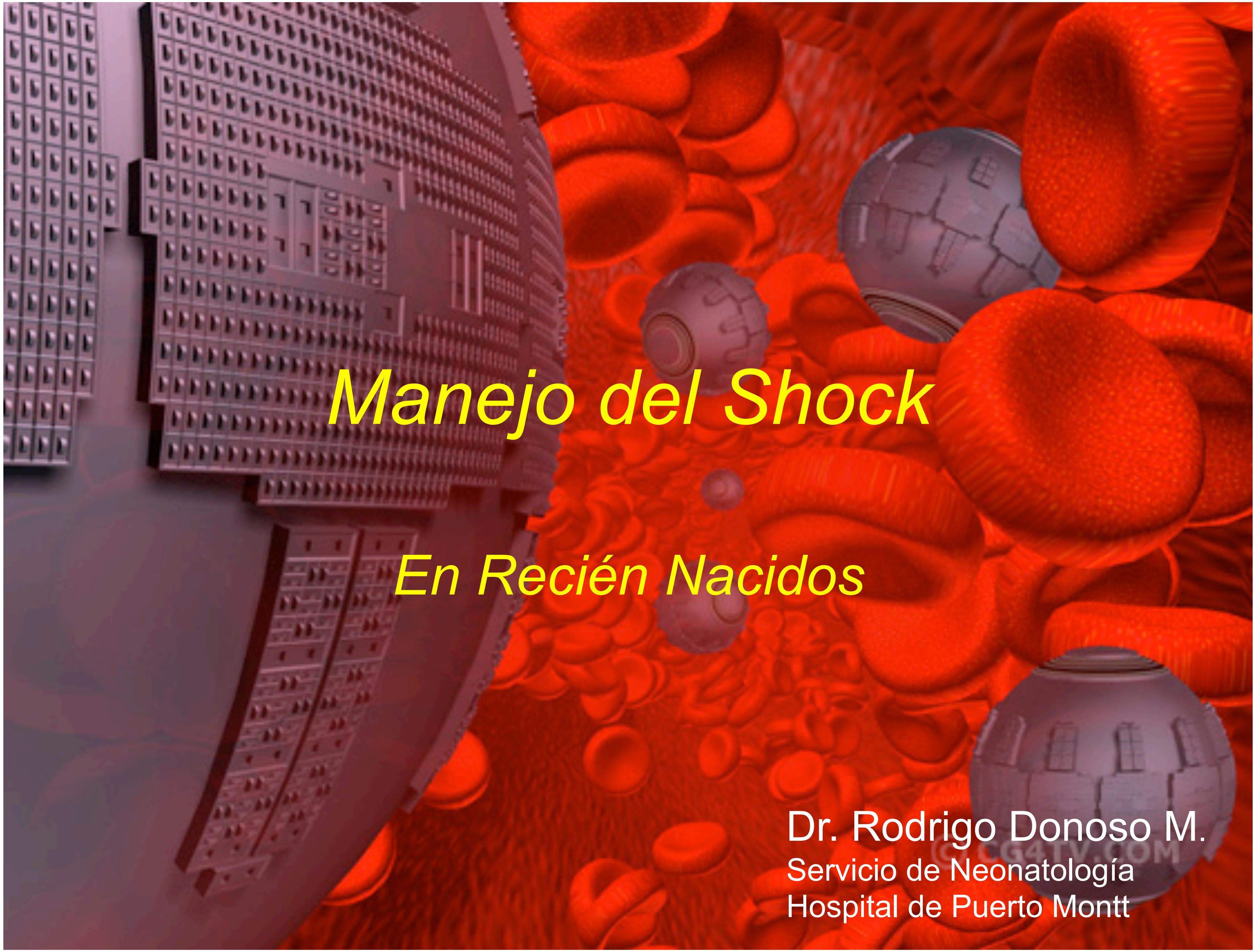

Manejo del Shock

En Recién Nacidos

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Introducción

- Las alteraciones de la PA son un problema frecuente en las UCIN, asociándose a otras patologías como hemorragias intraventriculares.

Seminars in Fetal & Neonatal Medicine Volume 11, Issue 3, Páginas 149-224 (Junio 2006)

Introducción

- Aunque existen valores epidemiológicos de PA normal para RNT y RNPT, aún es controversial el rango de PA para distintas EG y postnatales que asegure una adecuada y segura perfusión de órganos.

Early Human Development (2005) 81, 399—404

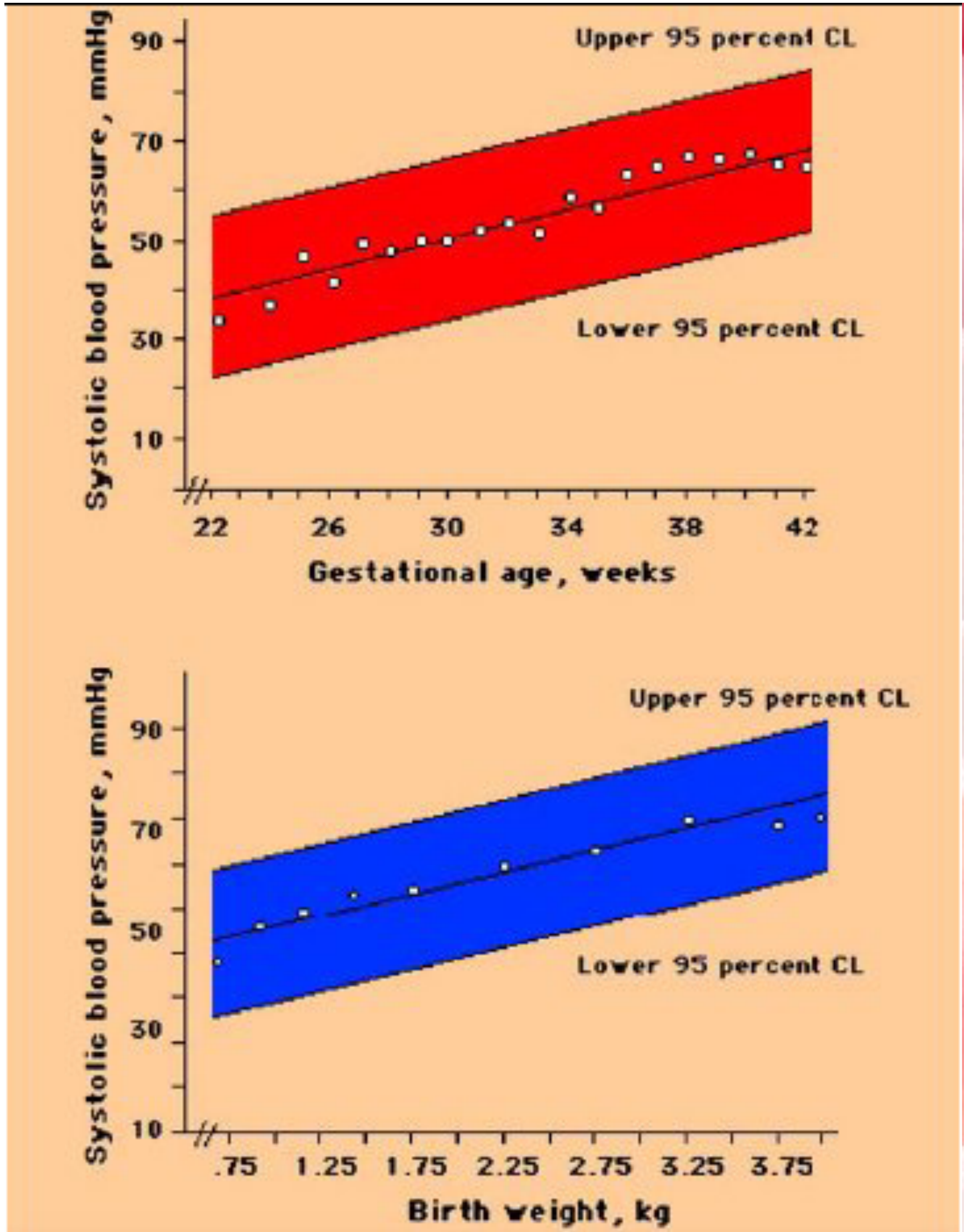


Figura 1.- Presión arterial neonatal. Regresión lineal de la mediana de presión arterial sistólica sobre edad gestacional y peso de nacimiento en 329 infantes ingresados a UCIN al día 1 de vida. La mediana de presión arterial sistólica y 95% de intervalo de confianza (CI) para edad gestacional y peso de nacimiento en aumento se trazan sobre las respectivas líneas de regresión (reproducidas con permiso de Zubrow y cols.
2).

Seminars in Fetal & Neonatal
Medicine Volume 11, Issue 3,
Páginas 149-224 (Junio 2006)

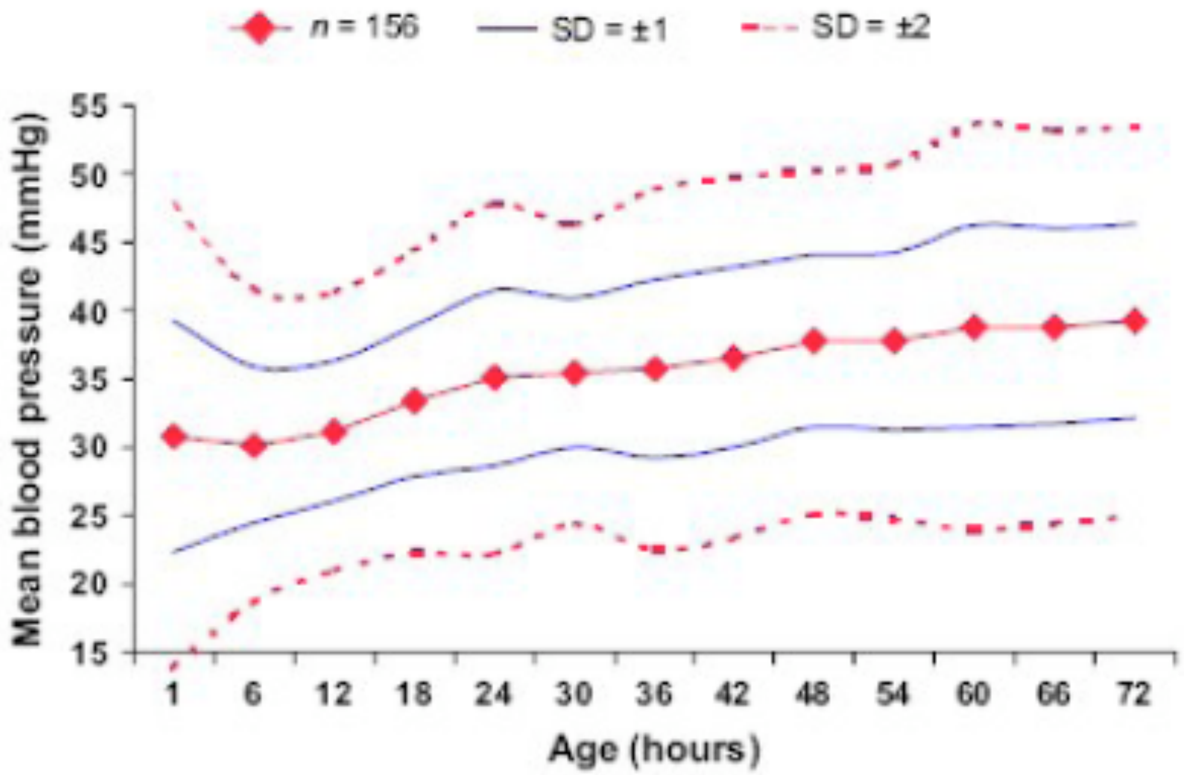


Figure 2 Mean blood pressure of all extremely low birth weight (ELBW) infants in the first 72 hours of life (from Fanaroff et al.[8]).

Figura 2.- Presión arterial media de todos los niños de extremo bajo peso de nacimiento (EBPN) en las primeras 72 horas de vida (de Fanaroff y cols 8).

Seminars in Fetal & Neonatal Medicine Volume 11, Issue 3, Páginas 149-224 (Junio 2006)

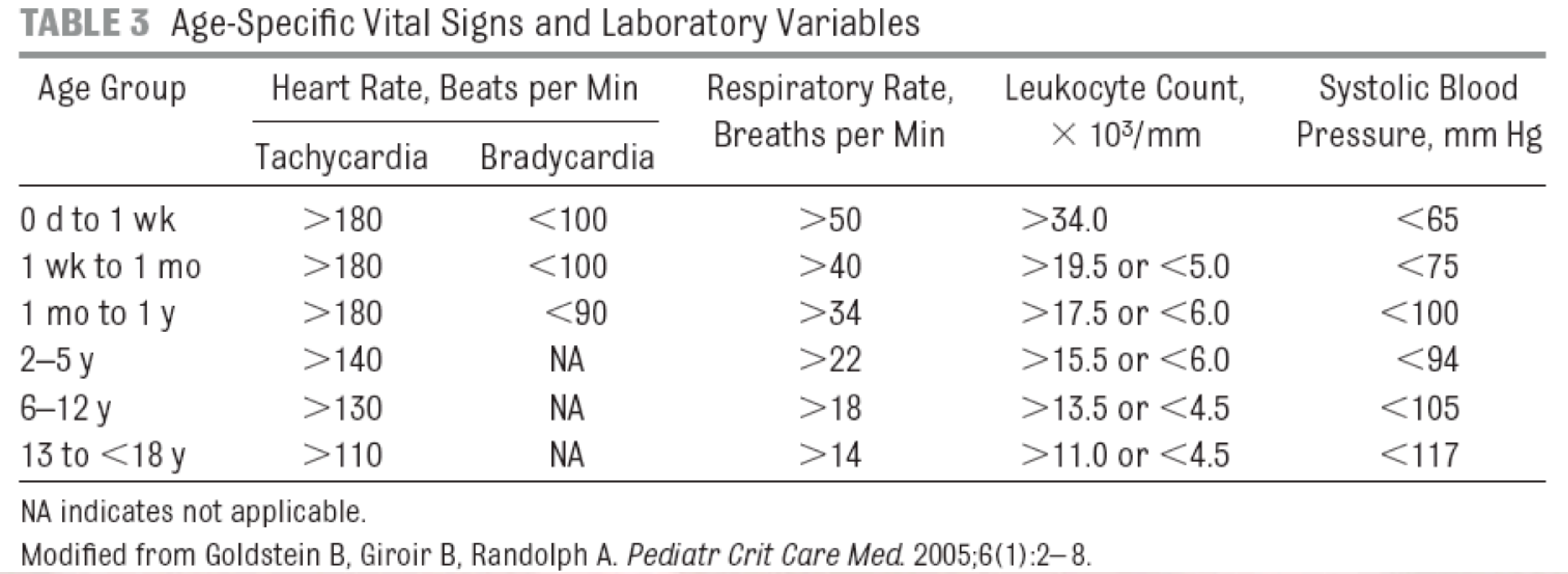


TABLE 3 Age-Specific Vital Signs and Laboratory Variables

Age Group	Heart Rate, Beats per Min		Respiratory Rate, Breaths per Min	Leukocyte Count, × 10³/mm	Systolic Blood Pressure, mm Hg
	Tachycardia	Bradycardia			
0 d to 1 wk	>180	<100	>50	>34.0	<65
1 wk to 1 mo	>180	<100	>40	>19.5 or <5.0	<75
1 mo to 1 y	>180	<90	>34	>17.5 or <6.0	<100
2–5 y	>140	NA	>22	>15.5 or <6.0	<94
6–12 y	>130	NA	>18	>13.5 or <4.5	<105
13 to <18 y	>110	NA	>14	>11.0 or <4.5	<117

NA indicates not applicable.

Modified from Goldstein B, Giroir B, Randolph A. *Pediatr Crit Care Med.* 2005;6(1):2–8.

PEDIATRICS Volume 125, Number 5, May 2010

Fisiopatología

- Muchos RNPT sufren de períodos de bajo flujo sistémico (BFS) durante el primer día de vida que puede repercutir en muerte o daño neurológico
- Estos períodos de BFS ocurre en 1/3 de < de 30 sem EG y la mayoría de < de 27 sem. Y en general en las primeras 12 hrs. de vida
- El BFS se asocia a pctes. con:

-PMVA alta en VM,

-DAP precoz de gran diámetro

-Resistencia vascular sistémica alta

-Miocardio inmaduro (que vence resistencia baja fetal, pero no resistencia alta RN por aumento de cortisol, catecolaminas)

Early Human Development (2005) 81, 413—422

Fisiopatología

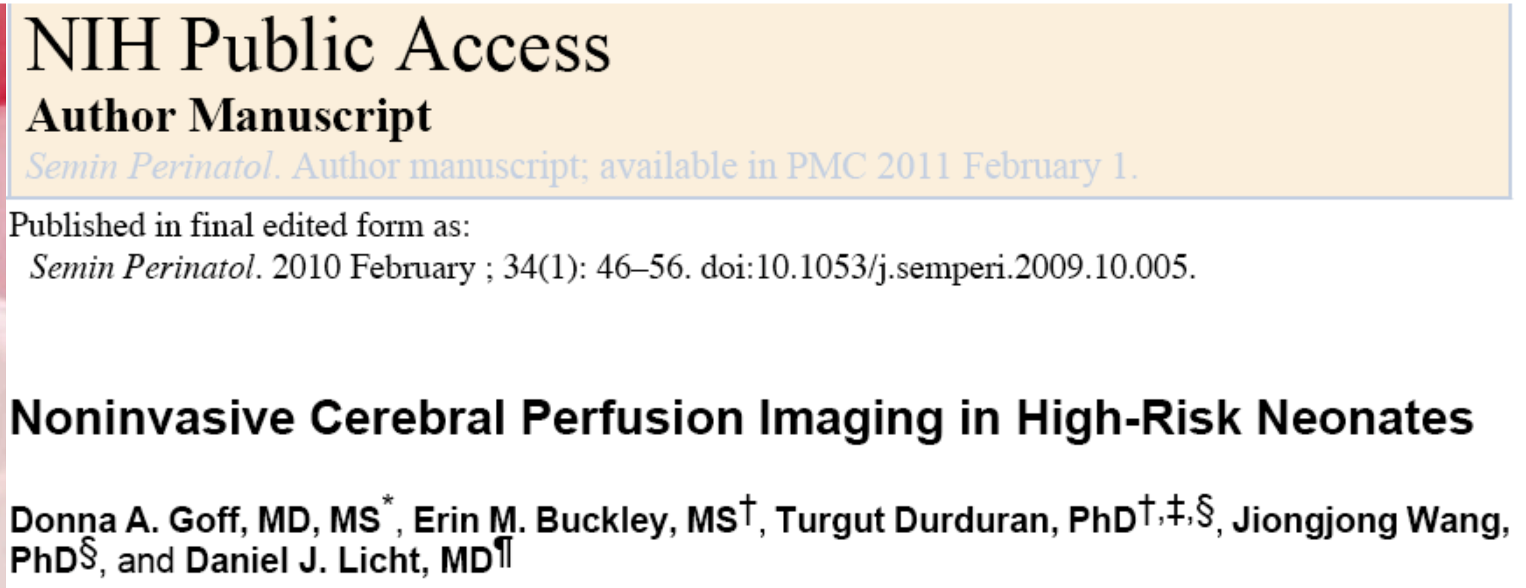
- BFS ocurre también en otras situaciones:
- RNT con GC bajo SDR severo e HTPP
- RN con asfixia con GC bajo con pobre contractilidad miocárdica
- RN con sepsis con resistencia vascular baja o alta
- Hipovolemia: es poco común en RNPT, estudios con cristaloides o coloides no han mostrado beneficio clínico en los primeros días de vida. Sospechar si historia obstétrica de pérdidas sanguíneas o ligadura precoz de cordón.

Early Human Development (2005) 81, 413—422

Dg de compromiso circulatorio

- Medición de PA: invasiva, no invasiva
- Signos de hipoperfusión: llene capilar prolongado, oliguria, acidosis
- Ecocardiografía: para confirmar DAP o HTP o descartar cardiopatía estructural. Permite junto a la PA invasiva determinar un estado de alta o baja resistencia vascular y por tanto escoger un mejor tto.
- Medición de flujo de VCS (SVCf)

Early Human Development (2005) 81, 413—422



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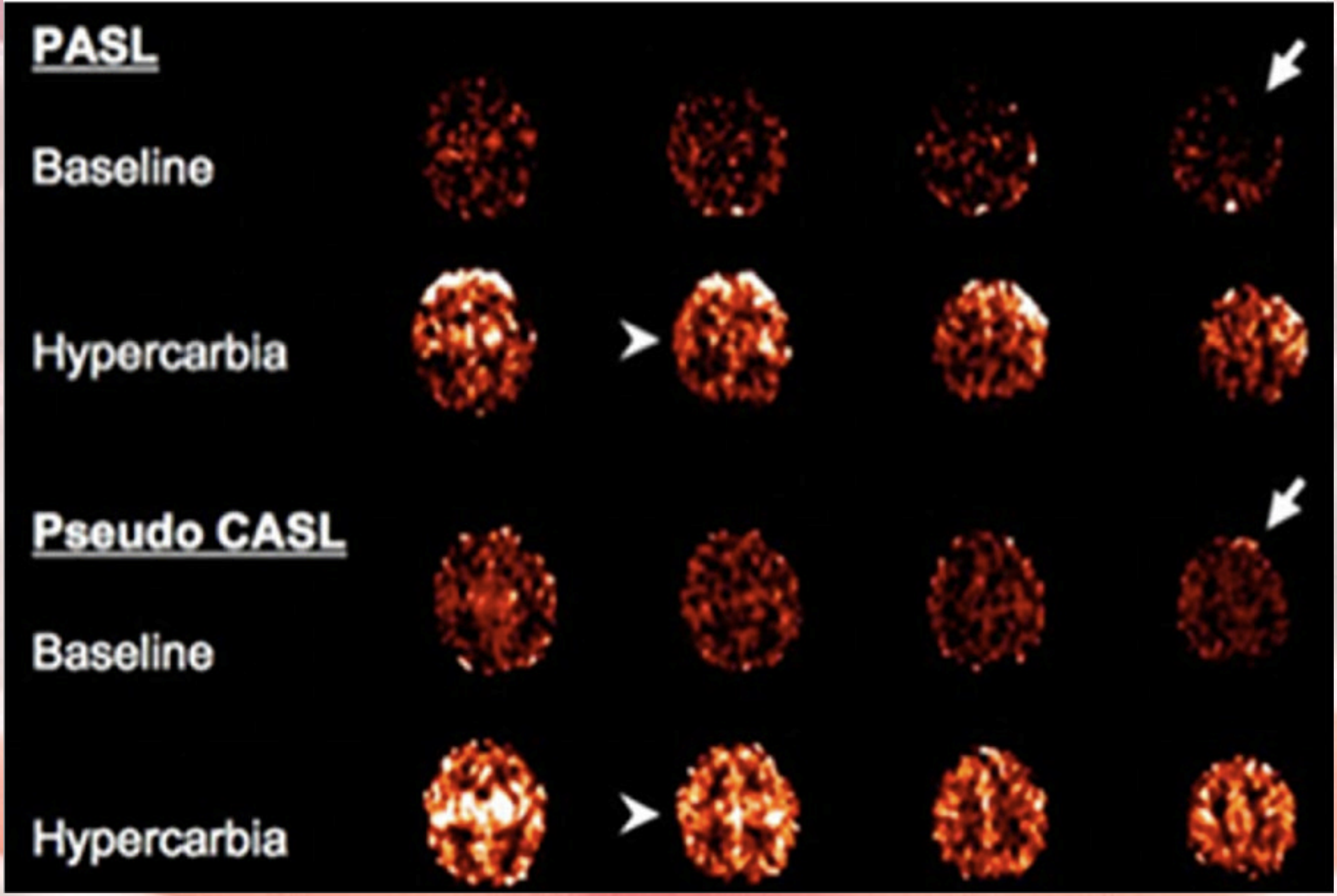
Semin Perinatol. 2010 February ; 34(1): 46–56. doi:10.1053/j.semperi.2009.10.005.

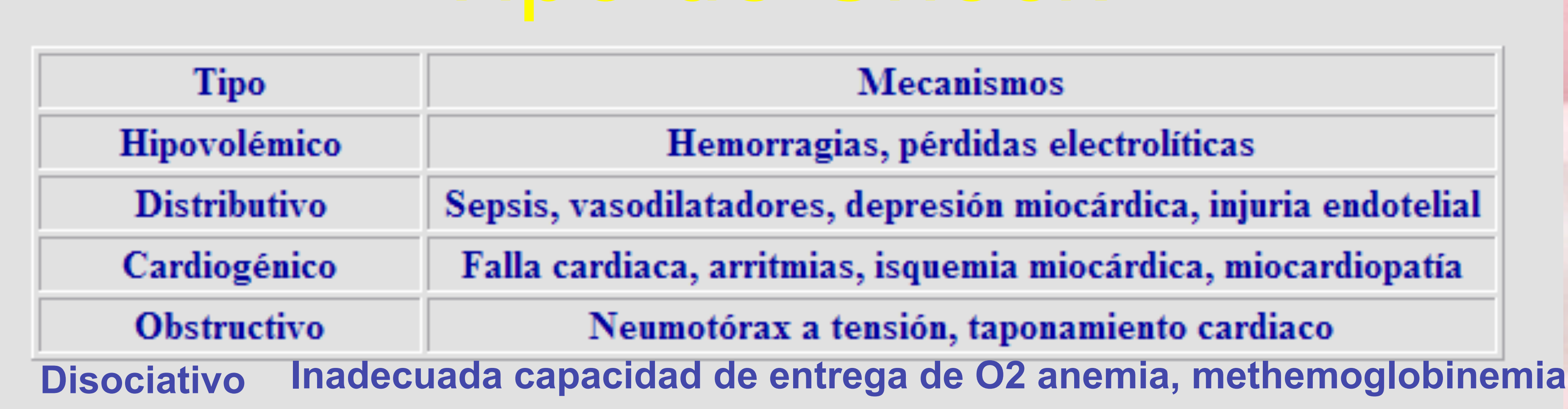
Noninvasive Cerebral Perfusion Imaging in High-Risk Neonates

Donna A. Goff, MD, MS[*], **Erin M. Buckley, MS**[†], **Turgut Durduran, PhD**[†,‡,§], **Jiongjong Wang, PhD**[§], and **Daniel J. Licht, MD**[¶]

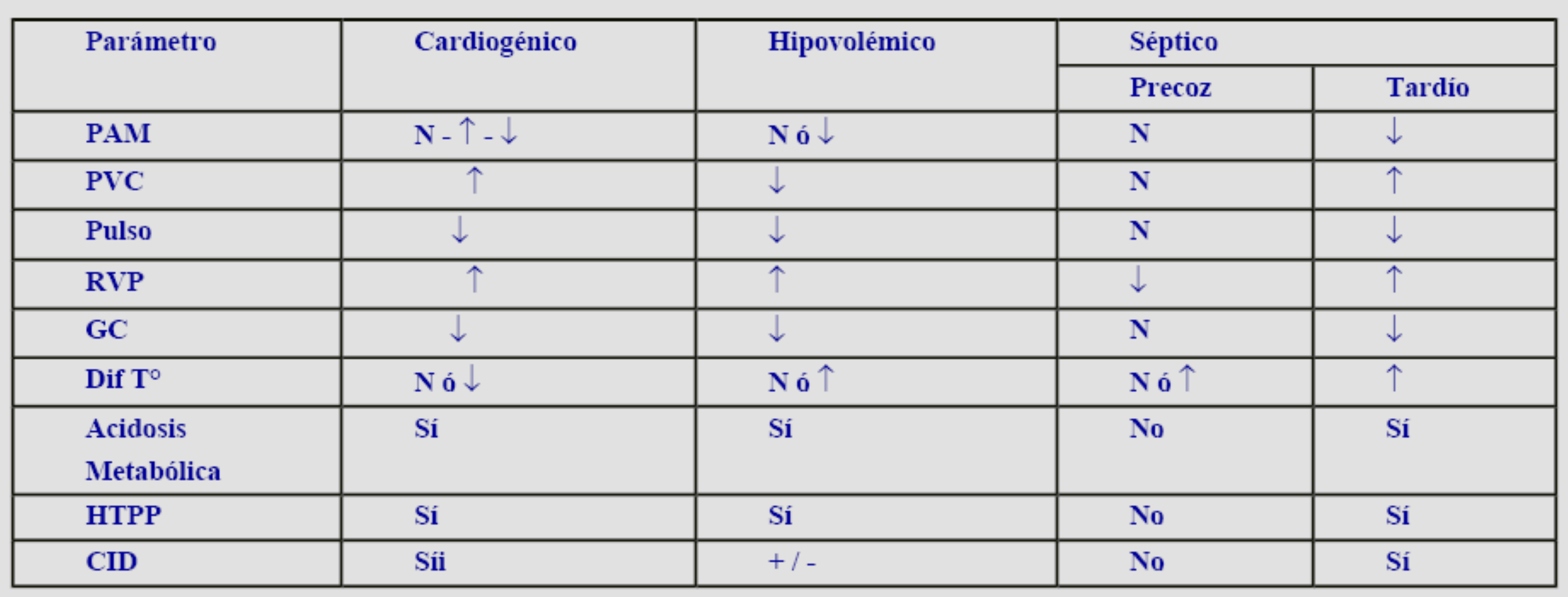
Optical near infrared spectroscopy
(NIRS) monitorea al lado de la cama la oxigenación cerebral y el volumen sanguíneo. Pero no mide directamente el Flujo Sang. Cerebral.
Arterial Spinlabeled Perfusion Magnetic Resonance Imaging and Optical Diffuse Correlation Spectroscopy, miden en forma directa y no invasiva la perfusión cerebral


PASL
Baseline
Hypercarbia
Pseudo CASL
Baseline
Hypercarbia

Tipo de Shock



Tipo	Mecanismos
Hipovolémico	Hemorragias, pérdidas electrolíticas
Distributivo	Sepsis, vasodilatadores, depresión miocárdica, injuria endotelial
Cardiogénico	Falla cardiaca, arritmias, isquemia miocárdica, miocardiopatía
Obstructivo	Neumotórax a tensión, taponamiento cardiaco
Disociativo	Inadecuada capacidad de entrega de O2 anemia, methemoglobinemia



Parámetro	Cardiogénico	Hipovolémico	Séptico	
			Precoz	Tardío
PAM	N - ↑ - ↓	N ó ↓	N	↓
PVC	↑	↓	N	↑
Pulso	↓	↓	N	↓
RVP	↑	↑	↓	↑
GC	↓	↓	N	↓
Dif T°	N ó ↓	N ó ↑	N ó ↑	↑
Acidosis Metabólica	Sí	Sí	No	Sí
HTPP	Sí	Sí	No	Sí
CID	Sii	+ / -	No	Sí

eMedicine Mayo, 2006

Tto Hipotensión

- Distintos criterios para iniciar tto:
- **PAM < 30 mm Hg** (Datos observacionales de Miall-Allen sugirieron que una PAM < 30 se asociaban con lesiones isquémicas cerebrales).
  Archives of Disease in Childhood, Vol 62, 1068-1069 (RNPT < de 31 sem EG)
- PAM ≤ a la Edad Gestacional (semanas) (1er a 3er día de vida)
- PAS < 40 mm Hg
- PA < p 10 de estudios de población

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eMedicine Mayo 2006

Tipos de tto

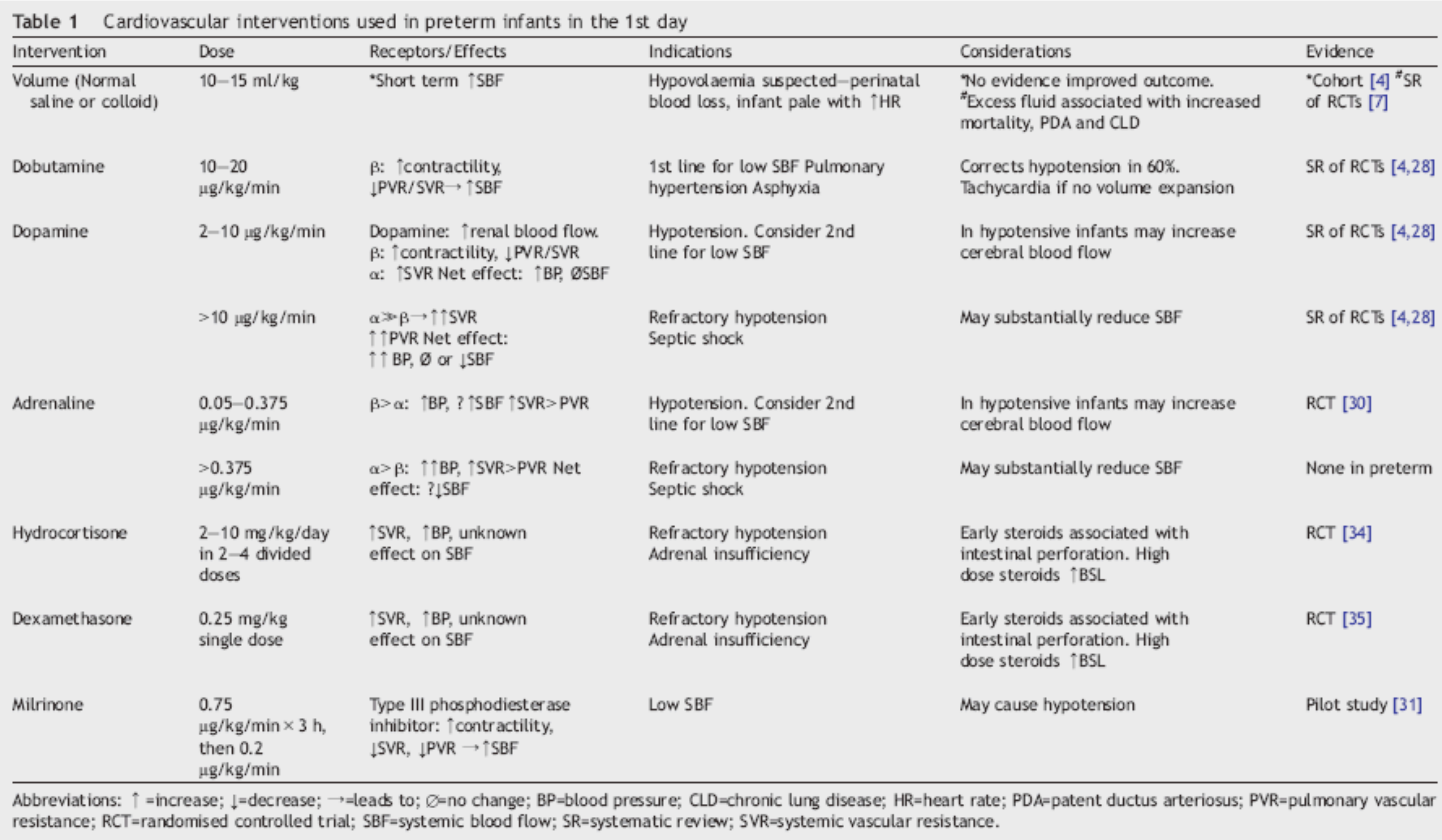


Table 1 Cardiovascular interventions used in preterm infants in the 1st day

Intervention	Dose	Receptors/Effects	Indications	Considerations	Evidence
Volume (Normal saline or colloid)	10–15 ml/kg	*Short term ↑SBF	Hypovolaemia suspected—perinatal blood loss, infant pale with ↑HR	*No evidence improved outcome. #Excess fluid associated with increased mortality, PDA and CLD	*Cohort [4] #SR of RCTs [7]
Dobutamine	10–20 µg/kg/min	β: ↑contractility, ↓PVR/SVR→ ↑SBF	1st line for low SBF Pulmonary hypertension Asphyxia	Corrects hypotension in 60%. Tachycardia if no volume expansion	SR of RCTs [4,28]
Dopamine	2–10 µg/kg/min	Dopamine: ↑renal blood flow. β: ↑contractility, ↓PVR/SVR α: ↑SVR Net effect: ↑BP, ØSBF	Hypotension. Consider 2nd line for low SBF	In hypotensive infants may increase cerebral blood flow	SR of RCTs [4,28]
	>10 µg/kg/min	α≫β→↑↑SVR ↑↑PVR Net effect: ↑↑ BP, Ø or ↓SBF	Refractory hypotension Septic shock	May substantially reduce SBF	SR of RCTs [4,28]
Adrenaline	0.05–0.375 µg/kg/min	β>α: ↑BP, ? ↑SBF ↑SVR>PVR	Hypotension. Consider 2nd line for low SBF	In hypotensive infants may increase cerebral blood flow	RCT [30]
	>0.375 µg/kg/min	α>β: ↑↑BP, ↑SVR>PVR Net effect: ?↓SBF	Refractory hypotension Septic shock	May substantially reduce SBF	None in preterm
Hydrocortisone	2–10 mg/kg/day in 2–4 divided doses	↑SVR, ↑BP, unknown effect on SBF	Refractory hypotension Adrenal insufficiency	Early steroids associated with intestinal perforation. High dose steroids ↑BSL	RCT [34]
Dexamethasone	0.25 mg/kg single dose	↑SVR, ↑BP, unknown effect on SBF	Refractory hypotension Adrenal insufficiency	Early steroids associated with intestinal perforation. High dose steroids ↑BSL	RCT [35]
Milrinone	0.75 µg/kg/min × 3 h, then 0.2 µg/kg/min	Type III phosphodiesterase inhibitor: ↑contractility, ↓SVR, ↓PVR →↑SBF	Low SBF	May cause hypotension	Pilot study [31]

Abbreviations: ↑ =increase; ↓=decrease; →=leads to; ∅=no change; BP=blood pressure; CLD=chronic lung disease; HR=heart rate; PDA=patent ductus arteriosus; PVR=pulmonary vascular resistance; RCT=randomised controlled trial; SBF=systemic blood flow; SR=systematic review; SVR=systemic vascular resistance.

Early Human Development (2005) 81, 413—422

Drogas Vasoactivas usadas en RN

- **Inótropos:**
- Aunque se usan frecuentemente los estudios en RN son limitados
- Su uso en falla cardiaca debe balancear el aumento en el consumo de O2 por el aumento del trabajo cardiaco de tal manera de asegurar un buen flujo sistémico pero sin disminuir el flujo miocárdico.

Dopamina

Precursor endógeno de la norepinefrina, aumenta la presión arterial, el debito cardiaco y la perfusión periférica.

Efecto dosis dependiente:

Dosis bajas → 0.3-3 ug/kg/min, estimulación de receptores dopaminergicos (D1), resultante en aumento del flujo sanguíneo renal, mesenterico y coronario.

Dosis medias → 3-10 ug/kg/min, efecto inotropico a traves de estimulación directa de receptores B1 e indirecta por liberación de norepinefrina.

Dosis altas → 10 ug/kg/min, estimulacion de alfa receptores, vasoconstricción periférica.

Limitaciones:

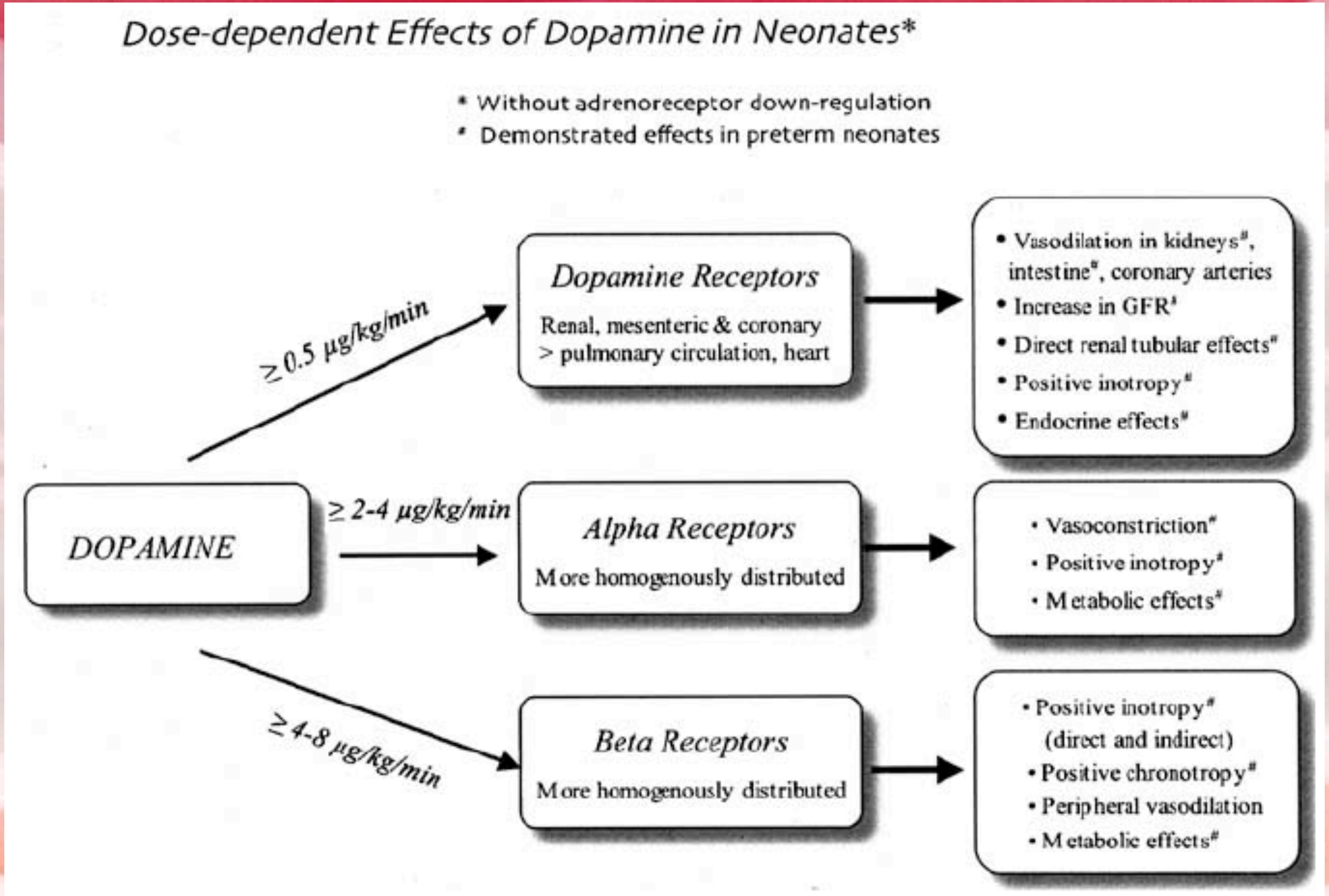
Fundamentalmente en dosis altas, aumento de RVS, taquicardia, arritmias y disminución del gasto cardiaco.

Debe usarse con precaucion en pacientes con HPT pulmonar pre-existente, ya que podria aumentar le RVP.

Produce supresión reversible de prolactina, hormona del crecimiento y liberadora de tirotropina.

Isquemia local y ulceración en sitios de extravasación (puede ser revertido con fentolamina en forma precoz).

Es inactivada por soluciones alcalinas, por le que no debe mezclarse con bicarbonato.



Dose-dependent Effects of Dopamine in Neonates*

* Without adrenoreceptor down-regulation
# Demonstrated effects in preterm neonates

DOPAMINE

≥ 0.5 μg/kg/min → **Dopamine Receptors**
Renal, mesenteric & coronary > pulmonary circulation, heart
→
- Vasodilation in kidneys#, intestine#, coronary arteries
- Increase in GFR#
- Direct renal tubular effects#
- Positive inotropy#
- Endocrine effects#

≥ 2-4 μg/kg/min → **Alpha Receptors**
More homogenously distributed
→
- Vasoconstriction#
- Positive inotropy#
- Metabolic effects#

≥ 4-8 μg/kg/min → **Beta Receptors**
More homogenously distributed
→
- Positive inotropy# (direct and indirect)
- Positive chronotropy#
- Peripheral vasodilation
- Metabolic effects#

I Seri Journal of Perinatology (2006) 26, S8–S13

Dopamina

- **Dopamina para la prevención de la morbilidad y mortalidad en recién nacidos a término con presunta asfixia perinatal (***Cochrane Plus, número 4, 2006*. update marzo 2002)
- El compromiso multisistémico con inclusión de hipotensión y gasto cardíaco bajo es común en recién nacidos con asfixia perinatal. Se usa comúnmente la dopamina para recién nacidos con hipotensión de cualquier etiología, con el objetivo de mejorar el gasto cardíaco y prevenir sus consecuencias perjudiciales.

Dopamina

- Actualmente no hay pruebas suficientes de ensayos controlados aleatorios de que el uso de dopamina en recién nacidos a término con presunta asfixia perinatal mejore la mortalidad o el resultado neurológico a largo plazo. Aún no se determinó si la dopamina mejora el resultado para los recién nacidos a término con presunta asfixia perinatal. Se necesitan investigaciones adicionales para determinar si el uso de la dopamina mejora la mortalidad y la morbilidad a largo plazo para estos recién nacidos y, de ser así, deben abordarse asuntos tales como qué recién nacidos, en qué dosis y con qué cointervenciones.

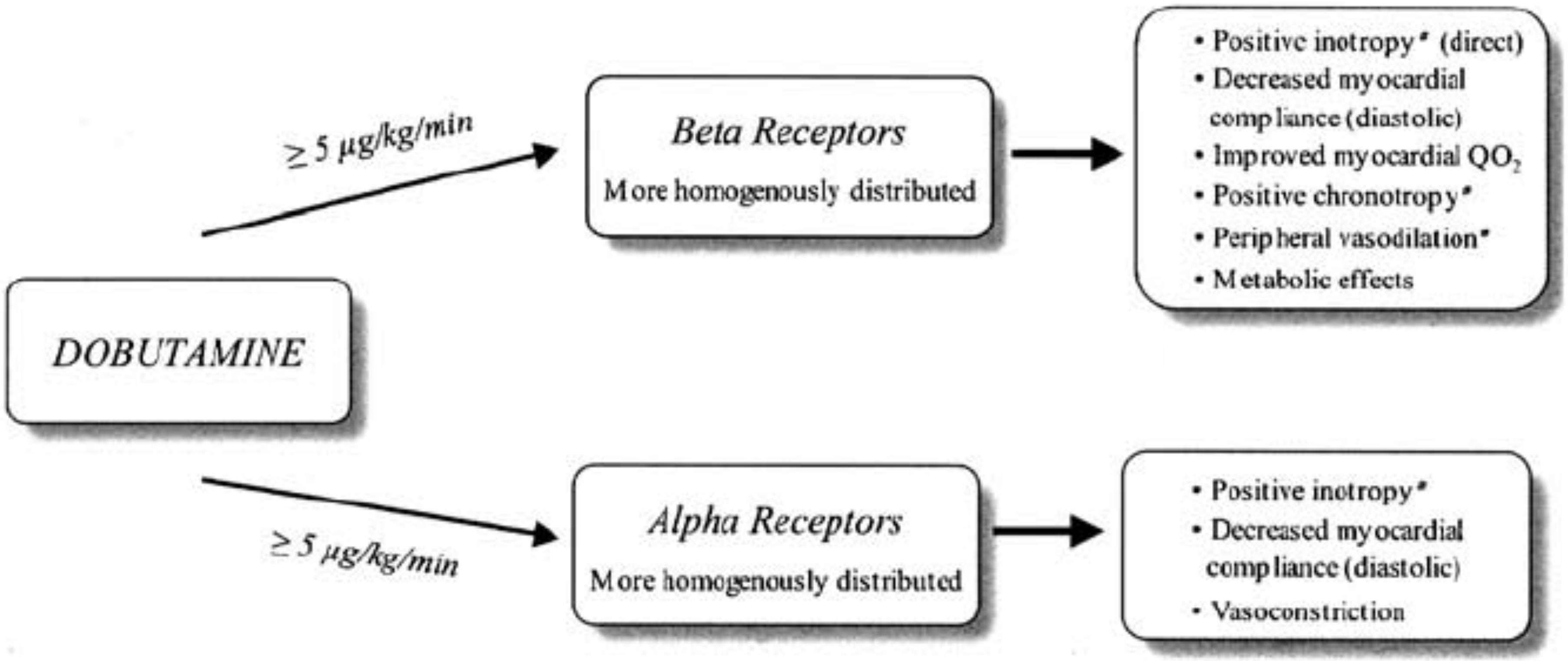
•*Cochrane Plus, número 4, 2006*. update marzo 2002)

Dobutamina

- Catecolamina sintética que estimula directamente receptores B1 y B2 adrenergicos, y a diferencia de la dopamina, no causa liberación de norepinefrina.
- Es mejor B2 agonista que la dopamina y causa vasodilatación sistémica y pulmonar.
- Uso cronico produce tolerancia.Taquifilaxis y tolerancia cruzada con dopamina.
- Limitaciones: menor efecto sobre perfusión renal, mayor costo.
- Dilución: igual a dopamina.

Cardiovascular Effects of Dobutamine Neonates*

* Without adrenoreceptor down-regulation
• Demonstrated effects in preterm neonates



DOBUTAMINE

≥ 5 μg/kg/min

Beta Receptors

More homogenously distributed

- Positive inotropy• (direct)
- Decreased myocardial compliance (diastolic)
- Improved myocardial QO_2
- Positive chronotropy•
- Peripheral vasodilation•
- Metabolic effects

≥ 5 μg/kg/min

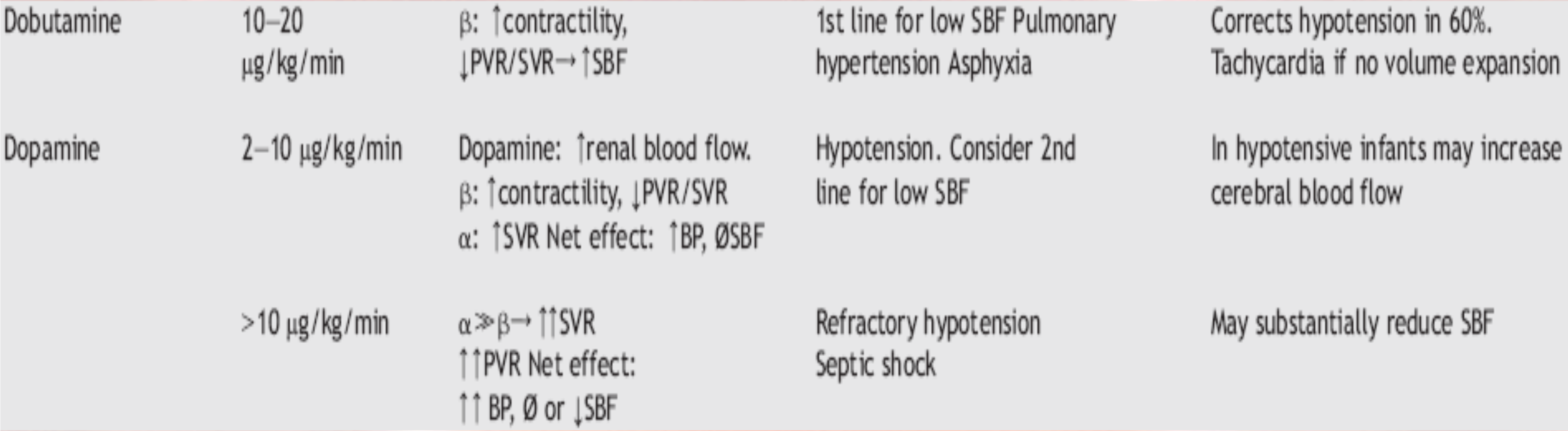
Alpha Receptors

More homogenously distributed

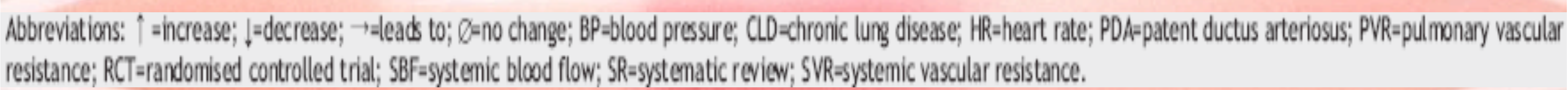
- Positive inotropy•
- Decreased myocardial compliance (diastolic)
- Vasoconstriction

I Seri Journal of Perinatology (2006) 26, S8–S13

Dopamina v/s Dobutamina



Dobutamine	10–20 μg/kg/min	β: ↑contractility, ↓PVR/SVR→↑SBF	1st line for low SBF Pulmonary hypertension Asphyxia	Corrects hypotension in 60%. Tachycardia if no volume expansion
Dopamine	2–10 μg/kg/min	Dopamine: ↑renal blood flow. β: ↑contractility, ↓PVR/SVR α: ↑SVR Net effect: ↑BP, ØSBF	Hypotension. Consider 2nd line for low SBF	In hypotensive infants may increase cerebral blood flow
	>10 μg/kg/min	α≫β→↑↑SVR ↑↑PVR Net effect: ↑↑ BP, Ø or ↓SBF	Refractory hypotension Septic shock	May substantially reduce SBF



Abbreviations: ↑ =increase; ↓=decrease; →=leads to; ∅=no change; BP=blood pressure; CLD=chronic lung disease; HR=heart rate; PDA=patent ductus arteriosus; PVR=pulmonary vascular resistance; RCT=randomised controlled trial; SBF=systemic blood flow; SR=systematic review; SVR=systemic vascular resistance.

David A. Osborn Early Human Development (2005) 81, 413—422

Dopamina v/s Dobutamina

- **Dopamina versus dobutamina para recién nacidos prematuros hipotensos** *Cochrane Plus, número 4, 2006 (update 2003)*
- **Conclusiones de los revisores:**

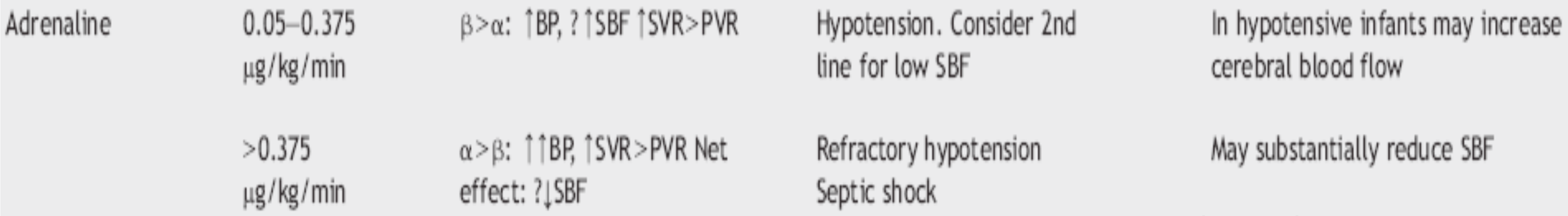
La dopamina es más efectiva que la dobutamina para el tratamiento a corto plazo de la hipotensión sistémica en recién nacidos prematuros. No hubo pruebas de un efecto sobre la incidencia de las secuelas neurorradiológicas adversas (hemorragia periventricular grave o leucomalacia periventricular) o sobre la incidencia de taquicardia. Sin embargo, ante la ausencia de datos que confirmen el beneficio y la seguridad a largo plazo de la dopamina en comparación con la dobutamina, no se pueden hacer recomendaciones firmes con respecto a la elección del fármaco para tratar la hipotensión.

Dopamina v/s Dobutamina

- Una revisión sistemática de 5 estudios en RN hipotensos no encontró diferencias significativas en mortalidad o tasas de HIC grado 3 o 4 o LPV
- La dopamina aumenta la PA alrededor de 30 mm Hg más rápidamente,pero el GC disminuía. La Dobutamina aumentaba el GC.
- Sin embargo los GC variaban dentro de rangos normales y no se reportó DAP.

Roze et al. Arch Dis Child 1993;69:59– 63.

Adrenalina



Adrenaline	0.05–0.375 µg/kg/min	β>α: ↑BP, ? ↑SBF ↑SVR>PVR	Hypotension. Consider 2nd line for low SBF	In hypotensive infants may increase cerebral blood flow
	>0.375 µg/kg/min	α>β: ↑↑BP, ↑SVR>PVR Net effect: ?↓SBF	Refractory hypotension Septic shock	May substantially reduce SBF

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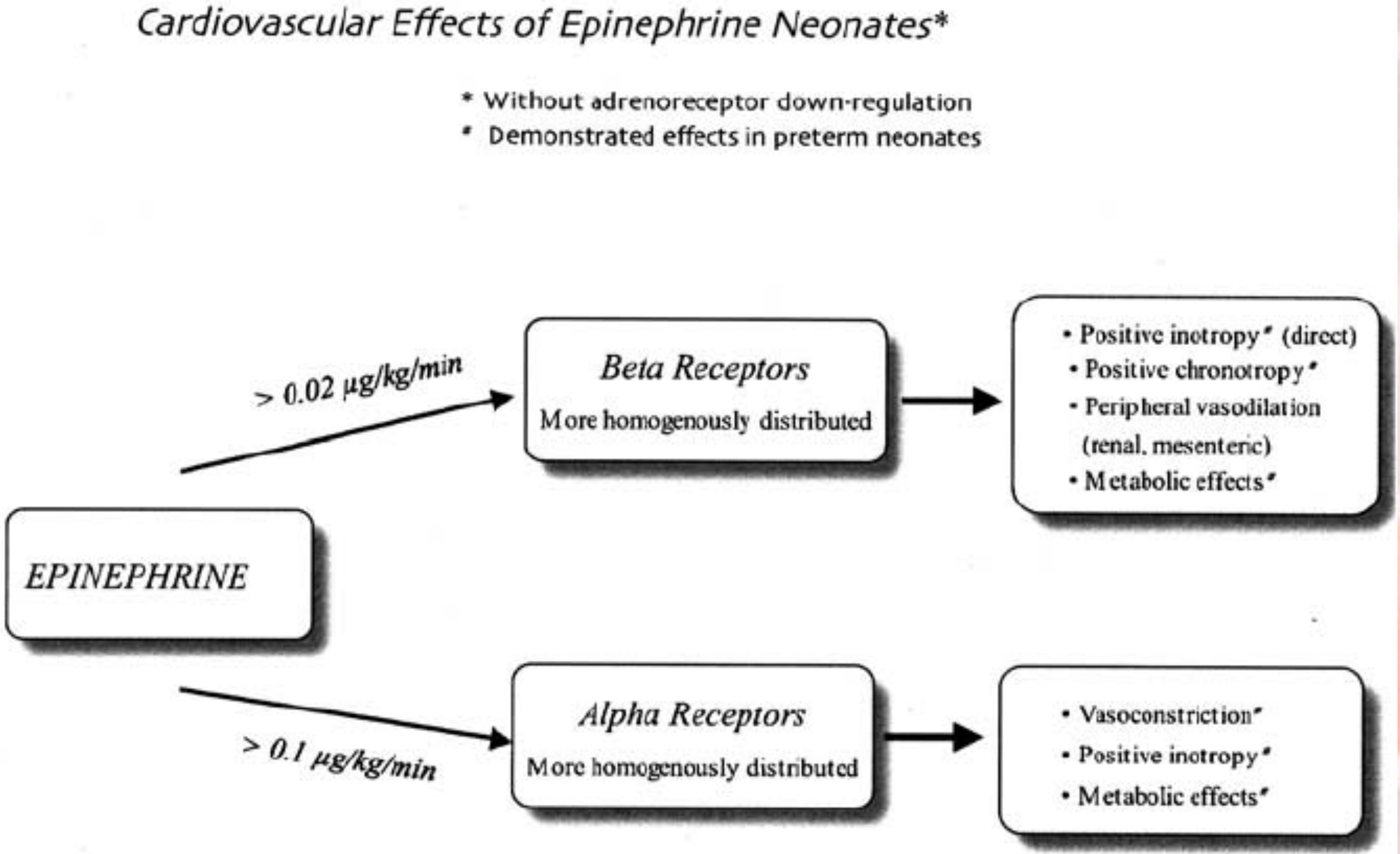

*Cardiovascular Effects of Epinephrine Neonates**

* Without adrenoreceptor down-regulation
* Demonstrated effects in preterm neonates

EPINEPHRINE

> 0.02 µg/kg/min

Beta Receptors
More homogenously distributed

- Positive inotropy* (direct)
- Positive chronotropy*
- Peripheral vasodilation (renal, mesenteric)
- Metabolic effects*

> 0.1 µg/kg/min

Alpha Receptors
More homogenously distributed

- Vasoconstriction*
- Positive inotropy*
- Metabolic effects*

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Adrenalina

- Producto final de síntesis de catecolaminas.
- Efecto inotropico potente. Uso en postoperados cardiacos.No se ocupa como agente inotropico de primera elección, por su tendencia a taquicardia y vasoconstricción.

Adrenalina

- **Adrenalina para la prevención de la morbilidad y mortalidad en recién nacidos prematuros con alteraciones cardiovasculares** (Cochrane Plus, número 4, 2006. Update septiembre 2003)
- **Conclusiones de los revisores:** No hay datos suficientes sobre el uso de las infusiones de adrenalina en los recién nacidos prematuros con alteraciones cardiovasculares para hacer las recomendaciones para la práctica. Existe la necesidad de ensayos más grandes a fin de determinar si la adrenalina es efectiva para la reducción de la morbilidad y la mortalidad en los recién nacidos prematuros con alteraciones cardiovasculares.

Adrenalina v/s Dopamina

- RN hipotensos en el 1er día de vida randomizados a dopamina y adrenalina aumentan su PAM y presentan incrementos similares de flujo sanguíneo cerebral (medido por NIRS)
- No hubo diferencias en mortalidad u otros outcomes clínicos.
- Resultados de neurodesarrollo no se han reportado.
- La adrenalina se ha usado comunmente para hipotensión refractaria a otros inótropos.

Pellicer et al. Pediatr Res 2004;55:426A.

Noradrenalina

- Derleth (Clinical experience with norepinephrine infusions in critically ill newborns. Pediatr Res 1997;41:145)
- Ha sugerido que las infusiones de noradrenalina son seguras en neonatos y no causan vasoconstricción cerebral o miocárdica significativa.
- Son necesarias más investigaciones para recomendar su uso rutinario..

Corticoides

- Dado que la expresión de receptores adrenérgicos y señales intracelulares es regulada por glucocorticoides, se ha sugerido que el desarrollo de hipotensión resistente a vasopresores en RN podría deberse a un down regulation de receptores adrenérgicos y a una relativa insuficiencia adrenal

Corticoides

La regulación de los receptores adrenérgicos cardiovasculares implica efectos genómicos y no genómicos como el aumento instantáneo en el calcio intracelular disponible a nivel cardiaco y en vasos sanguíneos, la inhibición de: 1) el metabolismo de las catecolaminas y 2) la liberación de sustancias vasoactivas como prostaciclina y óxido nítrico.

Estos efectos resultan en un rápido incremento de la respuesta cardiovascular a las catecolaminas y en la atenuación de vasodilatación patológica asociada a respuesta inflamatoria

Corticoides

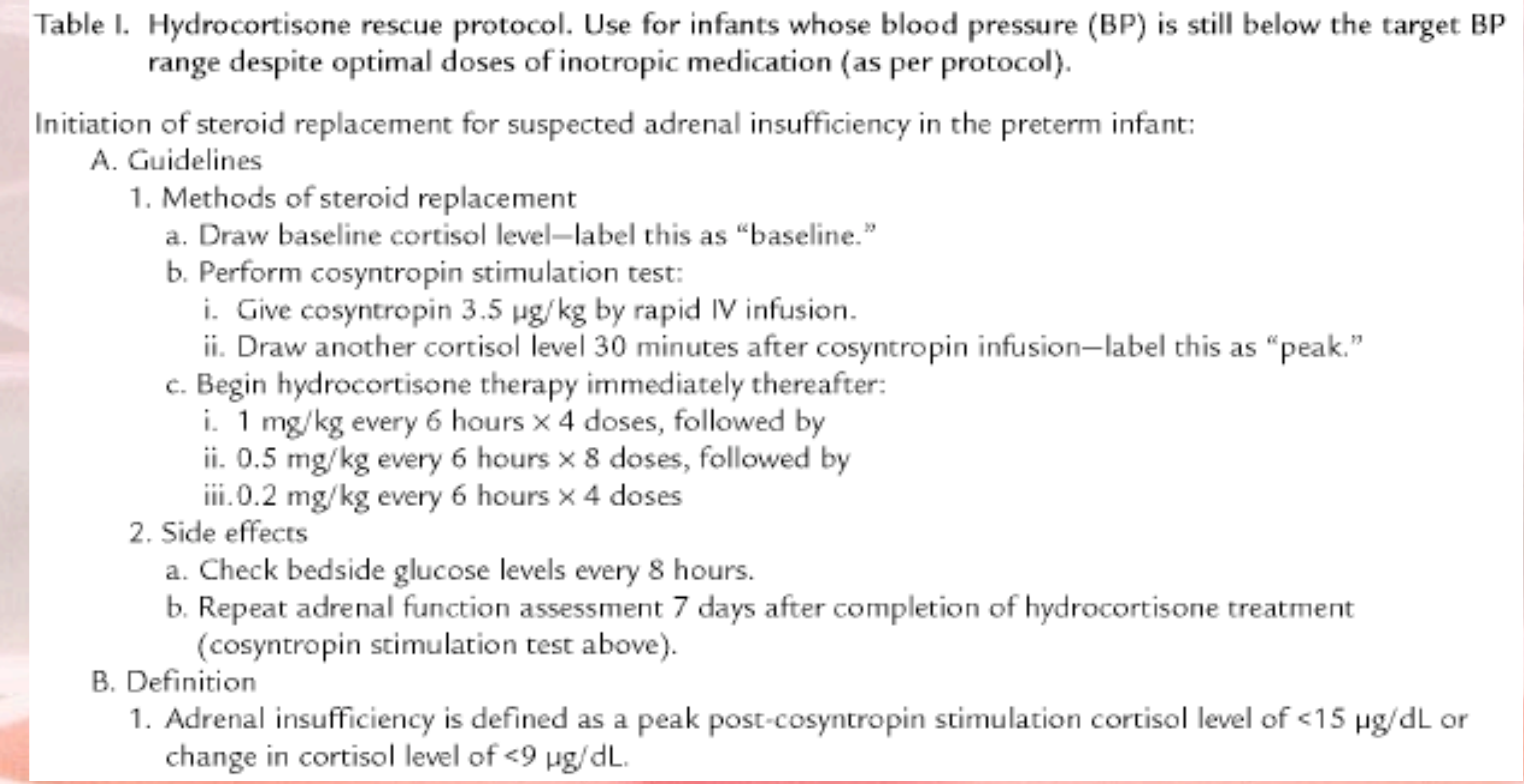


Table I. Hydrocortisone rescue protocol. Use for infants whose blood pressure (BP) is still below the target BP range despite optimal doses of inotropic medication (as per protocol).

Initiation of steroid replacement for suspected adrenal insufficiency in the preterm infant:

A. Guidelines
  1. Methods of steroid replacement
    a. Draw baseline cortisol level—label this as "baseline."
    b. Perform cosyntropin stimulation test:
      i. Give cosyntropin 3.5 µg/kg by rapid IV infusion.
      ii. Draw another cortisol level 30 minutes after cosyntropin infusion—label this as "peak."
    c. Begin hydrocortisone therapy immediately thereafter:
      i. 1 mg/kg every 6 hours × 4 doses, followed by
      ii. 0.5 mg/kg every 6 hours × 8 doses, followed by
      iii. 0.2 mg/kg every 6 hours × 4 doses
  2. Side effects
    a. Check bedside glucose levels every 8 hours.
    b. Repeat adrenal function assessment 7 days after completion of hydrocortisone treatment (cosyntropin stimulation test above).
B. Definition
  1. Adrenal insufficiency is defined as a peak post-cosyntropin stimulation cortisol level of <15 µg/dL or change in cortisol level of <9 µg/dL.

J.R. Evans et al. Clinical Therapeutics/Volume 28, Number 9, 2006

Cochrane Database Syst Rev. 2007 Jan 24;(1):CD003662.
Corticosteroids for treating hypotension in preterm infants.
Subhedar NV, Duffy K, Ibrahim H.

AUTHORS' CONCLUSIONS:

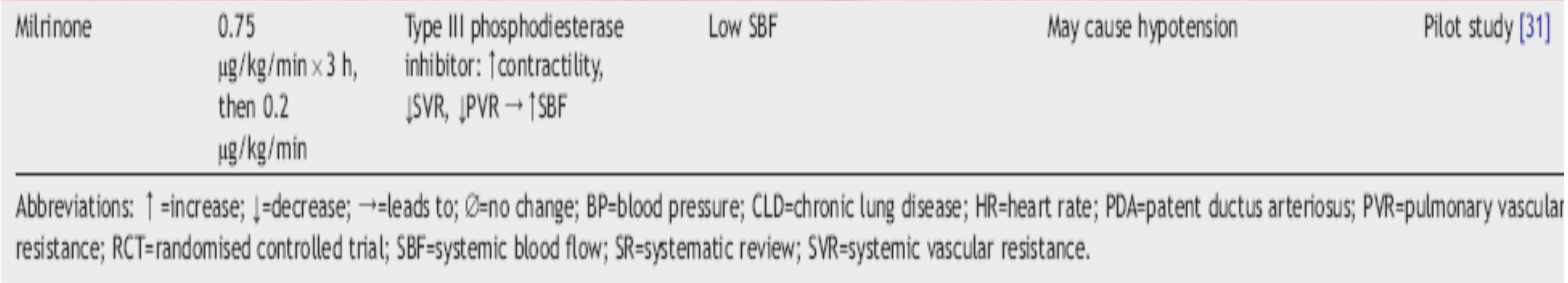
There is insufficient evidence to support the routine use of steroids in the treatment of primary or refractory neonatal hypotension. Hydrocortisone may be as effective as dopamine in treating primary hypotension, but there are no data regarding the long-term safety of steroids used for this indication.A single dose of dexamethasone may be effective in treating preterm infants with refractory hypotension receiving epinephrine. However, given the lack of data on long-term safety dexamethasone cannot be recommended for routine use in preterm hypotension.

Milrinona

- Es un inhibidor selectivo de la fosfodiesterasa que ha sido usado en infantes sometidos a cirugía cardiaca para tratar el Sd de bajo GC.
- Es inótropo y produce dilatación sistémica y pulmonar.
- En un estudio piloto, ninguno de los RNPT que fueron tratados profilácticamente presentaron bajo flujo sistémico en el primer día de vida.

Early Human Development (2005) 81, 413—422

Milrinona



Milrinone	0.75 µg/kg/min × 3 h, then 0.2 µg/kg/min	Type III phosphodiesterase inhibitor: ↑contractility, ↓SVR, ↓PVR → ↑SBF	Low SBF	May cause hypotension	Pilot study [31]

Abbreviations: ↑ =increase; ↓=decrease; →=leads to; ∅=no change; BP=blood pressure; CLD=chronic lung disease; HR=heart rate; PDA=patent ductus arteriosus; PVR=pulmonary vascular resistance; RCT=randomised controlled trial; SBF=systemic blood flow; SR=systematic review; SVR=systemic vascular resistance.

D.A. Osborn

Early Human Development (2005) 81, 413—422

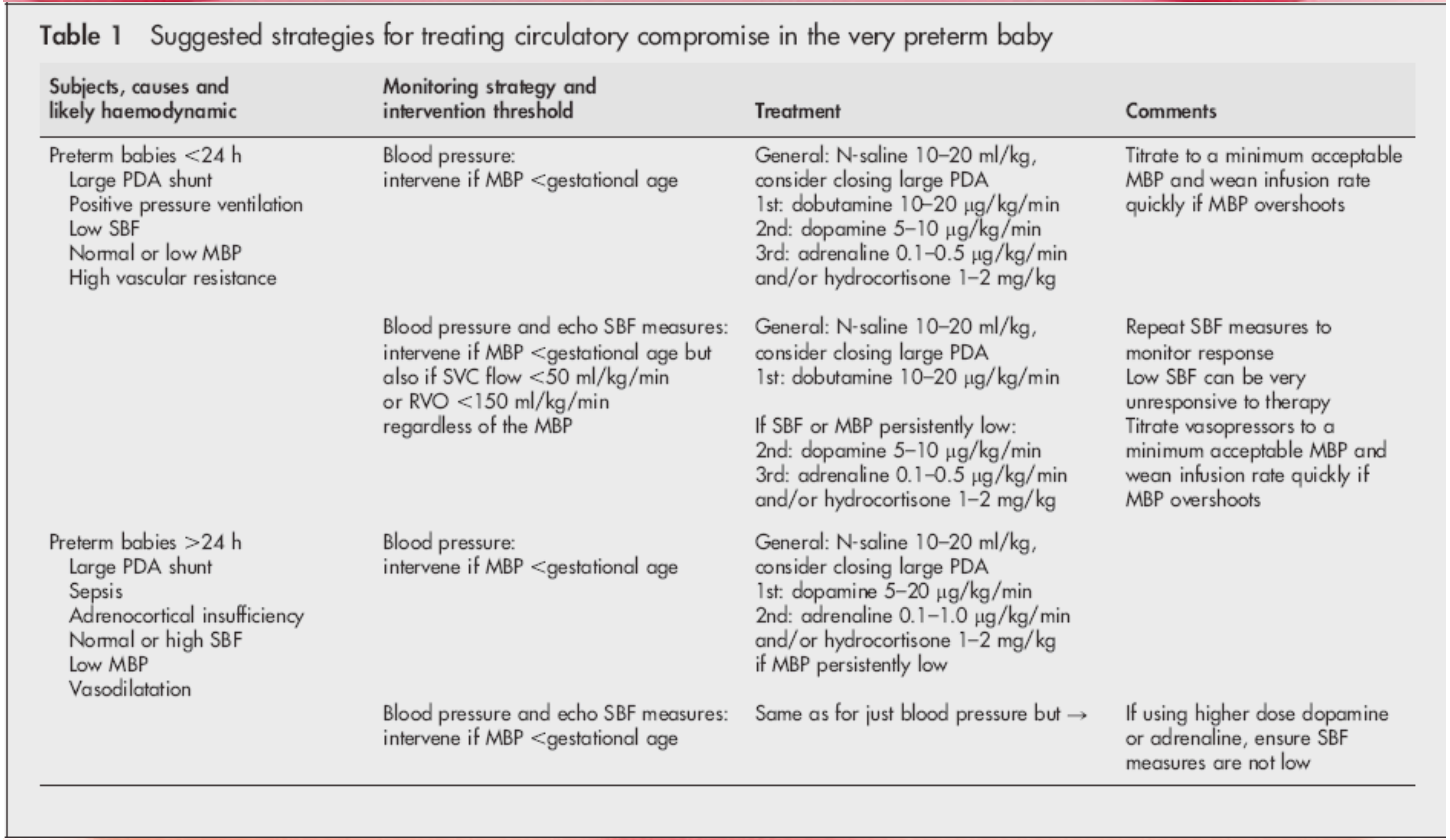


Table 1 Suggested strategies for treating circulatory compromise in the very preterm baby

Subjects, causes and likely haemodynamic	Monitoring strategy and intervention threshold	Treatment	Comments
Preterm babies <24 h Large PDA shunt Positive pressure ventilation Low SBF Normal or low MBP High vascular resistance	Blood pressure: intervene if MBP <gestational age	General: N-saline 10–20 ml/kg, consider closing large PDA 1st: dobutamine 10–20 µg/kg/min 2nd: dopamine 5–10 µg/kg/min 3rd: adrenaline 0.1–0.5 µg/kg/min and/or hydrocortisone 1–2 mg/kg	Titrate to a minimum acceptable MBP and wean infusion rate quickly if MBP overshoots
	Blood pressure and echo SBF measures: intervene if MBP <gestational age but also if SVC flow <50 ml/kg/min or RVO <150 ml/kg/min regardless of the MBP	General: N-saline 10–20 ml/kg, consider closing large PDA 1st: dobutamine 10–20 µg/kg/min If SBF or MBP persistently low: 2nd: dopamine 5–10 µg/kg/min 3rd: adrenaline 0.1–0.5 µg/kg/min and/or hydrocortisone 1–2 mg/kg	Repeat SBF measures to monitor response Low SBF can be very unresponsive to therapy Titrate vasopressors to a minimum acceptable MBP and wean infusion rate quickly if MBP overshoots
Preterm babies >24 h Large PDA shunt Sepsis Adrenocortical insufficiency Normal or high SBF Low MBP Vasodilatation	Blood pressure: intervene if MBP <gestational age	General: N-saline 10–20 ml/kg, consider closing large PDA 1st: dopamine 5–20 µg/kg/min 2nd: adrenaline 0.1–1.0 µg/kg/min and/or hydrocortisone 1–2 mg/kg if MBP persistently low	
	Blood pressure and echo SBF measures: intervene if MBP <gestational age	Same as for just blood pressure but →	If using higher dose dopamine or adrenaline, ensure SBF measures are not low

N. Evans. Arch Dis Child Fetal Neonatal Ed 2006;91:F213–F220

Otras Drogas

Arginina Vasopresina

- Ha mostrado ser más efectiva que dosis óptimas de epinefrina durante resucitación cardioplulmonar, cuando se administra ev o endotraqueal en humanos y animales.
- Landry et al. Reportaron el beneficio de usar AVP en pacientes adultos críticos con shock septic en quienes los inótropos y vasopresores habían fallado.
- Loeckinger et al.mostraron que además del incremento en la PA la AVP mejora el intecambio gaseoso en estados post resucitación

Arginina-vasopresina

- **“Arginine-vasopressin in catecholamine-refractory septic versus non-septic shock in extremely low birth weight infants with acute renal injury”**

- **Conclusion** AVP puede ser una promisoria terapia de rescate en el shock resistente a catecolaminas en RNMBP con falla renal.
- Se requieren más trabajos prospectivos para asegurar su eficacia y seguridad como presor coadyudante en shock séptico-no séptico en RNMBP

Meyer *et al.* *Critical Care* 2006, **10**:R71

Cita Relacionada: Anaesthesia. 2008 Mar; 63(3):228-34. Epub 2007 Dec 13.

Terlipresina

- Terlipresina (tricycl-lysine-vasopressin), es un análogo sintético de larga acción de la vasopresina con farmacodinamia comparable, pero con diferentes propiedades farmacocinéticas.
- Su vida media es de 6 hrs, y la duración de ación es de 2 a 10 hrs en oposición a la corta vida media de la vasopresina (sólo 6 min) y una duración de acción de 30 a 60 min.
- Tiene una acción vasoconstrictora mediada por los receptores V1 en los músculatura de los vasos sanguíneos. Esta acción es más potente que la de la angiotensina II o epinefrina.
- En la práctica clinica se usa para parar sangrados de várices esofágicas.
- Sus ventajas sobre la vasopresina serían:
- - se puede administrar en bolos en vez de infusión (dada su VM más larga).

  - una dosis única de terlipresina (1–2 mg) aumenta la PA dentro de 10 a 20 min en pacientes con shock séptico (lo que se mantiene por al menos 5 horas).

  - Un efecto adicional importante es que permite la disminución de catecolaminas agonistas, especialmente la epinefrina.

Cita relacionada: Ann Pharmacother. 2010 Oct;44(10):1545-53. Epub 2010 Sep 14.

Terlipresina

- **TERLIPRESSIN AS RESCUE THERAPY FOR INTRACTABLE HYPOTENSION DUE TO SEPTIC SHOCK IN CHILDREN**

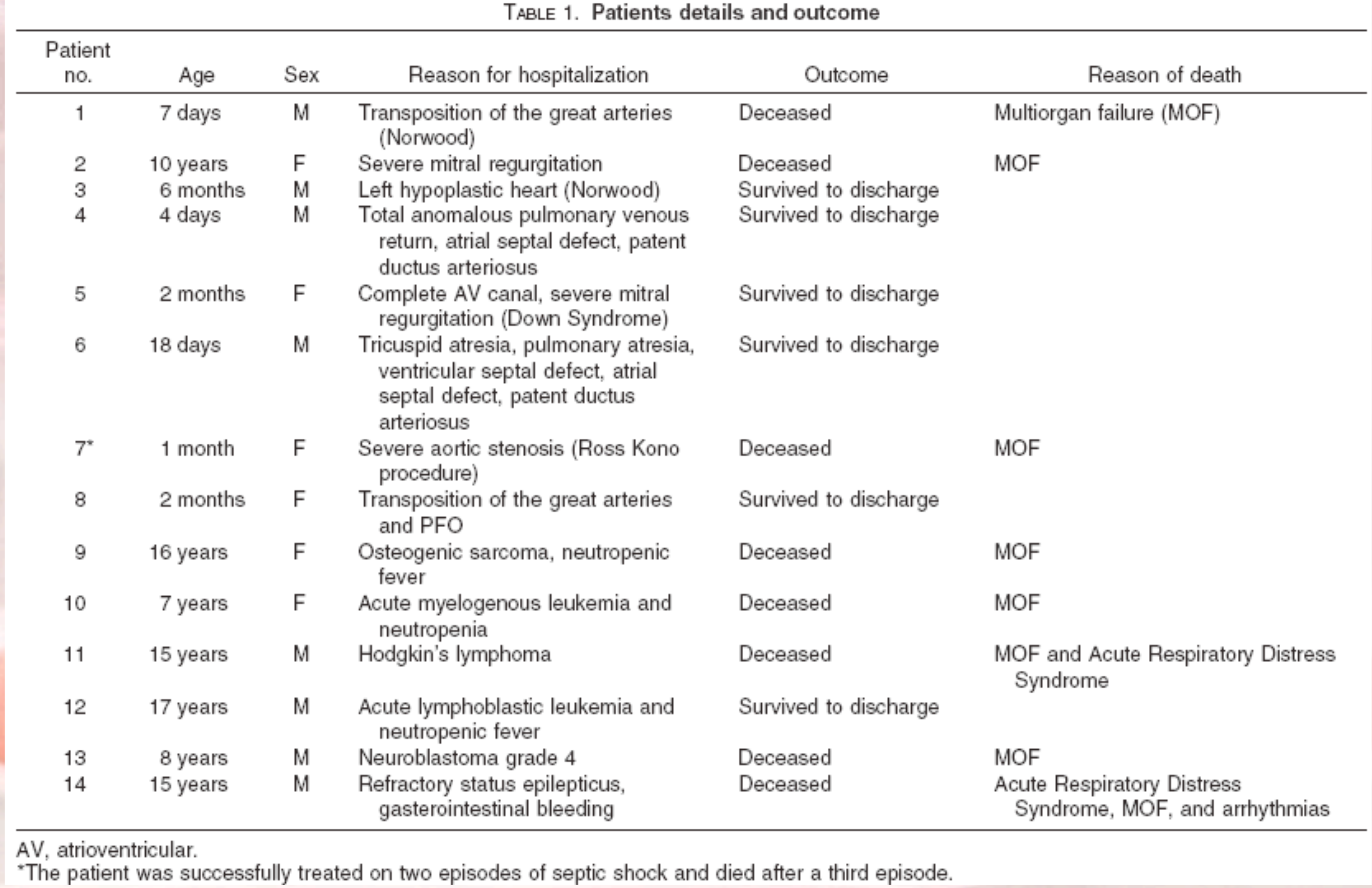


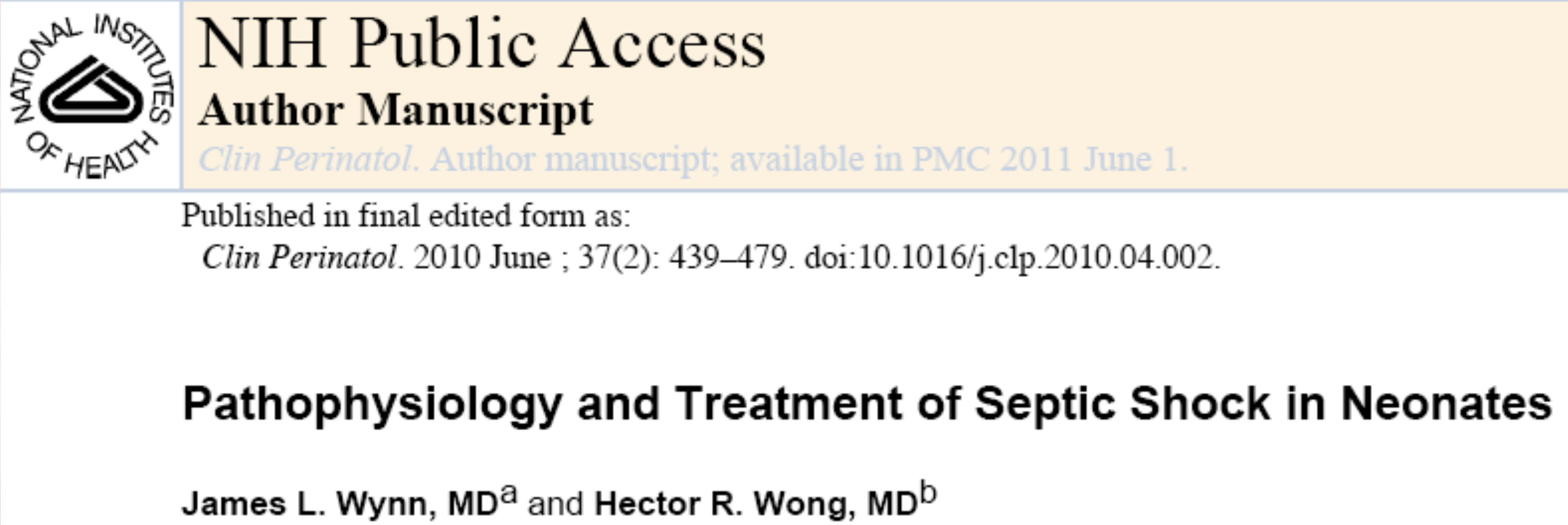
TABLE 1. **Patients details and outcome**

Patient no.	Age	Sex	Reason for hospitalization	Outcome	Reason of death
1	7 days	M	Transposition of the great arteries (Norwood)	Deceased	Multiorgan failure (MOF)
2	10 years	F	Severe mitral regurgitation	Deceased	MOF
3	6 months	M	Left hypoplastic heart (Norwood)	Survived to discharge	
4	4 days	M	Total anomalous pulmonary venous return, atrial septal defect, patent ductus arteriosus	Survived to discharge	
5	2 months	F	Complete AV canal, severe mitral regurgitation (Down Syndrome)	Survived to discharge	
6	18 days	M	Tricuspid atresia, pulmonary atresia, ventricular septal defect, atrial septal defect, patent ductus arteriosus	Survived to discharge	
7*	1 month	F	Severe aortic stenosis (Ross Kono procedure)	Deceased	MOF
8	2 months	F	Transposition of the great arteries and PFO	Survived to discharge	
9	16 years	F	Osteogenic sarcoma, neutropenic fever	Deceased	MOF
10	7 years	F	Acute myelogenous leukemia and neutropenia	Deceased	MOF
11	15 years	M	Hodgkin's lymphoma	Deceased	MOF and Acute Respiratory Distress Syndrome
12	17 years	M	Acute lymphoblastic leukemia and neutropenic fever	Survived to discharge	
13	8 years	M	Neuroblastoma grade 4	Deceased	MOF
14	15 years	M	Refractory status epilepticus, gasterointestinal bleeding	Deceased	Acute Respiratory Distress Syndrome, MOF, and arrhythmias

AV, atrioventricular.

*The patient was successfully treated on two episodes of septic shock and died after a third episode.

MATOK ET AL. **SHOCK,** Vol. 23, No. 4, pp. 305–310, 2005



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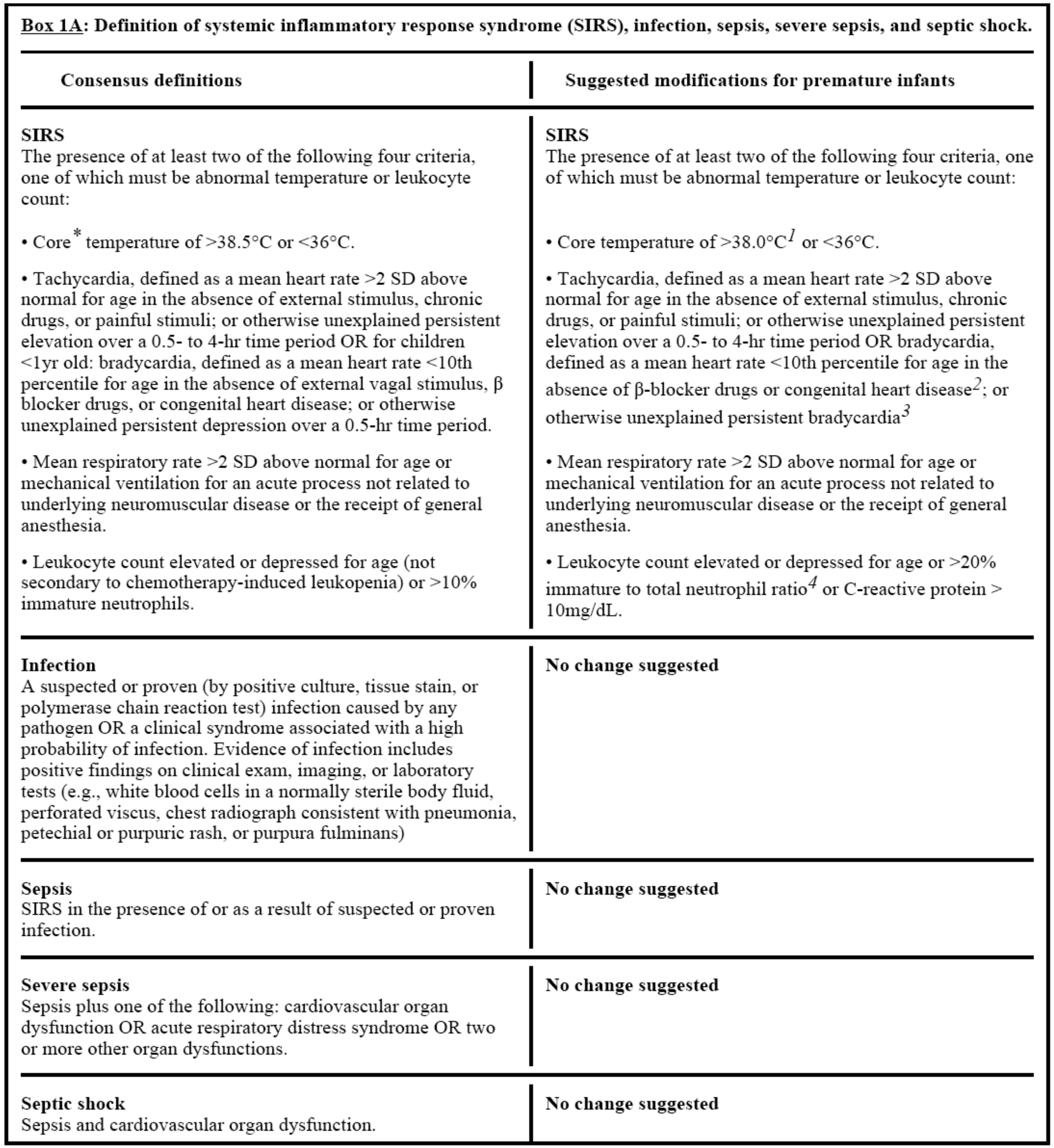
Pathophysiology and Treatment of Septic Shock in Neonates

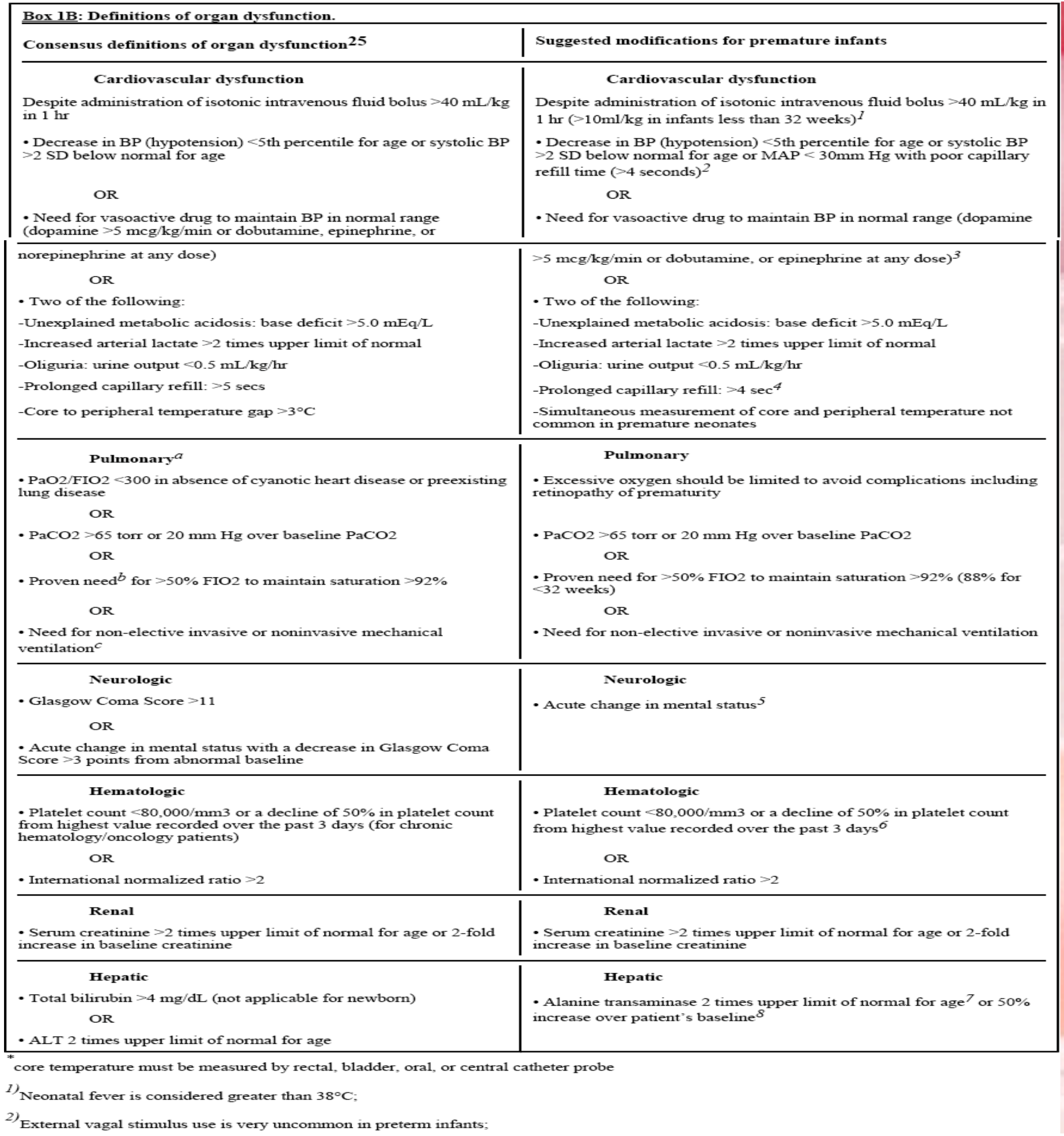
James L. Wynn, MD[a] and **Hector R. Wong, MD**[b]



Box 1A: Definition of systemic inflammatory response syndrome (SIRS), infection, sepsis, severe sepsis, and septic shock.

Consensus definitions	Suggested modifications for premature infants
SIRS The presence of at least two of the following four criteria, one of which must be abnormal temperature or leukocyte count: • Core[*] temperature of >38.5°C or <36°C. • Tachycardia, defined as a mean heart rate >2 SD above normal for age in the absence of external stimulus, chronic drugs, or painful stimuli; or otherwise unexplained persistent elevation over a 0.5- to 4-hr time period OR for children <1yr old: bradycardia, defined as a mean heart rate <10th percentile for age in the absence of external vagal stimulus, β blocker drugs, or congenital heart disease; or otherwise unexplained persistent depression over a 0.5-hr time period. • Mean respiratory rate >2 SD above normal for age or mechanical ventilation for an acute process not related to underlying neuromuscular disease or the receipt of general anesthesia. • Leukocyte count elevated or depressed for age (not secondary to chemotherapy-induced leukopenia) or >10% immature neutrophils.	**SIRS** The presence of at least two of the following four criteria, one of which must be abnormal temperature or leukocyte count: • Core temperature of >38.0°C[1] or <36°C. • Tachycardia, defined as a mean heart rate >2 SD above normal for age in the absence of external stimulus, chronic drugs, or painful stimuli; or otherwise unexplained persistent elevation over a 0.5- to 4-hr time period OR bradycardia, defined as a mean heart rate <10th percentile for age in the absence of β-blocker drugs or congenital heart disease[2]; or otherwise unexplained persistent bradycardia[3] • Mean respiratory rate >2 SD above normal for age or mechanical ventilation for an acute process not related to underlying neuromuscular disease or the receipt of general anesthesia. • Leukocyte count elevated or depressed for age or >20% immature to total neutrophil ratio[4] or C-reactive protein > 10mg/dL.
Infection A suspected or proven (by positive culture, tissue stain, or polymerase chain reaction test) infection caused by any pathogen OR a clinical syndrome associated with a high probability of infection. Evidence of infection includes positive findings on clinical exam, imaging, or laboratory tests (e.g., white blood cells in a normally sterile body fluid, perforated viscus, chest radiograph consistent with pneumonia, petechial or purpuric rash, or purpura fulminans)	**No change suggested**
Sepsis SIRS in the presence of or as a result of suspected or proven infection.	**No change suggested**
Severe sepsis Sepsis plus one of the following: cardiovascular organ dysfunction OR acute respiratory distress syndrome OR two or more other organ dysfunctions.	**No change suggested**
Septic shock Sepsis and cardiovascular organ dysfunction.	**No change suggested**

Clin Perinatol. 2010 June ; 37(2): 439–479



Box 1B: Definitions of organ dysfunction.

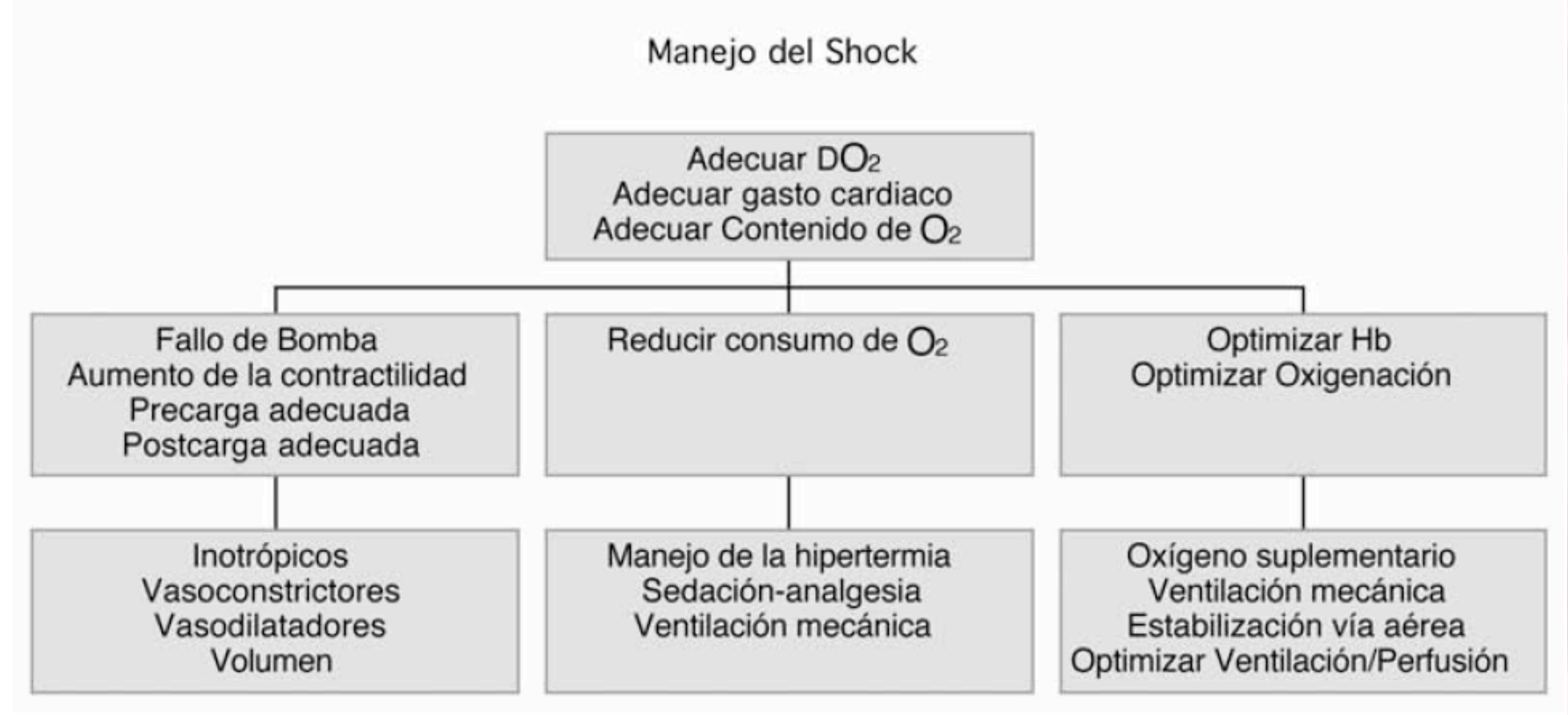
Consensus definitions of organ dysfunction[25]	Suggested modifications for premature infants
Cardiovascular dysfunction Despite administration of isotonic intravenous fluid bolus >40 mL/kg in 1 hr • Decrease in BP (hypotension) <5th percentile for age or systolic BP >2 SD below normal for age OR • Need for vasoactive drug to maintain BP in normal range (dopamine >5 mcg/kg/min or dobutamine, epinephrine, or norepinephrine at any dose) OR • Two of the following: -Unexplained metabolic acidosis: base deficit >5.0 mEq/L -Increased arterial lactate >2 times upper limit of normal -Oliguria: urine output <0.5 mL/kg/hr -Prolonged capillary refill: >5 secs -Core to peripheral temperature gap >3°C	**Cardiovascular dysfunction** Despite administration of isotonic intravenous fluid bolus >40 mL/kg in 1 hr (>10ml/kg in infants less than 32 weeks)[1] • Decrease in BP (hypotension) <5th percentile for age or systolic BP >2 SD below normal for age or MAP < 30mm Hg with poor capillary refill time (>4 seconds)[2] OR • Need for vasoactive drug to maintain BP in normal range (dopamine >5 mcg/kg/min or dobutamine, or epinephrine at any dose)[3] OR • Two of the following: -Unexplained metabolic acidosis: base deficit >5.0 mEq/L -Increased arterial lactate >2 times upper limit of normal -Oliguria: urine output <0.5 mL/kg/hr -Prolonged capillary refill: >4 sec[4] -Simultaneous measurement of core and peripheral temperature not common in premature neonates
Pulmonary[a] • PaO2/FIO2 <300 in absence of cyanotic heart disease or preexisting lung disease OR • PaCO2 >65 torr or 20 mm Hg over baseline PaCO2 OR • Proven need[b] for >50% FIO2 to maintain saturation >92% OR • Need for non-elective invasive or noninvasive mechanical ventilation[c]	**Pulmonary** • Excessive oxygen should be limited to avoid complications including retinopathy of prematurity • PaCO2 >65 torr or 20 mm Hg over baseline PaCO2 OR • Proven need for >50% FIO2 to maintain saturation >92% (88% for <32 weeks) OR • Need for non-elective invasive or noninvasive mechanical ventilation
Neurologic • Glasgow Coma Score >11 OR • Acute change in mental status with a decrease in Glasgow Coma Score >3 points from abnormal baseline	**Neurologic** • Acute change in mental status[5]
Hematologic • Platelet count <80,000/mm3 or a decline of 50% in platelet count from highest value recorded over the past 3 days (for chronic hematology/oncology patients) OR • International normalized ratio >2	**Hematologic** • Platelet count <80,000/mm3 or a decline of 50% in platelet count from highest value recorded over the past 3 days[6] OR • International normalized ratio >2
Renal • Serum creatinine >2 times upper limit of normal for age or 2-fold increase in baseline creatinine	**Renal** • Serum creatinine >2 times upper limit of normal for age or 2-fold increase in baseline creatinine
Hepatic • Total bilirubin >4 mg/dL (not applicable for newborn) OR • ALT 2 times upper limit of normal for age	**Hepatic** • Alanine transaminase 2 times upper limit of normal for age[7] or 50% increase over patient's baseline[8]

* core temperature must be measured by rectal, bladder, oral, or central catheter probe

1) Neonatal fever is considered greater than 38°C;

2) External vagal stimulus use is very uncommon in preterm infants;

Clin Perinatol. 2010 June ; 37(2): 439–479



Manejo del Shock

Adecuar DO_2
Adecuar gasto cardiaco
Adecuar Contenido de O_2

Fallo de Bomba
Aumento de la contractilidad
Precarga adecuada
Postcarga adecuada

Reducir consumo de O_2

Optimizar Hb
Optimizar Oxigenación

Inotrópicos
Vasoconstrictores
Vasodilatadores
Volumen

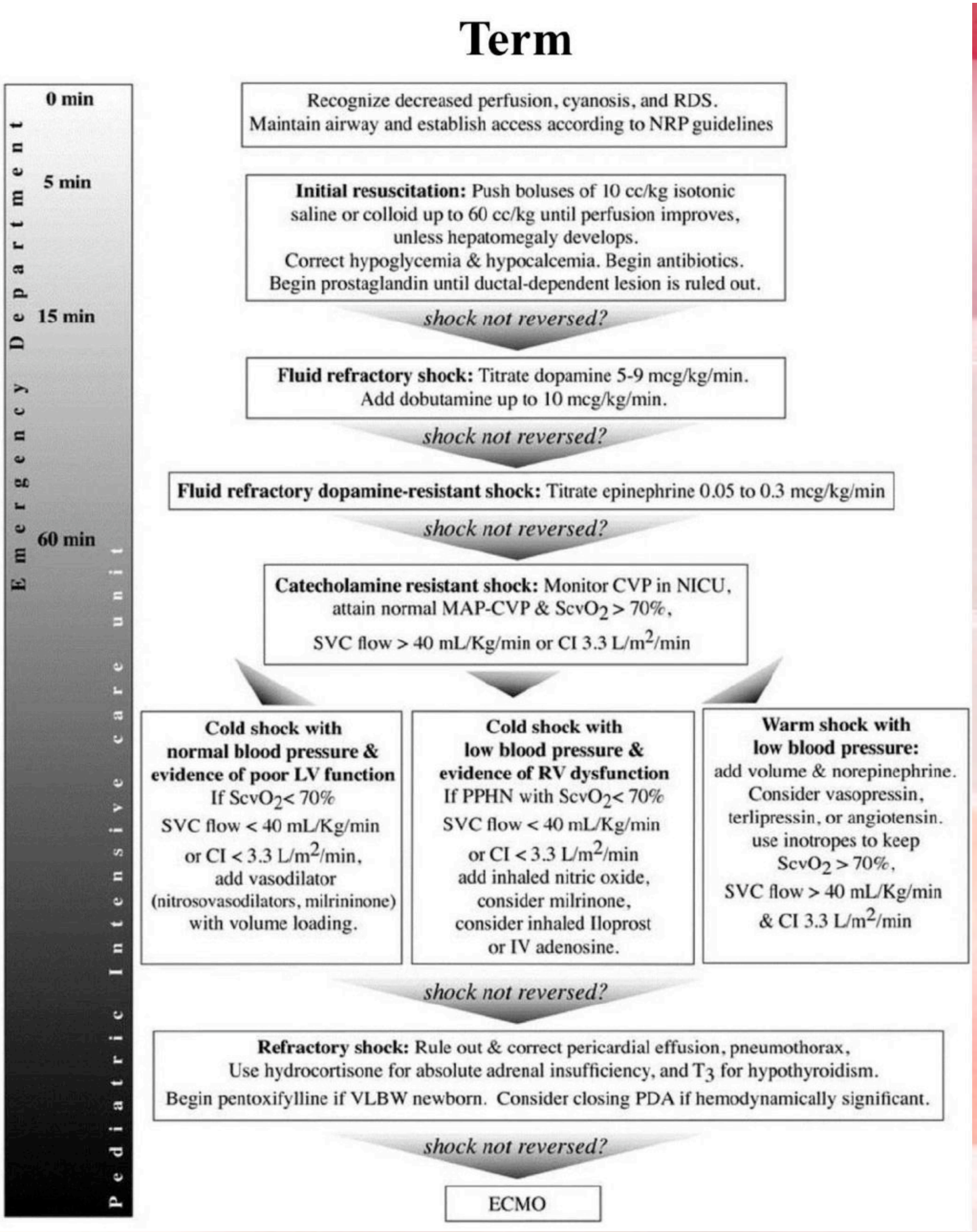
Manejo de la hipertermia
Sedación-analgesia
Ventilación mecánica

Oxígeno suplementario
Ventilación mecánica
Estabilización vía aérea
Optimizar Ventilación/Perfusión

Protocolos Diagnóstico Terapeúticos de la
AEP: Neonatología 2008

Type of Infants	Problem	Cardiovascular Associations	Suggested Interventions
Extreme prematurity	Low SBF First day after birth	Normal or low BP Low SVC flow± RVO or LVO Large ductus arteriosus High systemic (±pulmonary) VR Poor myocardial contractility	Normal saline 10 to 20 mL/kg and Dobutamine 10 to 20 mcg/kg per minute titrated to maintain: –SVC flow >40 mL/kg per minute/ RVO >120 mL/kg per minute Second-line: Add dopamine 5 mcg/kg per minute titrated to BP Third line: Adrenaline 0.05 mcg/kg per minute titrated to BP
Preterm infant	Low blood pressure Especially after first day	Normal or high SVC flow/ RVO Low systemic VR	Dopamine 5 mcg/kg per minute titrated to BP
Infant who has asphyxia	Low SBF	Normal or low blood pressure Poor myocardial contractility	Normal saline 10 to 20 mL/kg and Dobutamine 10 to 20 mcg/kg per minute titrated to maintain: –SVC flow >40 mL/kg per minute/ RVO >120 mL/kg per minute Second-line: Either dopamine or adrenaline
Infant who has suspected sepsis	"Hyperdynamic sepsis"	Normal or low BP High systemic SVC flow/RVO Low systemic VR±fluid leak	Normal saline—may need larger volumes Dopamine 5 mcg/kg per minute titrated to BP Second-line: Adrenaline 0.05 mcg/kg per minute titrated to BP
Infant with suspected sepsis	"Nonhyperdynamic sepsis"	Normal or low BP Normal or low SVC flow/RVO High systemic (±pulmonary) VR	Normal saline 10 to 20 mL/kg per minute Dobutamine 10 to 20 mcg/kg per minute titrated to maintain: –SVC flow >40 mL/kg per minute/ RVO >120 mL/kg per minute Second-line (low flows): Adrenaline Second-line (hypotension): Dopamine or adrenaline
Infant who has respiratory distress	Pulmonary hypertension	Normal or low BP Normal or low SVC flow/RVO High pulmonary VR	Dobutamine 10 to 20 mcg/kg per minute titrated to maintain: –SVC flow >40 mL/kg per minute/ RVO >120 mL/kg per minute Second-line: Adrenaline

SBF=systemic blood flow; BP=blood pressure; SVC=superior vena cava; LVO=left ventricular output; RVO=right ventricular output; VR=vascular resistance



Term

Emergency Department

Pediatric Intensive care unit

0 min

Recognize decreased perfusion, cyanosis, and RDS.
Maintain airway and establish access according to NRP guidelines

5 min

Initial resuscitation: Push boluses of 10 cc/kg isotonic saline or colloid up to 60 cc/kg until perfusion improves, unless hepatomegaly develops.
Correct hypoglycemia & hypocalcemia. Begin antibiotics.
Begin prostaglandin until ductal-dependent lesion is ruled out.

15 min

shock not reversed?

Fluid refractory shock: Titrate dopamine 5-9 mcg/kg/min.
Add dobutamine up to 10 mcg/kg/min.

shock not reversed?

Fluid refractory dopamine-resistant shock: Titrate epinephrine 0.05 to 0.3 mcg/kg/min

60 min

shock not reversed?

Catecholamine resistant shock: Monitor CVP in NICU, attain normal MAP-CVP & $ScvO_2 > 70\%$,
SVC flow > 40 mL/Kg/min or CI 3.3 L/m^2/min

Cold shock with normal blood pressure & evidence of poor LV function
If $ScvO_2 < 70\%$
SVC flow < 40 mL/Kg/min or CI < 3.3 L/m^2/min,
add vasodilator (nitrosovasodilators, milrininone) with volume loading.

Cold shock with low blood pressure & evidence of RV dysfunction
If PPHN with $ScvO_2 < 70\%$
SVC flow < 40 mL/Kg/min or CI < 3.3 L/m^2/min
add inhaled nitric oxide, consider milrinone, consider inhaled Iloprost or IV adenosine.

Warm shock with low blood pressure:
add volume & norepinephrine.
Consider vasopressin, terlipressin, or angiotensin.
use inotropes to keep $ScvO_2 > 70\%$,
SVC flow > 40 mL/Kg/min & CI 3.3 L/m^2/min

shock not reversed?

Refractory shock: Rule out & correct pericardial effusion, pneumothorax,
Use hydrocortisone for absolute adrenal insufficiency, and T_3 for hypothyroidism.
Begin pentoxifylline if VLBW newborn. Consider closing PDA if hemodynamically significant.

shock not reversed?

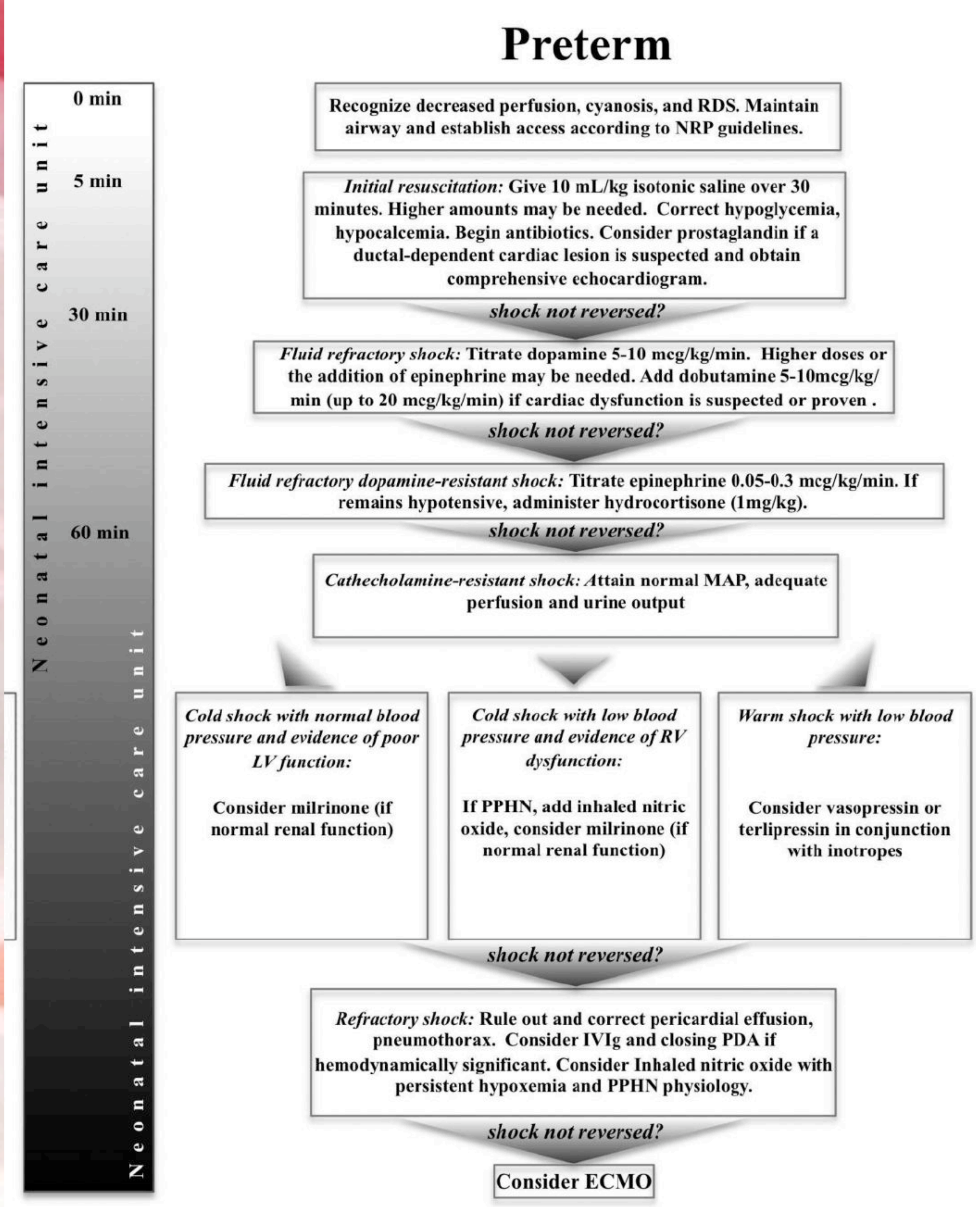
ECMO

ACCCM consensus guidelines for treatment of shock in term infants and suggested modifications for preterm infants

Clin Perinatol. Author manuscript; available in PMC 2011 June 1.

ACCCM consensus guidelines for treatment of shock in term infants and suggested modifications for preterm infants

Clin Perinatol. Author manuscript; available in PMC 2011 June 1.



Preterm

Recognize decreased perfusion, cyanosis, and RDS. Maintain airway and establish access according to NRP guidelines.

Initial resuscitation: Give 10 mL/kg isotonic saline over 30 minutes. Higher amounts may be needed. Correct hypoglycemia, hypocalcemia. Begin antibiotics. Consider prostaglandin if a ductal-dependent cardiac lesion is suspected and obtain comprehensive echocardiogram.

shock not reversed?

Fluid refractory shock: Titrate dopamine 5-10 mcg/kg/min. Higher doses or the addition of epinephrine may be needed. Add dobutamine 5-10mcg/kg/min (up to 20 mcg/kg/min) if cardiac dysfunction is suspected or proven .

shock not reversed?

Fluid refractory dopamine-resistant shock: Titrate epinephrine 0.05-0.3 mcg/kg/min. If remains hypotensive, administer hydrocortisone (1mg/kg).

shock not reversed?

Catecholamine-resistant shock: Attain normal MAP, adequate perfusion and urine output

Cold shock with normal blood pressure and evidence of poor LV function:

Consider milrinone (if normal renal function)

Cold shock with low blood pressure and evidence of RV dysfunction:

If PPHN, add inhaled nitric oxide, consider milrinone (if normal renal function)

Warm shock with low blood pressure:

Consider vasopressin or terlipressin in conjunction with inotropes

shock not reversed?

Refractory shock: Rule out and correct pericardial effusion, pneumothorax. Consider IVIg and closing PDA if hemodynamically significant. Consider Inhaled nitric oxide with persistent hypoxemia and PPHN physiology.

shock not reversed?

Consider ECMO

Gracias por su atención!