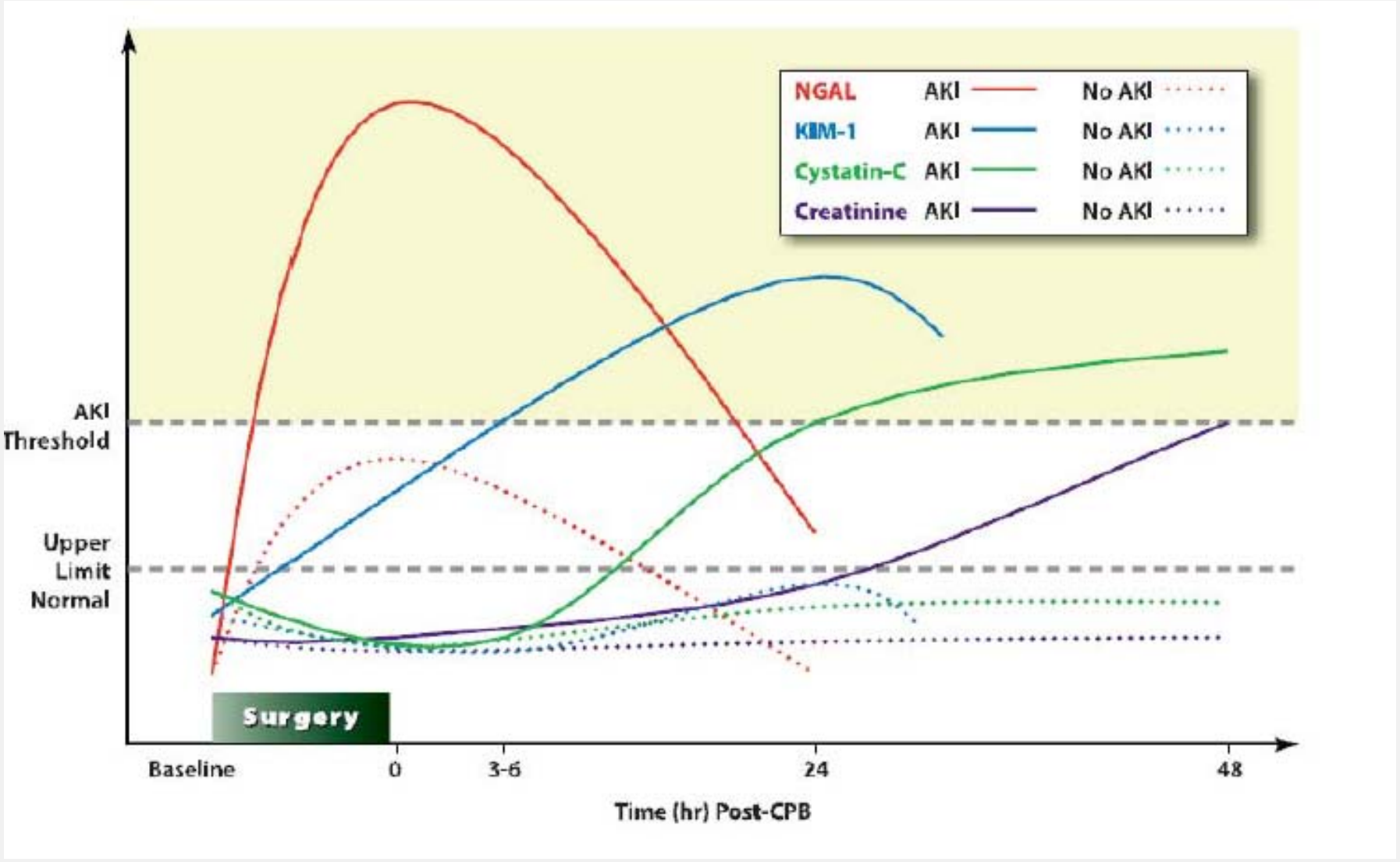
Mai T. Nguyen · Prasad Devarajan

Table 1 Current status of promising acute kidney injury (AKI) biomarkers in various clinical situations

Biomarker Name	Sample Source	Cardiac Surgery	Contrast Nephropathy	Sepsis or ICU	Kidney Transplant	Commercial Test?
NGAL	Plasma	Early	Early	Early	Early	Biosite[a]
Cystatin C	Plasma	Intermediate	Intermediate	Intermediate	Intermediate	Dade-Behring
NGAL	Urine	Early	Early	Early	Early	Abbott[a]
IL-18	Urine	Intermediate	Absent	Intermediate	Intermediate	None
KIM-1	Urine	Intermediate	Not tested	Not tested	Not Tested	None

NGAL neutrophil gelatinase-associated lipocalin, *IL-18* interleukin 18, *KIM-1* kidney injury molecule 1
[a] In development

Nuevos marcadores…



KDIGO® AKI Guideline March 2012

pRIFLE

- Risk
- Injury
- Failure

Kidney International (2007) **71,** 1028–1035

pRIFLE

Table 1 Comparison between the pRIFLE acute kidney injury classification and the KDIGO classification

pRIFLE classification			KDIGO classification		
Category	Estimated Cr clearance[a]	Urine output	Stage	SCr	Urine output
Risk (R)	Decrease by 25 %	<0.5 ml/kg/hr for 8 h	1	Rise of 0.3 mg/dL or 26.5 μmol/L within 48 h OR 50-99 % rise from baseline within 7 days[b]	<0.5 ml/kg/h for 6–12 h
Injury (I)	Decrease by 50 %	<0.5 ml/kg/h for 16 h	2	100–199 % increase in SCr level from baseline within 7 days[b] (2–2.99 × baseline)	<0.5 ml/kg/h for >12 h
Failure (F)	Decrease by 75 % or < 35 mL/min per 1.73 m^2	<0.3 ml/kg/h for 24 h or anuric for 12 h	3	≥200 % increase in SCr level from baseline within 7 day[b] (3.00 × baseline) OR Need for RRT OR In patients <18 years, decrease in eGFR to ≤35 mL/min per 1.73 m^2	<0.3 ml/kg/h for ≥ 4 h OR Anuria for ≥12 h

Kidney International (2007) **71,** 1028–1035

Estimación del Filtrado Glomerular:

FG_e (ml/min/1,73m^2):

$$\frac{\text{Talla (cm)} \times \mathbf{k}}{\text{Cr plasmática (mg/dl)}}$$

k: RN < 1 año: 0,45
1-12 años: 0,55
Mujeres 13 a 21a: 0,55
Varones 13 a 21a: 0,70
(Método Colorimétrico)
Schwartz 1976

k: 1-18años: 0,413
(Método Enzimático)
Schwartz 2009

pRIFLE

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Kidney International (2007) **71,** 1028–1035

INJURIA RENAL AGUDA COMPROMISO SISTEMICO

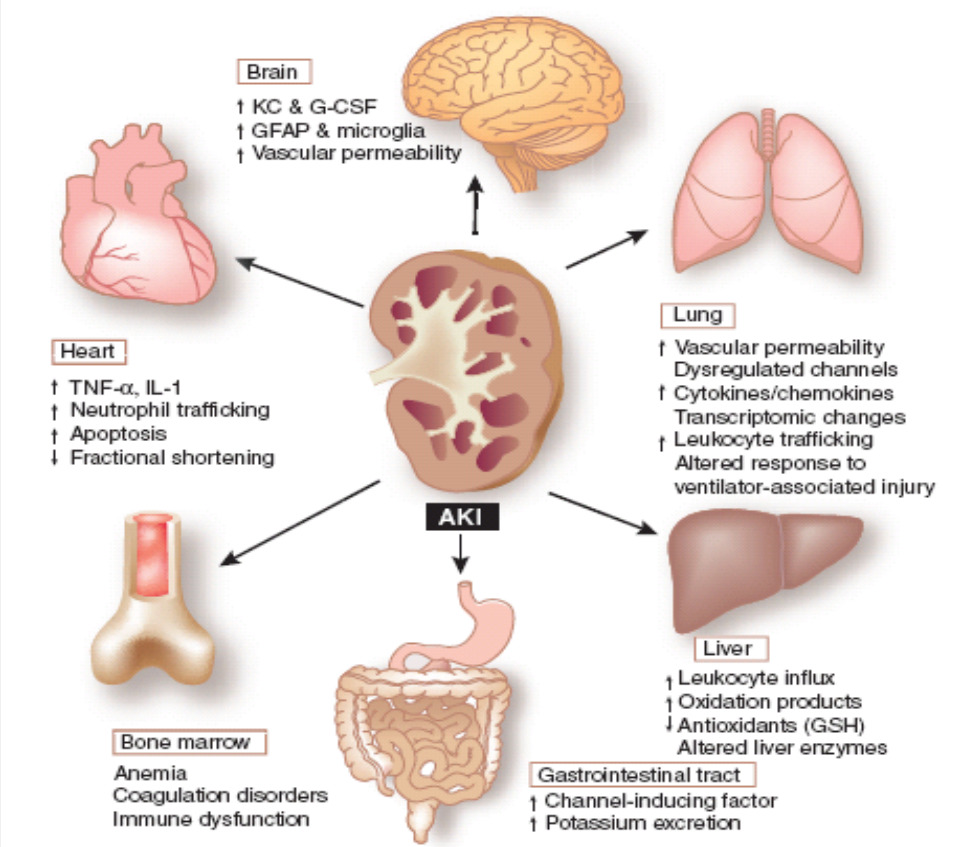


Figure 1 | AKI-induced distant organ effects. AKI leads to changes in distant organs, including brain, lungs, heart, liver, gastrointestinal tract, and bone marrow. Changes have been described in organ function, microvascular inflammation and coagulation, cell apoptosis, transporter activity, oxidative stress, and transcriptional responses. Abbreviations: AKI, acute kidney injury; G-CSF, granular colony-stimulating factor; GFAP, glial fibrillary acidic protein; GSH, glutathione; IL-1, interleukin-1; KC, keratinocyte-derived chemokine; TNF-α, tumor necrosis factor-α.

Consecuencias de la AKI:

Incrementa:

- Los días de internación
- El riesgo de ingresar a Terap
- Requerimientos de ARM
- La mortalidad
- El riesgo de progresar a ERC

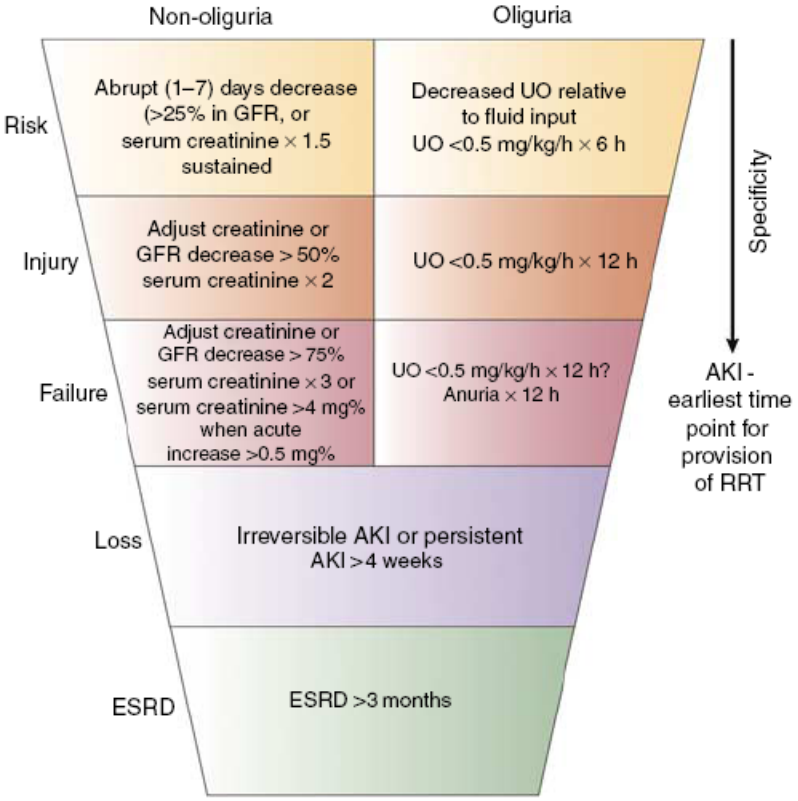
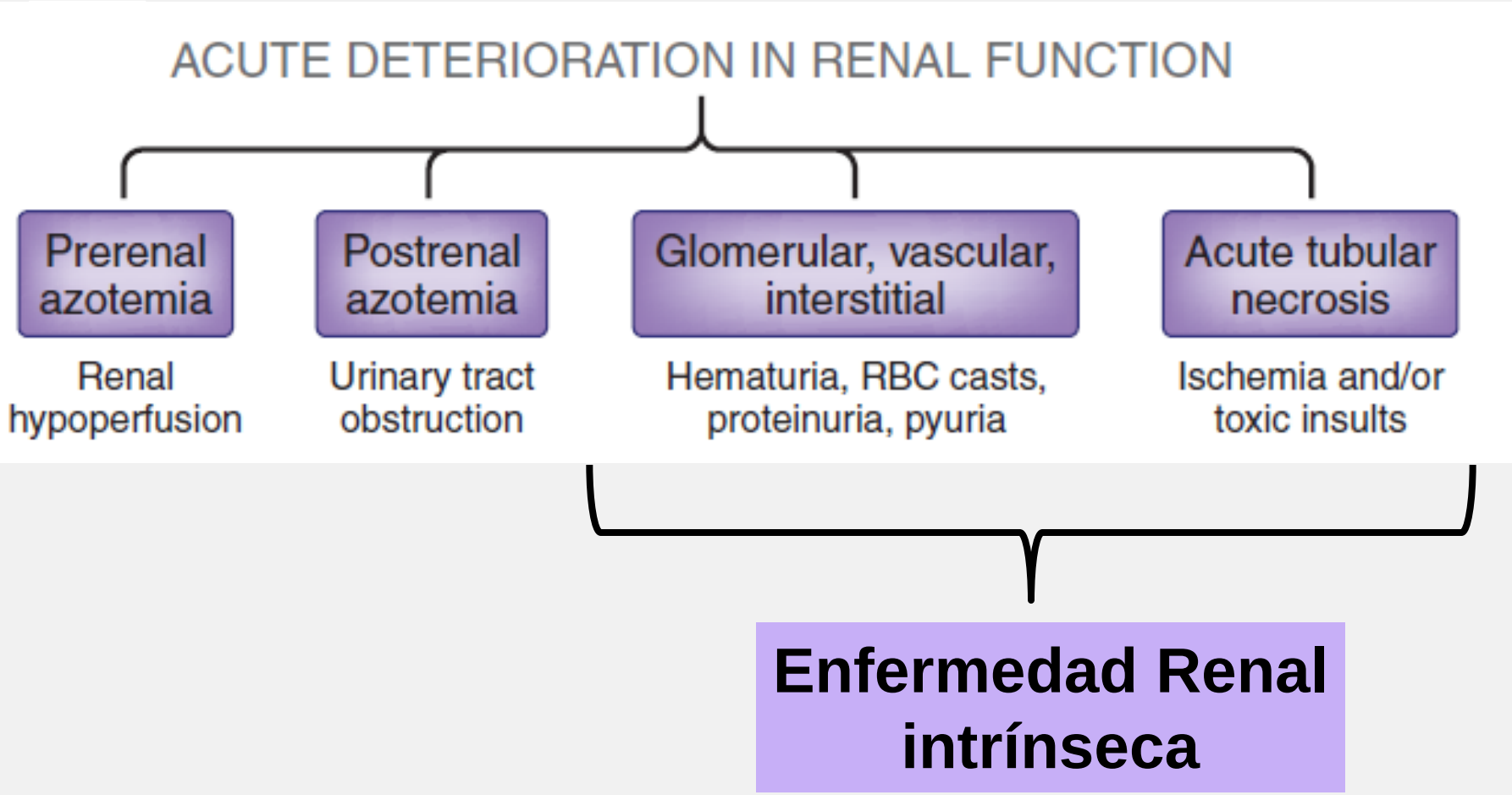


Figure 1 | RIFLE Criteria for Diagnosis of AKI. Adapted with permission from Lameire *et al.*[16]

Pediatr Nephrol (2009) 24:253–263

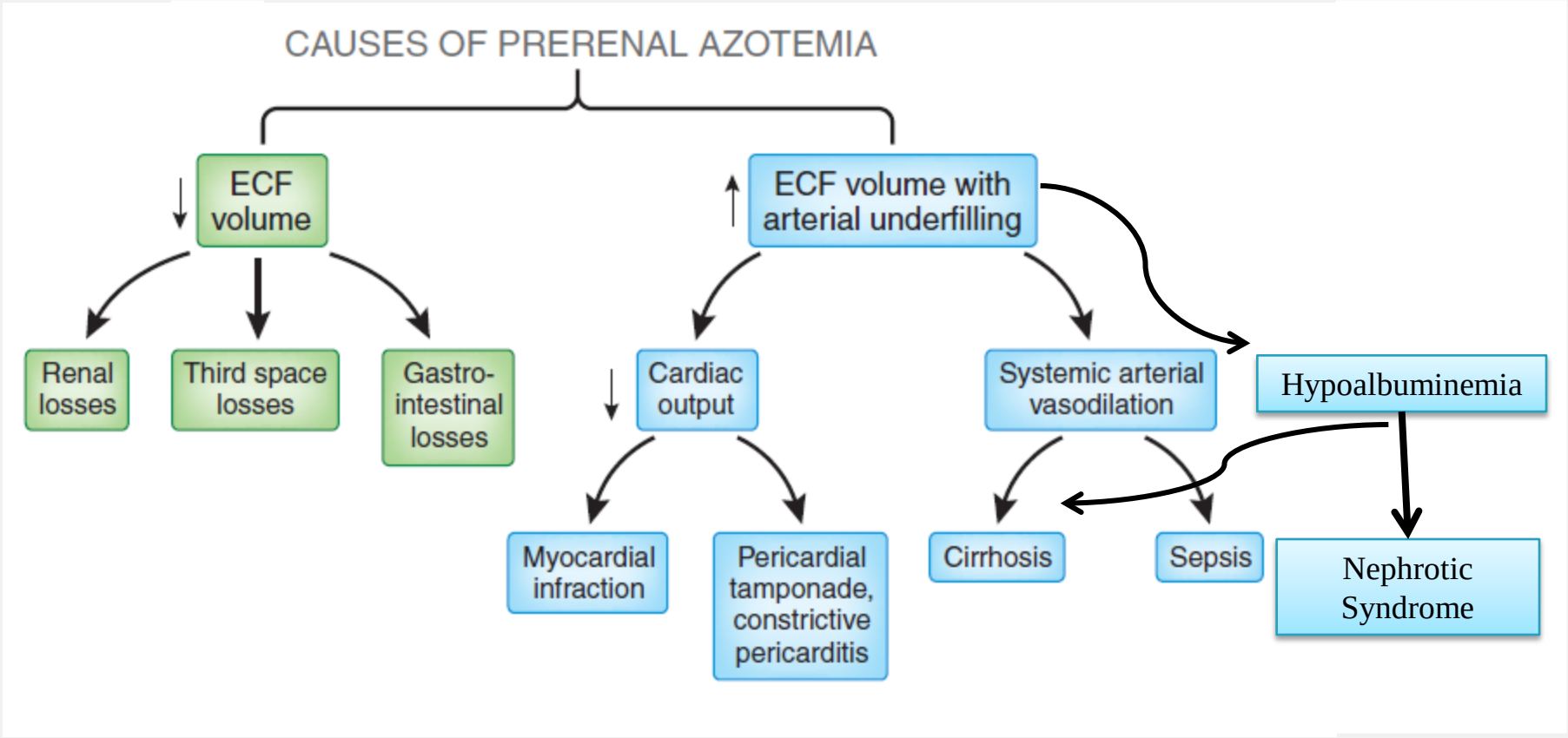
Kidney International (2007) **71,** 1028–1035

¿Cómo la puedo clasificar y estudiar?



Enfermedad Renal intrínseca

J Am Soc Nephrol 22: 1610–1613, 2011

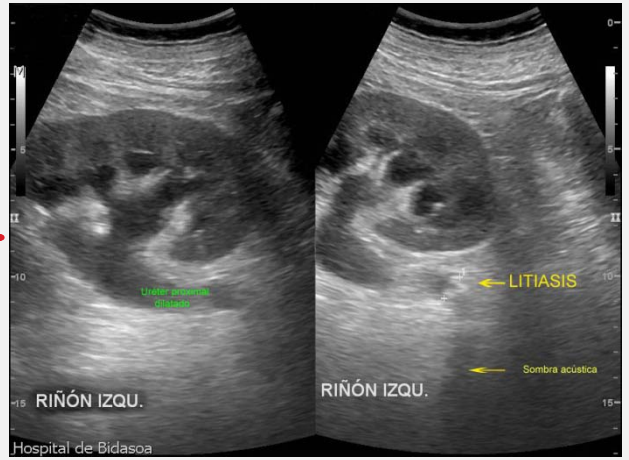


J Am Soc Nephrol 22: 1610–1613, 2011

Table 1 Etiology of common causes of acute kidney injury

Type	Etiology
Pre-renal injury	Decreased true intravascular volume
	Decreased effective intravascular volume
Intrinsic renal disease	Acute tubular necrosis (vasomotor nephropathy)
	Hypoxic/ischemic insults
	Drug induced
	Toxin mediated
	Endogenous toxins—hemoglobin, myoglobin
	Exogenous toxins—ethylene glycol, methanol
	Uric acid nephropathy and tumor lysis syndrome
	Interstitial nephritis
	Drug induced
	Idiopathic
	Glomerulonephritis—RPGN
	Vascular lesions
	Renal artery thrombosis
	Renal vein thrombosis
	Cortical necrosis
	Hemolytic uremic syndrome
	Hypoplasia/dysplasia with or without obstructive uropathy
	Idiopathic
	Exposure to nephrotoxic drugs in utero
Obstructive uropathy	Obstruction in a solitary kidney
	Bilateral ureteral obstruction
	Urethral obstruction

Estudio de imágenes



Pediatr Nephrol (2009) 24:253–263

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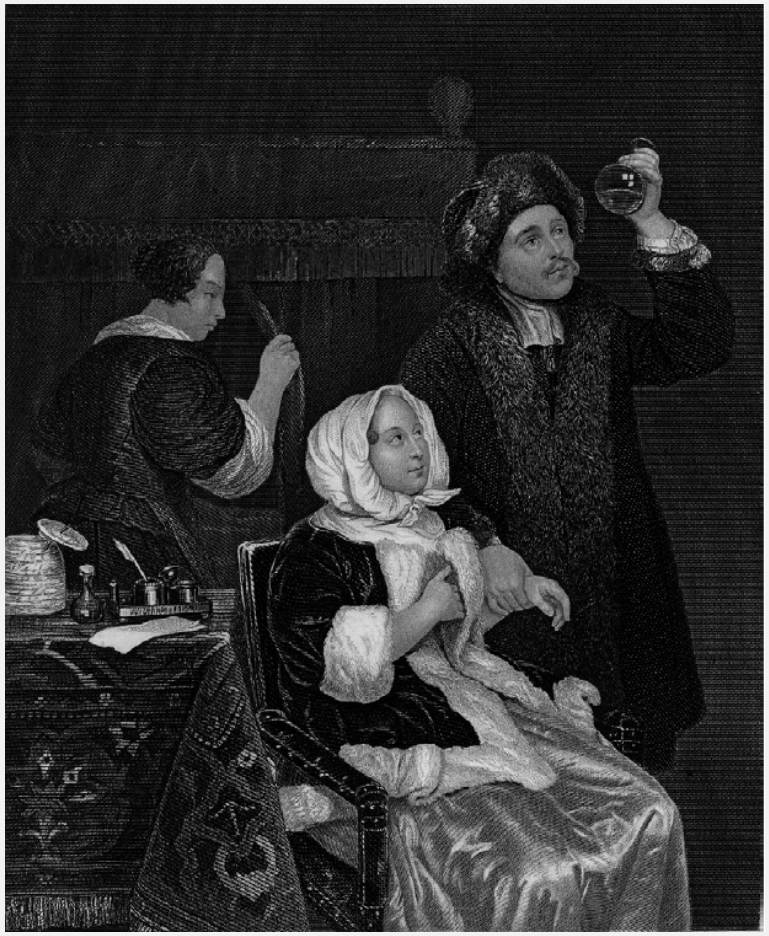
Pediatr Nephrol (2009) 24:253–263

WORLD KIDNEY FORUM

Looking at the Urine: The Renaissance of an Unbroken Tradition

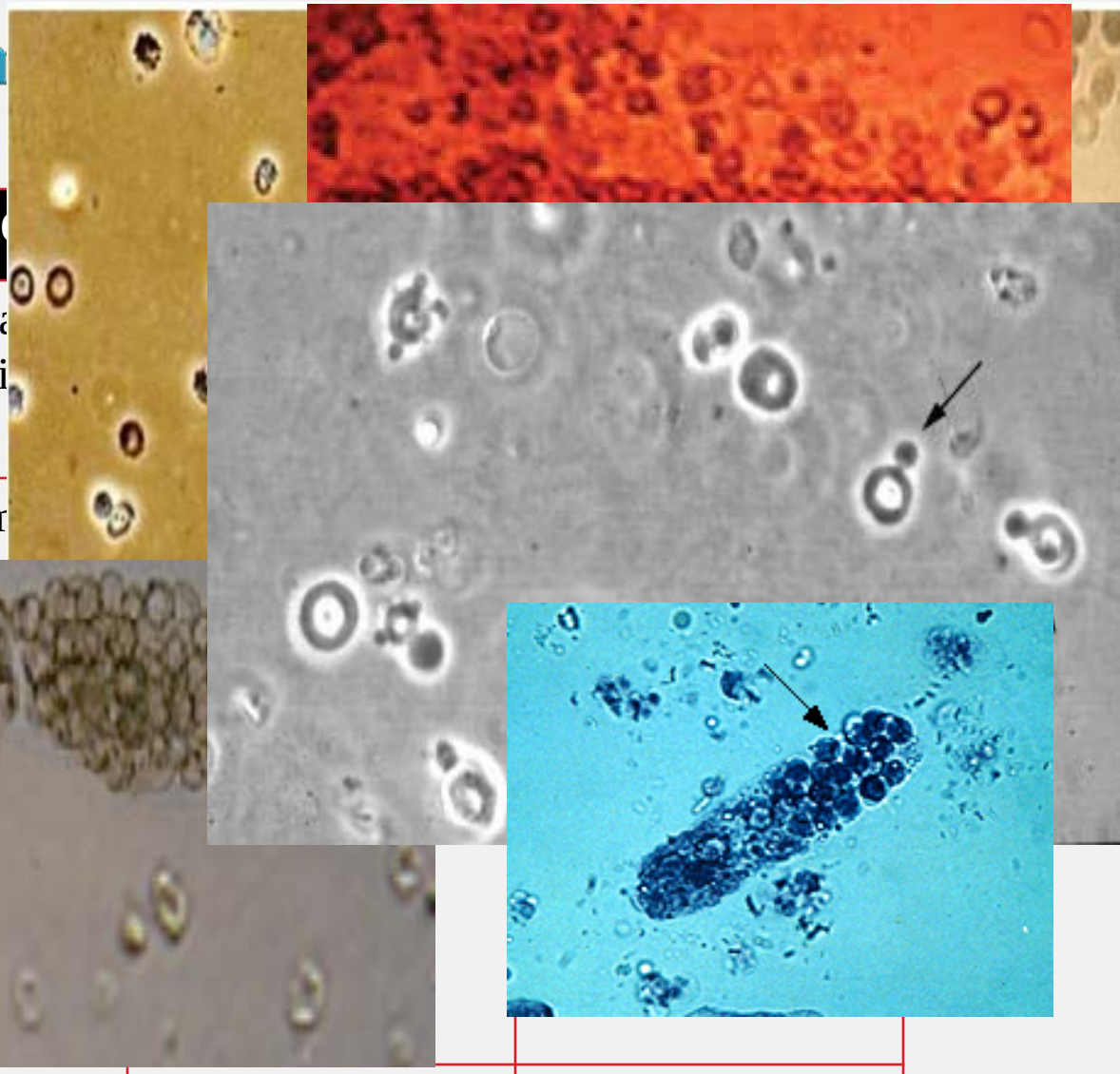
Garabed Eknoyan, MD



American Journal of Kidney Diseases, Vol 49, No 6 (June), 2007: pp 865-872

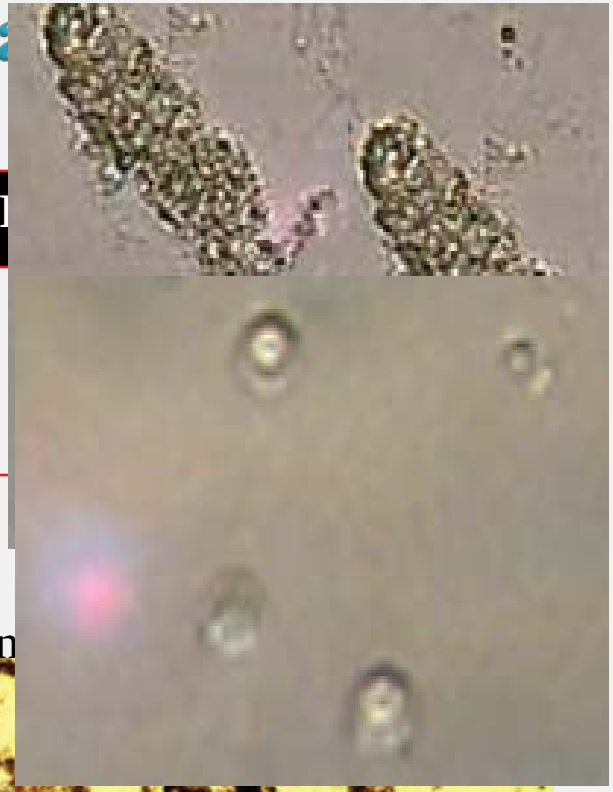
Diagnóstico de AKI
Utilidad del exam

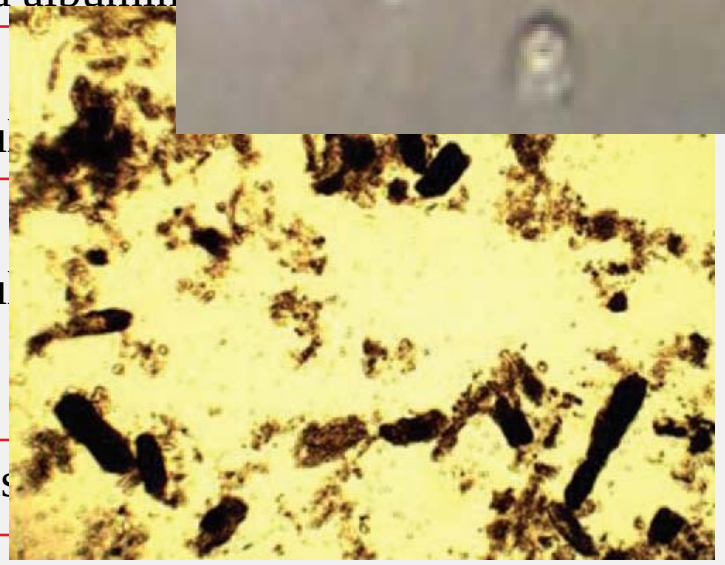
SITIO	SEDIMENT		
PRERENAL	Normal / Esca cilindros hiali granulosos		
RENAL GNAguda	Cilindros hem Leucoc Hemat		
RENAL NTA	Cel. Tu Cil. gra		
RENAL NEFRITIS INTERST. AGUDA	leucoc eosino leucoc cél. tub		
POSTRENAL	Hematíes,cristales	trazas	>1.010



Diagnóstico de AKI
Utilidad del examen de orina

SITIO	SEDIMENTO U.	PROTEINU
PRERENAL	Normal / Escasos cilindros hialinos y granulosos	trazas
RENAL GNAguda	Cilindros hemát. Leucoc. y granul. Hematíes dismorf.	++ a ++++ Glomerular (Pred albúmin
RENAL NTA	Cel. Tubul. Renal. Cil. granulosos	++ Tubu
RENAL NEFRITIS INTERST. AGUDA	leucocitos, hemat., eosinofilos, cilind leucoc y granul, cél. tubul. renal.	++ Tubu
POSTRENAL	Hematíes,cristales	trazas

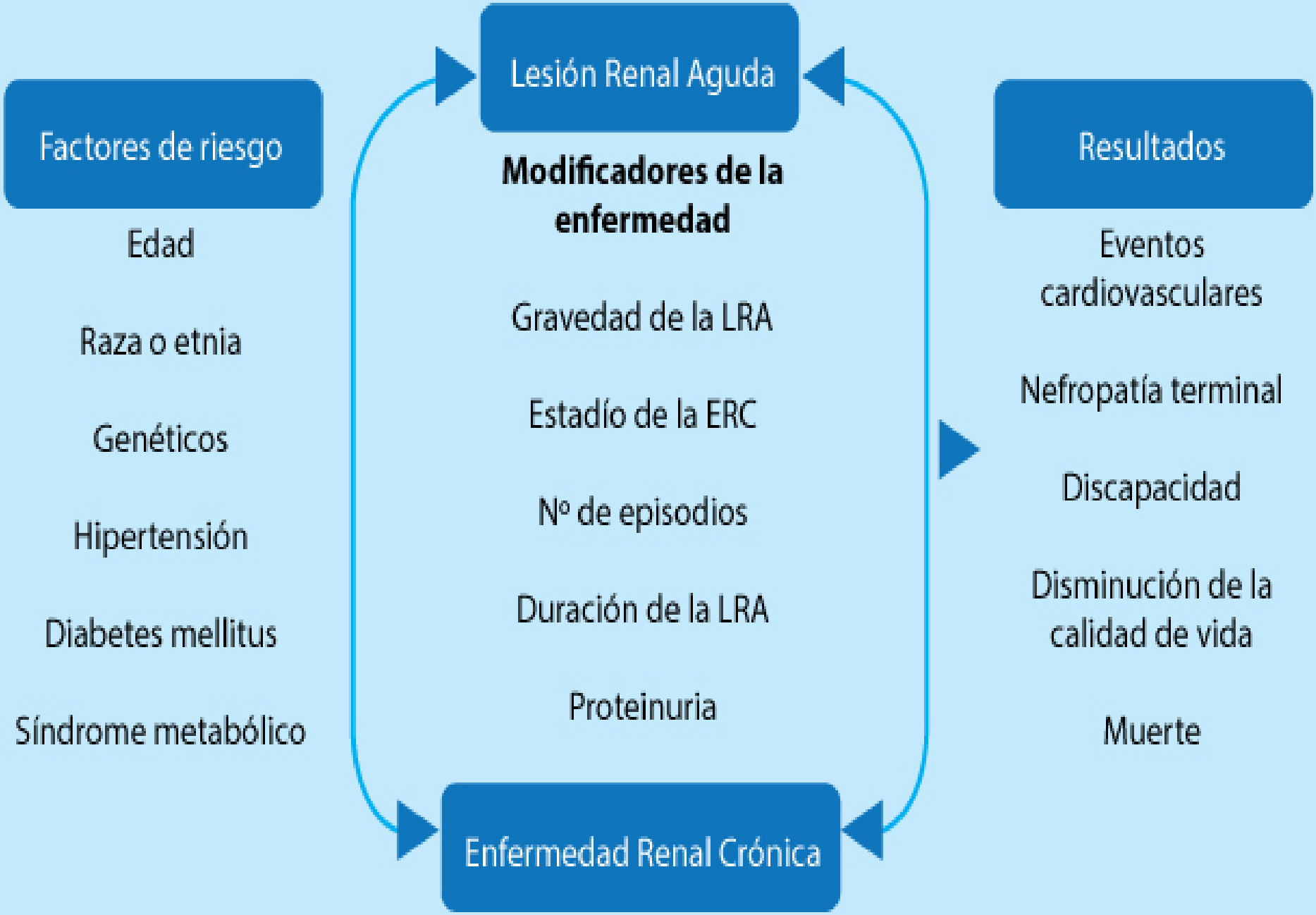




Indices urinarios

Indices	Prerenal	Renal
Urine sediment	Hyaline casts	Abnormal
Specific gravity	>1.020	~1.010
Urine osmolality (mOsm per kg H_2O)	>500	<350
U_{Na} (mmol/l)	<20	>40
Fractional excretion		
Sodium (%)	<1	>2
Urea (%)	<35	>35
Uric acid (%)	<7	>15
Lithium (%)	<7	>20
Low molecular weight proteins	Low	High
Brush border enzymes	Low	High

KDIGO® AKI Guideline March 2012


Lesión Renal Aguda
Factores de riesgo
Edad
Raza o etnia
Genéticos
Hipertensión
Diabetes mellitus
Síndrome metabólico
Modificadores de la enfermedad
Gravedad de la LRA
Estadío de la ERC
Nº de episodios
Duración de la LRA
Proteinuria
Resultados
Eventos cardiovasculares
Nefropatía terminal
Discapacidad
Disminución de la calidad de vida
Muerte
Enfermedad Renal Crónica

Acute Kidney Injury Associated with High Nephrotoxic Medication Exposure Leads to Chronic Kidney Disease after 6 Months

Shina Menon, MD[1], Eric S. Kirkendall, MD[2], Hovi Nguyen, MPH[1], and Stuart L. Goldstein, MD[1]

Table IV. Comparison between subjects with AKI and controls

	Subjects with AKI	Controls (NTMx exposure without AKI)	*P* value
Age (y)	8.9 (7.0)	7.1 (6.1)	.13
Males	51 (66.2)	29 (50.9)	.07
Primary team			
BMT/oncology	44 (57.1)	32 (56.1)	.92
Gastrointestinal/liver	15 (19.5)	14 (24.6)	.48
Pulmonary	9 (11.7)	8 (14)	.71
Cardiology	5 (6.5)	2 (3.5)	
Other	4 (5.2)	1 (1.8)	
Baseline eGFR (mL/min/1.73 m^2)	118 (15.1)	119.9 (15.4)	.48
Subjects on ≥1 NTMx at follow-up	41 (53.2)	23 (40.4)	.14
eGFR at 6 mo (mL/min/1.73 m^2)	(n = 77) 113.8 (30.6)	(n = 57) 123.4 (14.5)	.04
Distribution of eGFR at 6 mo (mL/min/1.73 m^2)	(n = 77)	(n = 57)	
<60	2	0	
60-90	16	0	
90-150	50	56	
>150	9	1	
GFR by cystatin C (mL/min/1.73 m^2)	(n = 52) 80.2 (23.4)	(n = 25) 111.4 (24.3)	<.01
Up/c ratio, mg/mg	(n = 35)	(n = 15)	
<0.3	11	10	
0.3-3	20	5	
>3	4	0	
Up/c ratio at 6 mo	0.9 (1.14)	0.27 (0.21)	.04
Subjects with hypertension	29/77 (37.7)	11/57 (19.3)	.01
Subjects with ≥1 sign of CKD	26 (33.7)	5 (8.8)	<.01

J Pediatr 2014;165:522-7

Prevención, sostén y tratamiento

Cual es el mejor fluídos para la expansión inicial del volumen intravascular, para prevenir la AKI?

1. Solución Fisiológica (ClNa 9%)
2. Ringer Lactato
3. Albúmina 20%
4. Coloides Sintéticos (Hidroximetilalmidón al 6%)
5. No existe la solución ideal

Fluid Management and Use of Diuretics in Acute Kidney Injury

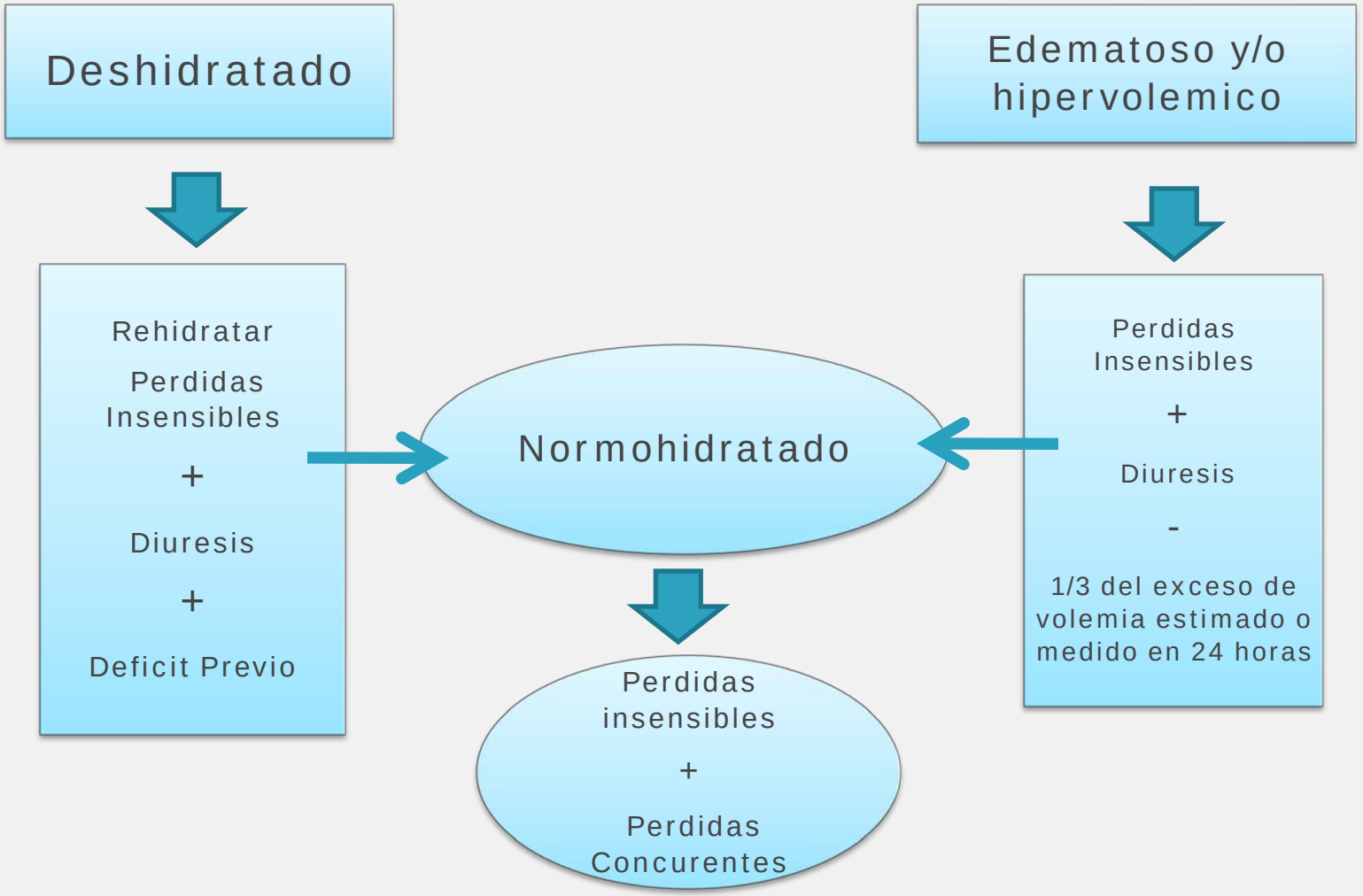
Annie-Claire Nadeau-Fredette and Josée Bouchard

CLINICAL SUMMARY

- There is increasing evidence suggesting that isotonic crystalloids should be used instead of colloids as initial management for expansion of intravascular volume in critically ill adult patients at risk for AKI or with AKI, such as those with sepsis, septic shock, or trauma.
- The optimal timing and amount of initial volume resuscitation to prevent AKI, to reduce its severity, and to improve mortality in these clinical settings still needs to be defined, although a more aggressive early fluid repletion is probably beneficial.
- Once AKI occurs and that hemodynamic status is stabilized, the relevance of restrictive fluid management and the use of diuretics or renal replacement therapy to prevent or treat fluid overload and improve outcomes in this population, without worsening kidney function, needs to be confirmed with randomized controlled trials.

Advances in Chronic Kidney Disease, Vol 20, No 1 (January), 2013: pp 45-55

AKI: Fluidoterapia



Prevención de AKI:

- Uso racional de drogas potencialmente nefrotóxicas.

Antivirales
Aciclovir, Ganciclovir, Foscarnet

AINEs

QMT
Ifosfamida, Cisplatino
Metrotexate

Anticonvulsivante

ATB
Beta-Lactámicos, Aminoglucósidos
Vancomicina

Contrastes endovenosos

Antifúngicos

Pediatr Nephrol (2016) 31:145–151

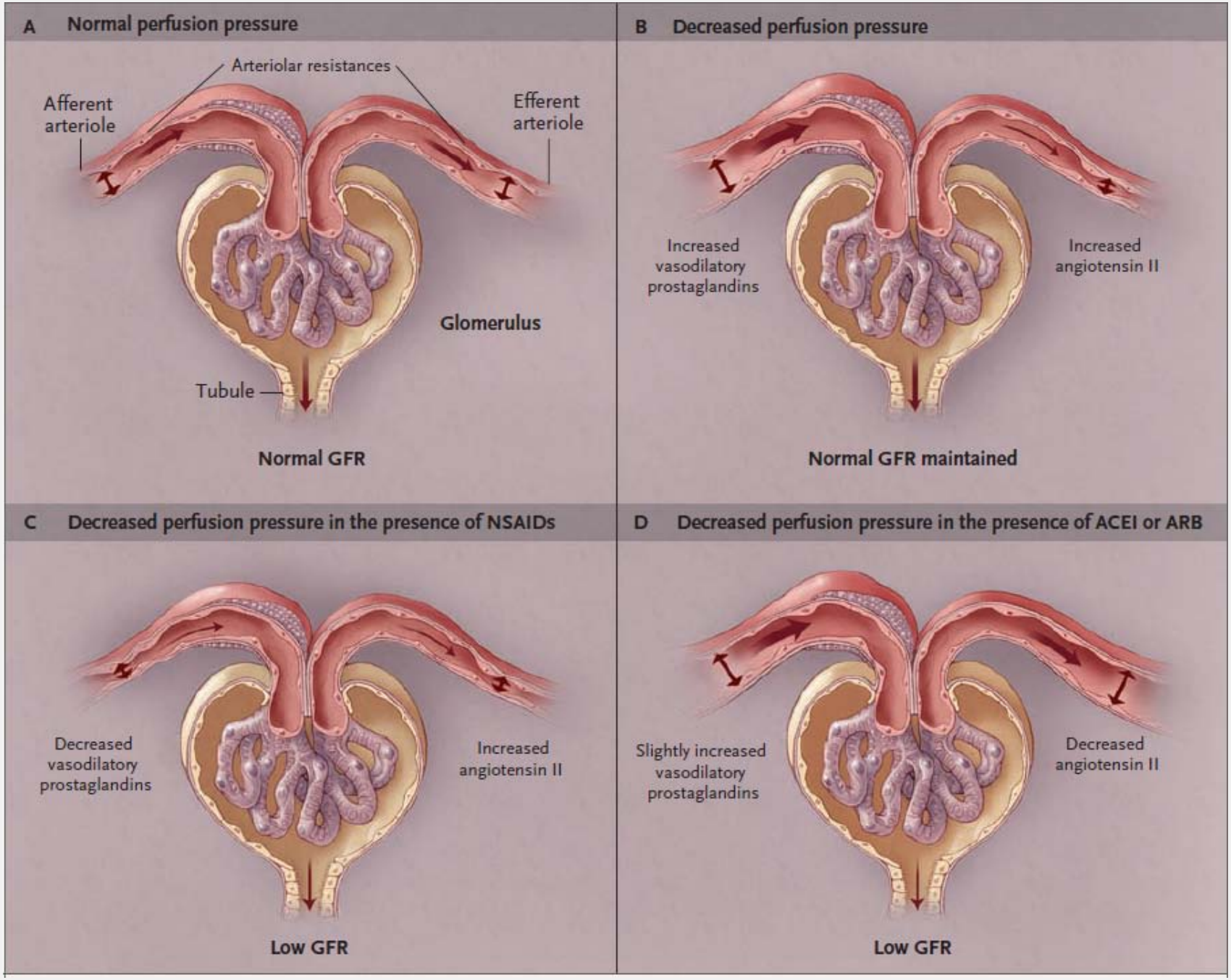
Pediatr Nephrol (2015) 30:1873–1878
DOI 10.1007/s00467-015-3105-7

ORIGINAL ARTICLE

Ibuprofen-associated acute kidney injury in dehydrated children with acute gastroenteritis

Alejandro Balestracci[1] · Mauricio Ezquer[2] · María Eugenia Elmo[2] · Andrea Molini[2] · Claudia Thorel[2] · Milagros Torrents[2] · Ismael Toledo[1]

Characteristic	No acute kidney injury (n=59)	Acute kidney injury (n=46)	p value
Gender (female/male)	28/31	27/19	0.25
Age (years)	1.74 (0.16–14)	0.66 (0.16–15.75)	<0.001
Weight (kg)	10.8 (3.5–37)	7.72 (3.15–56.7)	<0.001
Age- and sex-specific body mass index percentile[a]	46 (3–99)	37 (3–99)	0.36
Percentage of dehydration	7 (3–10)	7 (3.5–10)	0.08
Vomiting	10 (17 %)	12 (26 %)	0.25
Fever	24 (41 %)	14 (31 %)	0.27
Ibuprofen exposure	29 (49 %)	34 (74 %)	0.01



N Engl J Med 2007;357:797-805.

Prevención de AKI:

- Uso racional de drogas potencialmente nefrotóxicas.
- Hidratación agresiva en niños con tratamientos de quimioterapia.
- No se recomienda:
  - «Dosis bajas" (*0.5 a 3 microgramos* ***(µg)/kg/minuto) de dopamina para prevenir AKI, ni en el AKI establecido.*** Uso de inotrópicos en el paciente con shock vasomotor y AKI o riesgo de AKI.(1)
  - Utilizar furosemida para aumentar el ritmo diurético, excepto para el tratamiento de la hipervolemia. (2)
  - Utilizar manitol para aumentar el ritmo diurético. (3)

(1) Ann. Intern. Med. 2005; 142: 510.
(2) BMJ 2006; 333 (7565): 420.
(3)*Anaesthesia 2008; 63: 576–582.*

AKI: Diálisis

- Oliguria/Anuria para mantener un adecuado aporte nutricional.
- Hipervolemia con ICC, edema pulmonar y/o hipertensión arterial severa no tratable con medidas conservadoras.
- Anomalías electrolíticas y del estado ácido base con riesgo de vida: hiperkalemia ***≥ 7 mEq/l con manifestaciones ECG, hipernatremia, hiponatremia, acidosis metabólica no corregida con bicarbonato.***
- Signos y síntomas de uremia: pericarditis, alteración del sensorio.
- Aumento progresivo de los niveles de urea (*>160-200 mg/dl) con recuperación de la función renal no esperable.*
- Síndrome de lisis tumoral con hiperuricemia *>10 mg/dl y oliguria.*
- Error congénito del metabolismo con acidosis orgánica severa o hiperamoniemia.
- Ingestión de tóxicos: salicilatos, metanol, etanol, teofilina, paraquat (según concentraciones séricas y criterios clínicos)

RRT in AKI: Start Early or Wait?

Kathleen D. Liu and Paul M. Palevsky†‡*

Clin J Am Soc Nephrol 11: 1867–1871, 2016. doi: 10.2215/CJN.06690616

	AKIKI Trial, n=620	
	31 KDIGO stage 3 AKI and one of the following: catecholamine infusion and/or invasive mechanical ventilation Modality/dosing at discretion of study site	
	Early RRT, n=311	Delayed RRT, n=308
Criteria for initiation of RRT	<6 h after Reaching KDIGO stage 3 AKI	Presence of BUN>112 mg/dl, serum K^+ >6 mmol/L, pH<7.15, pulmonary edema caused by fluid overload, or oliguria or anuria >72 h
SOFA score at randomization	10.9±3.2	10.8±3.1
Received RRT (%)	305 (98)	157 (51)
Median time from KDIGO stage 2 AKI to RRT (IQR), h	4.3 (2.7–5.9)	57 (28–83)
Median time from KDIGO stage 3 AKI to RRT (IQR), h		
Serum creatinine at initiation of RRT, mg/dl	3.3±1.4	5.3±2.3
BUN at initiation of RRT, mg/dl	52±24	90±34
Serum K^+ at initiation of RRT, mmol/L	4.4±0.7	5.1±0.9
Serum tCO_2 at initiation of RRT, mmol/L	18.9±4.9	16.6±5.6
Initial modality of RRT, %		
CRRT	44	45
IHD	56	55
Mortality, %		
28 d	41.6	43.5
60 d	48.5	49.7 (P=0.79)
90 d		
Dependence on RRT among survivors (%)		
Day 28	22/179 (12.3)	17/178 (9.6; P=0.51)
Day 60	3/157 (1.9)	8/155 (5.2; P=0.12)
Day 90		

Caso clínico:

	Día 4	Día 5	Día 8
Hto (%)			42
Urea (mg/dl)	104	106	76
Creatinina (mg/dl)	6,14	5,79	2,1
CPK (U/l)	1639	1186	166
Iono (mEq/L)	138/4,68/104	137/5/107	140/4,9/100
Bicarbonato (mEq/L)	16,9	20,5	26,3

Orina completa: δ1010, pH7,5, Prot ++, Hb +++

Sedimento: leuco 4-6/cpo, hemat 0-1/cpo

Orina 24hs: FGm: 47 ml/min/1,73m2 vs FGe 20ml/min/1,73m2

Rabdomiólisis

Nefritis Intersticial

Prerrenal / NTA

Hipoxia/ NTA

~~Glomerulonefritis~~

Conclusiones:

- Medir siempre creatinina sérica y diuresis en los pacientes internados. Estratificar el riesgo de AKI.
- Determinar la etiología de la AKI siempre que sea posible, detectar causas potencialmente reversibles (Evitar nefrotóxicos).
- Utilidad del sedimento urinario en el diagnóstico etiológico
- Evaluar la evolución del paciente a largo plazo, luego *de un episodio de AKI*

Muchas Gracias