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**AD-COR Program inovativ de formare in domeniul cardiologiei pediatrice**
**POSDRU/179/3.2/S/152012**

***Data:*** **16-11-2015**

MODUL TEORETIC

# Post-operative Care in Pediatric Open-Heart Surgery

**Imputernicit: Prof. Dr. Tammam Youssef**

**Activitate prestata de I.R.C.C.S. POLICLINICO SAN DONATO – MILANO, ITALIA in baza contractului nr. 18/22144/29.07.2015**

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Acest material a fost documentat/ validat/ prezentat la sesiunile de formare în cadrul proiectului *„AD-COR Program inovativ de formare în domeniul cardiologiei pediatrice”* - POSDRU/179/3.2/S/152012, proiect cofinanțat din Fondul Social Operațional Sectorial Dezvoltarea Resurselor Umane 2007-2013.

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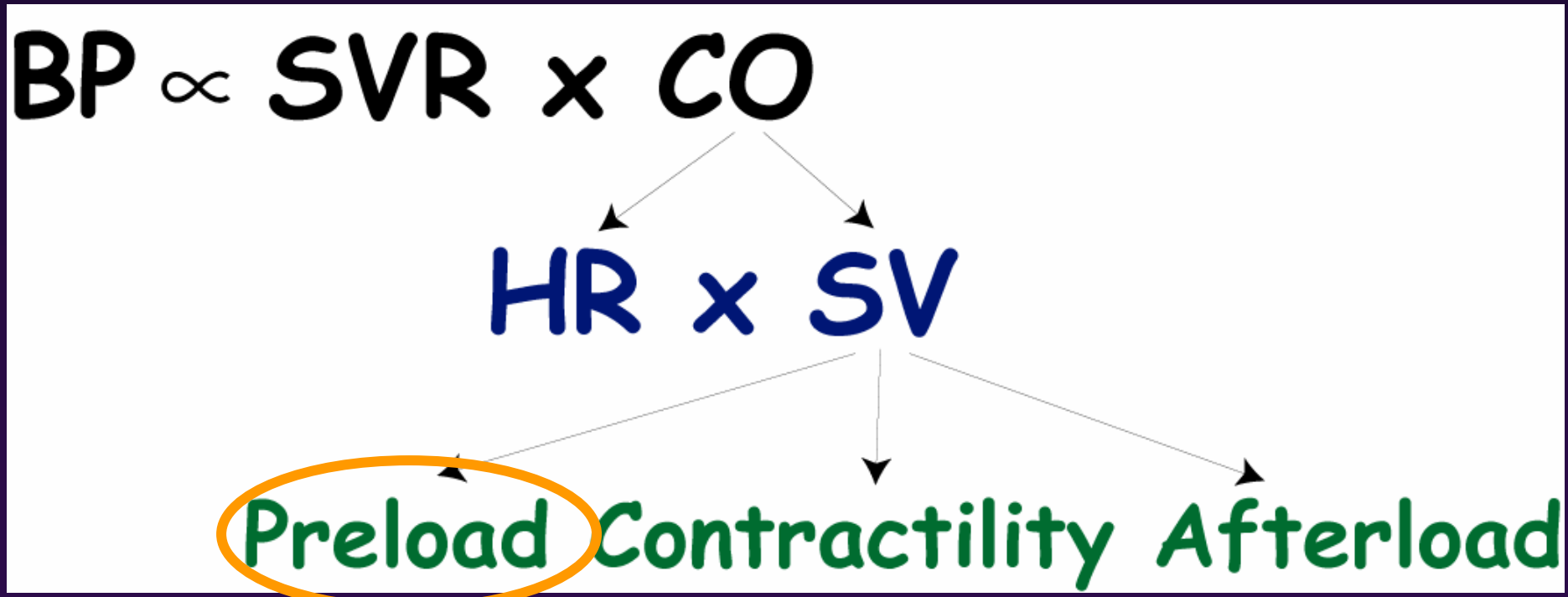
# Post-operative Care in Pediatric Open-Heart Surgery

Anna Cazzaniga
IRCCS Policlinico San Donato
Milano

# Cardiovascular - Basic



# Preload

- Amount of volume filling ventricles during diastole
- Proportional to volume status
- Increasing preload, increases stroke volume (in general)
- Monitor Preload using CVP,RAP, LAP

# Preload Problems in post-op Patients

Either there is not enough preload

or

The heart needs more than usual

# Why too little?

- Post-operative blood loss
- Third Spacing (capillary leak syndrome)

# Why might they need more preload than usual?

- Stiff Right Ventricle
- Right Ventricular Hypertrophy
  - Tetrology of Fallot

- Myocardial edema
  - Prolonged pump run, long cross clamp

# Why else?

- Atrial arrhythmias or Junctional rhythms
  - No atrial ‘kick’
- Passive blood flow to the lungs
- (Glenn Fontan Operation)

# Preload - treatment

Crystalloids

vs.

Colloids

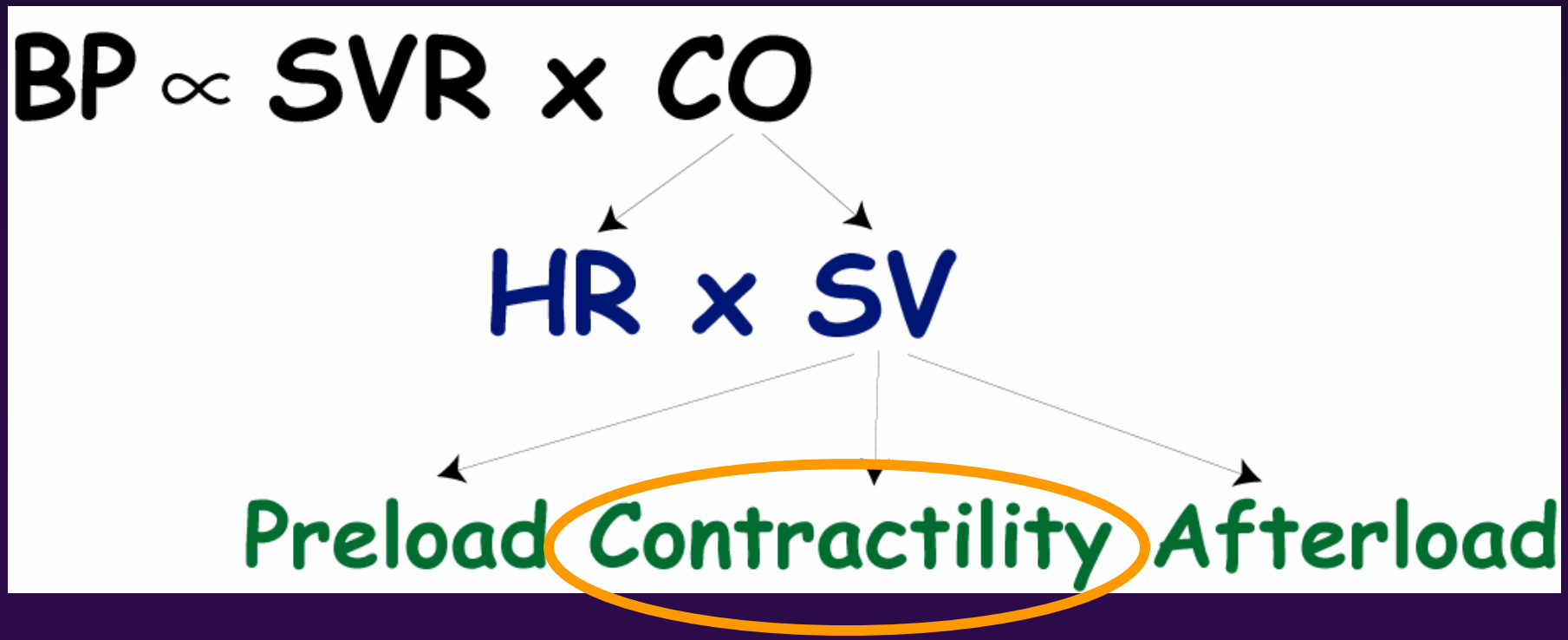
# Crystalloids

- Isotonic Fluid
- Normal Saline
  - 154 mEq NaCl/l
- Lactated Ringers
  - 130mEq $Na^{+}$
  - 4mEq $K^{+}$
  - 3mEq $Ca^{+2}$
  - 109mEq $Cl^{-}$
  - 28mEq Lactate

# Colloids

- Oncotic properties
- More likely to stay intravascular
- Longer duration of action
- Less likely to contribute to edema

# Back to our diagram



# Contractility

- Often impaired
- Secondary to surgery
- CPB

# Inotropic Agents

- Dopamine
- Dobutamine
- Epinephrine
- Milrinone
- Levosimendan

# Dopamine

- Alpha, beta and dopaminergic agonist
- Dose range: 2-10mcg/kg/min
- Effects: Low dose 2-5mcg/kg/min
  - 'renal' dose
  - Middle range: more beta
  - Higher range: alpha starts to predominate
- Use: inotrope, vasoconstriction
- Risk: vasoconstriction, tachycardia

# Dobutamine

- β1 selective
- Dose range: 5-10mcg/kg/min
- Effect: increased inotropy and chronotropy
- Use: to increase contractility, strength of contraction
- Risk: vasodilation in higher dose range, tachycardia

# Epinephrine

- Trade name Adrenalin

- works at all receptors $\beta > \alpha$
- Dose range: 0.05mcg/kg/min – 0.2 mcg/kg/min
- Use: most potent inotropic effect
- Risk: vasoconstriction, ischemia, acidosis, tachycardia

# Milrinone

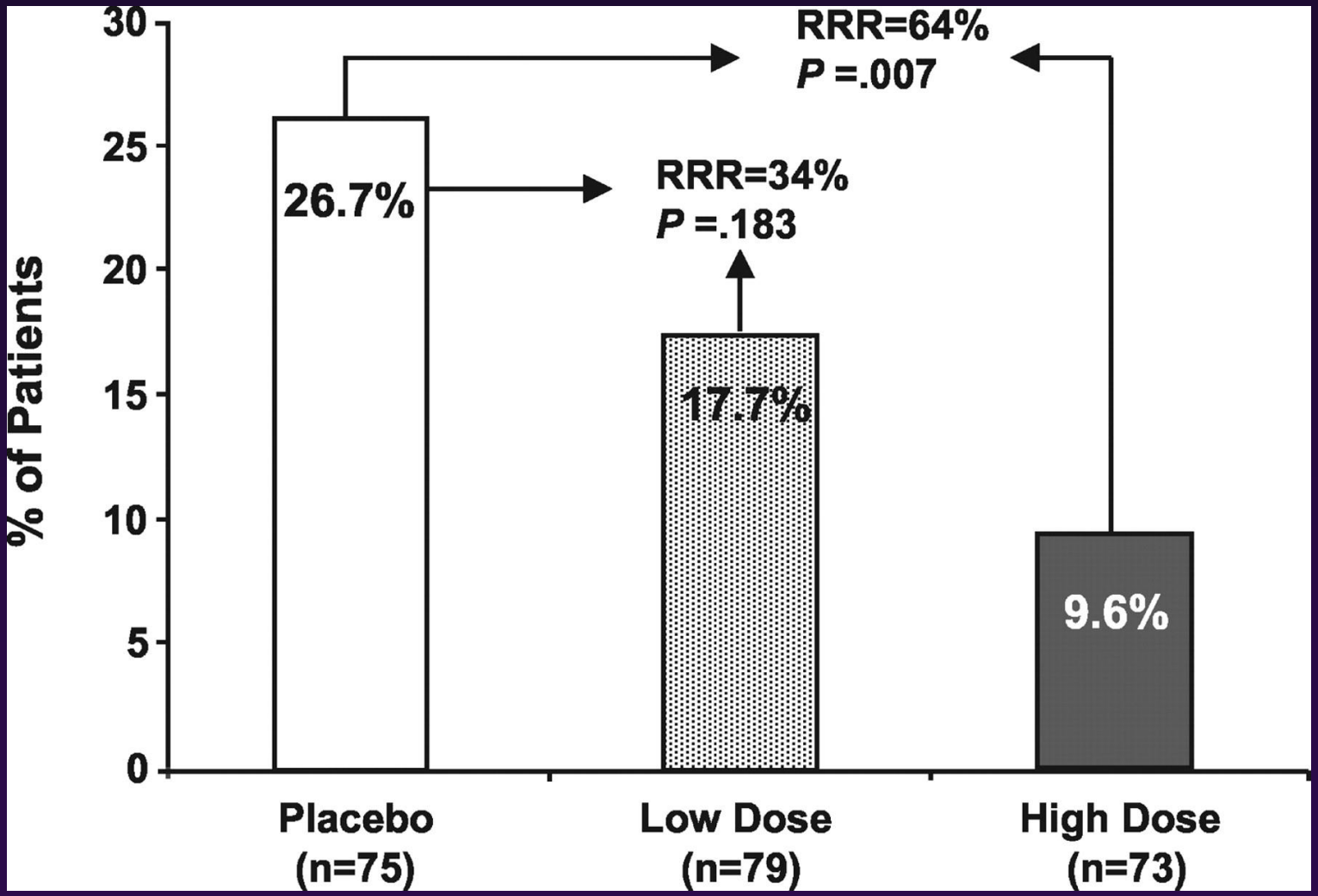
- A phosphodiesterase inhibitor
- Inhibits breakdown of cAMP
- Dose range: 0.375-0.750 mcg/kg/min

# Efficacy and Safety of Milrinone in Preventing Low Cardiac Output Syndrome in Infants and Children After Corrective Surgery for Congenital Heart Disease

*by Timothy M. Hoffman, Gil Wernovsky, Andrew M. Atz, Thomas J. Kulik, David P. Nelson, Anthony C. Chang, James M. Bailey, Akbar Akbary, John F. Kocsis, Raymond Kaczmarek, Thomas L. Spray, and David L. Wessel*

*Circulation*
*Volume 107(7):996-1002*
*February 25, 2003*

Figure 2. Primary end point: development of LCOS/death in the first 36 hours (per-protocol population, n=227).

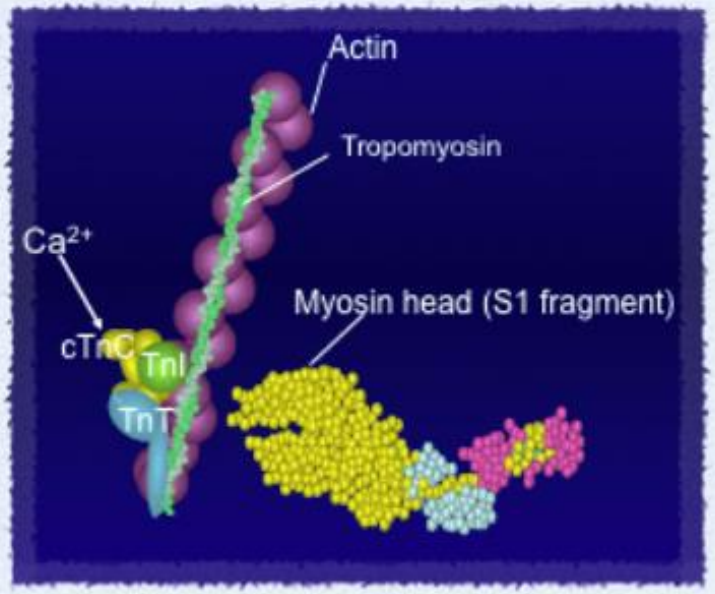



Timothy M. Hoffman et al. Circulation. 2003;107:996-1002

American Heart Association

# LEVOSIMENDAN

## Calcium sensitisation for enhanced cardiac contractility




Inotropic and lusitropic effect

Short-term treatment

## DOSE

The usual dosage of intravenous levosimendan used in clinical trials of patients with heart failure is 6 to 12 µg/kg loading dose over 10 minutes followed by 0.05 to 0.2 µg/kg/min as a continuous infusion.

Hemodynamic response is generally observed within 5 minutes of commencement of infusion of the loading dose. Peak effects are observed within 10 to 30 minutes of infusion; duration of action of levosimendan is about 75-78 hours to 1 week due to active metabolites.

OR - 1896

It is now believed that levosimendan increases cardiac output by several mechanisms, involving its effects on heart rate, improvement of cardiac performance and vasodilation

Lille- berg et al., 1995; Nieminen et al., 2000; Slawsky et al., 2000; Follath et al., 2002; Kivikko et al., 2002a,b

..”Theoretically, levosimendan could increase cardiac output partly by increasing heart rate”...

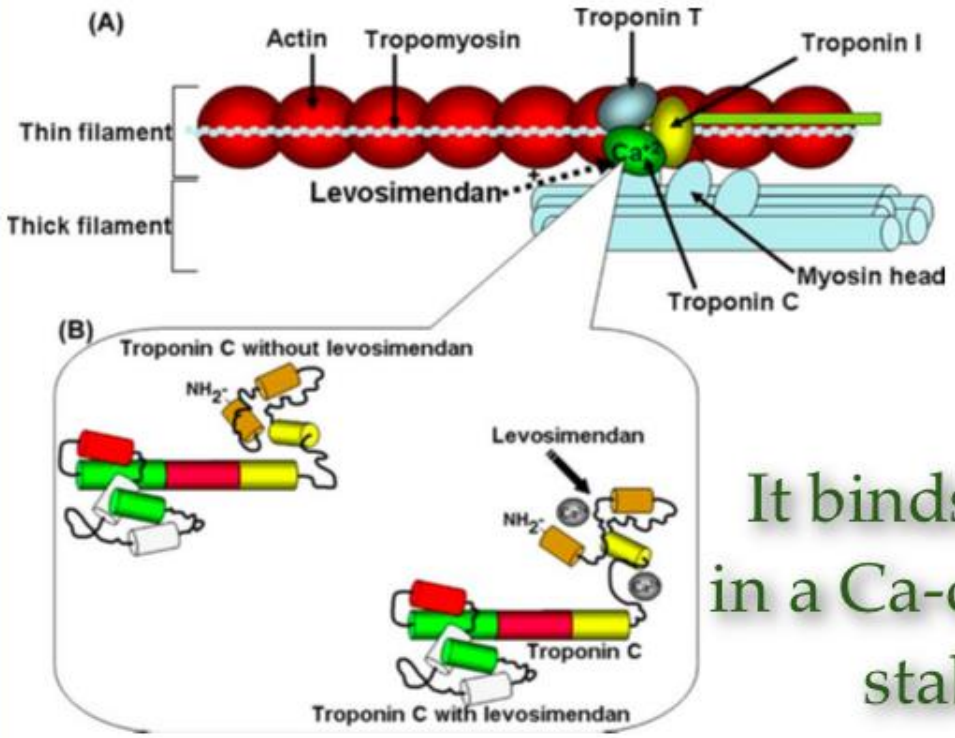
Todaka et al., 1996

..“Although the exact mechanism of the effect of levosimendan on heart rate is unknown, it seems to be partly mediated by compensatory vasodilation-induced activation of baroreceptor reflexes”..

Harkin et al., 1995

# LEVOSIMENDAN:

## IS A PYRIDAZONE-DINITRILE DERIVATIVE




This causes actin-myosin cross-bridges, without increasing myocardial consumption of ATP.

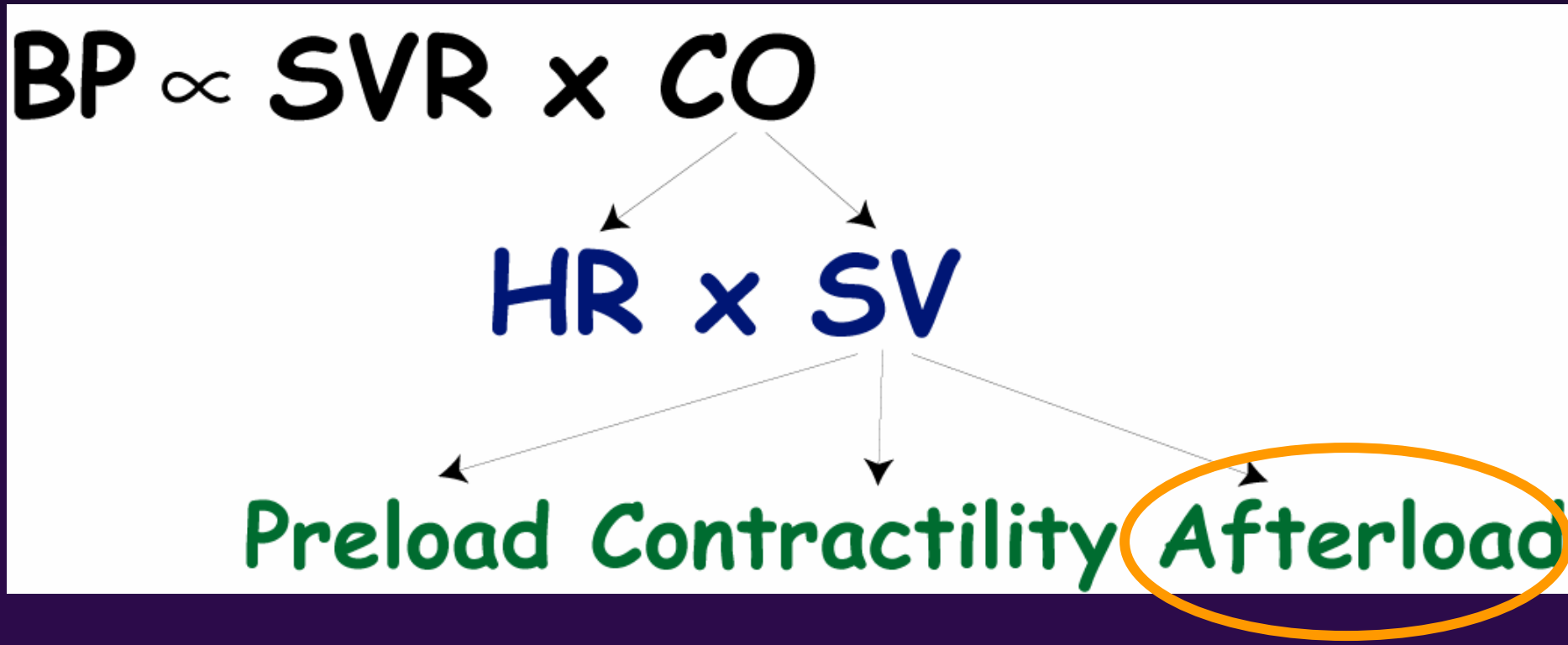
It binds to cardiac troponin C in a Ca-dependent manner and stabilises troponin C.

# COMPARISON BETWEEN LEVOSIMENDAN, MILRINONE AND DOBUTAMINE

**TABLE I** COMPARISON BETWEEN LEVOSIMENDAN, MILRINONE AND DOBUTAMINE

| Feature | Levosimendan | Milrinone | Dobutamine |
|---|---|---|---|
| Class | Calcium channel sensitizer | Phosphodiesterase-III inhibitor | Catecholamine ($\beta$-adrenergic agent) |
| Increases intracellular calcium concentrations | No | Yes | Yes |
| Vasodilator | Coronary and systemic | Peripheral | Mild peripheral |
| Increase myocardial oxygen demand | No | No | Yes |
| Arrhythmogenic potential | Rare and may be due to QTc prolongation | Ventricular and supraventricular arrhythmias | Ventricular ectopic activity; less arrhythmogenic than milrinone |
| Adverse events | Headache, hypotension | Ventricular irregularities, hypotension, headache | Tachycardia and increased SBP on overdosage |

# Remember that diagram?



# Afterload

- Refers to work against which the heart is contracting
- Either an immediate obstruction such as valvular stenosis or hypertrophy
- Or related to systemic vascular resistance
- As you might imagine decreasing the afterload will help the heart to contract

# Afterload Reduction

- Nitroprusside
- Nitric Oxide
- Milrinone
- Levosimendan

# Nitroprusside

- Mechanism of action: NO donor
- Site of action: primarily on arteries
- Action: vasodilator
- Dose range: 0.5-4.0mcg/kg/min
- Risks: profound hypotension, cyanide toxicity, methemoglobinemia

# Who needs afterload reduction?

- Decreases force against which heart has to contract
- Particularly needed for patients with aortic insufficiency or mitral regurgitation
  - Can help to decrease the amount of regurgitation
- Poor LV or RV function

# Pulmonary Hypertension and CHD

- Increased pulmonary blood flow
- Pulmonary venous obstruction
- Cardiopulmonary bypass effects
- Worsened or triggered by :
  - Hypoxia
  - Hypercapnia
  - Acidosis
  - Pain

# The most common pathologies where we can meet PHT

- Complete AV- canal
- VSD (in natural history)
- Truncus arteriosus
- Total anomalous pulmonary venous connection
- Partial anomalous pulmonary venous connection (scimitar syndrome)
- Cor triatriatum
- Aorto-pulmonary window
- Congenital mitral stenosis

# Pulmonary vasoconstriction due to impaired nitric oxide production after cardiopulmonary bypass.

Morita K, Ihnken K, Buckberg GD, Sherman MP, Ignarro LJ.

Division of Cardiothoracic Surgery, UCLA School of Medicine, USA.

CONCLUSIONS. Cardiopulmonary bypass impairs pulmonary NO production, resulting in pulmonary vasoconstriction and right ventricular dysfunction, which can be reduced by antioxidants. These findings imply the validity of NO inhalation therapy for postoperative pulmonary hypertension as a supplementation of endogenous endothelium-derived relaxing factor.

## How common is severe pulmonary hypertension after pediatric cardiac surgery?

L. Lindberg, MD, PhD
A. K. Olsson, MD, PhD
P. Jögi, MD
C. Jonmarker, MD, PhD

SEVERE PHT (mean PAP = mean SAP) IS A RARE EVENT (< 5%)

CONCLUSION: Severe postoperative pulmonary hypertension occurred after 2% of the cardiac procedures and in most cases was managed successfully with conventional treatment and had a favorable postoperative outcome. The low incidence relative to previous reports may reflect the benefits of early correction and improved intraoperative and postoperative care.

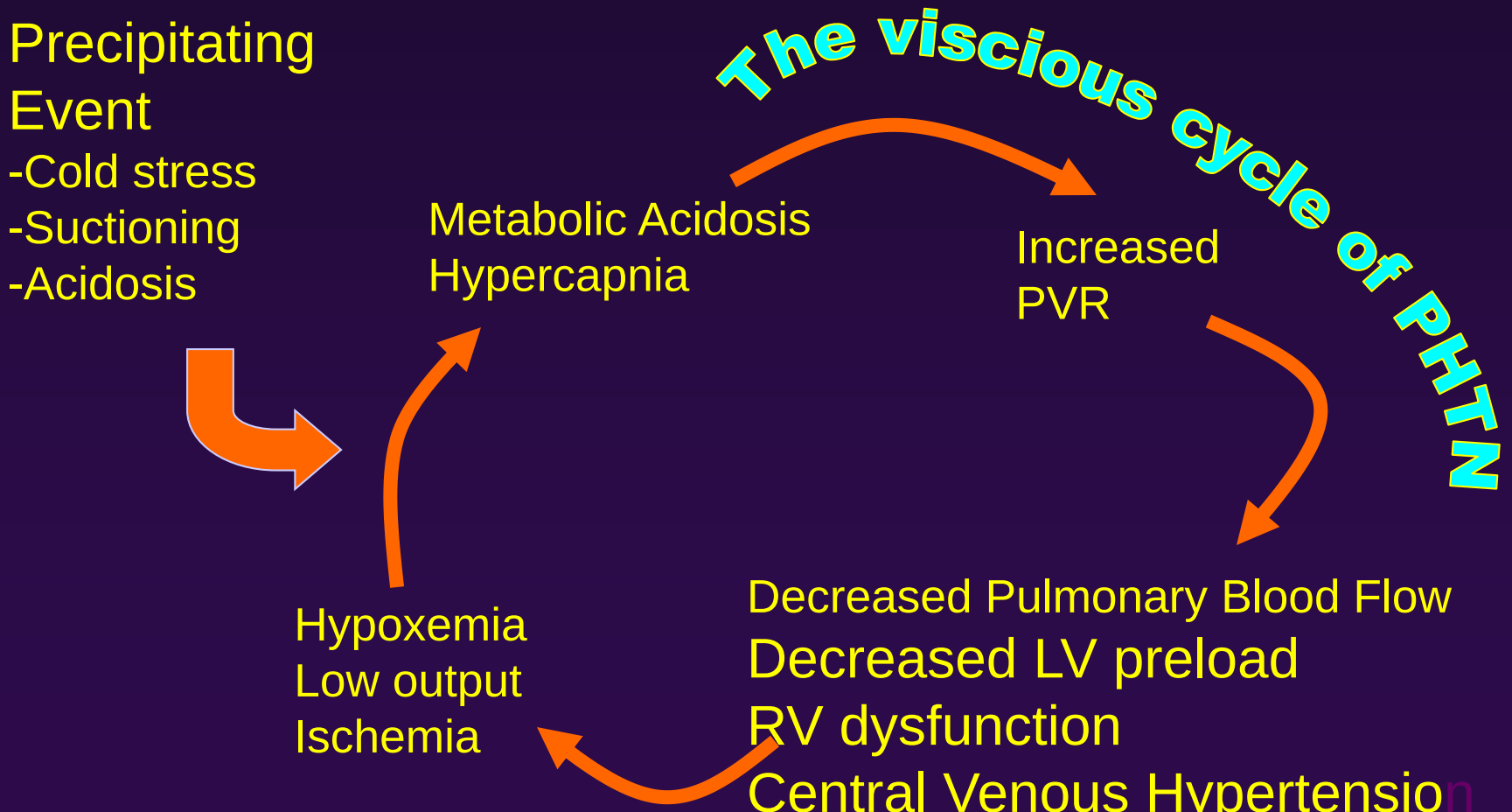
# Pain Control/Sedation

- Stress response attenuation
- Analgesia/anxiolysis
- Fentanyl doses are suggested before suction

# Treatment for Pulmonary HTN

- Classic:
- Hyperventilation
  - pH 7.50-7.55
  - Similar to treatment of PPHN in the neonate
- Oxygen
  - A potent pulmonary vasodilator, keep oxygen high

# Ventilator Strategies: Pulmonary Hypertension



# NO

Duncan J. Macrae
David Field
Jean-Christophe Mercier
Jens Møller
Tom Stiris
Paolo Biban
Paul Cornick
Allan Goldman
Sylvia Göthberg
Lars E. Gustafsson
Jürg Hammer
Per-Arne Lönnqvist
Manuel Sanchez-Luna
Gunnar Sedin
Nim Subhedar

**Inhaled nitric oxide therapy in neonates and children: reaching a European consensus**

# A starting point

Pulmonary hypertension is an important problem in many children with acquired or congenital heart disease. As a selective pulmonary vasodilator, as in neonatal PPHN, iNO has the potential to improve the management of these patients. Numerous reports of iNO usage in such patients have been published including its use in the assessment of the reversibility of pulmonary hypertension as a diagnostic procedure [64, 65] and in the perioperative management of pulmonary hypertension or RV afterload reduction [66, 67, 68]. Inhaled NO has also been shown to complement standard methods of differentiating reactive from fixed pulmonary vascular disease [64, 65].

# A starting point

Inhaled NO has been shown to be effective in the management of some patients with severe reactive pulmonary hypertensive episodes following cardiac surgery [69, 70]. In these patients, iNO is believed to replace endogenous NO production, which is temporarily impaired due to the effects of cardiopulmonary bypass on the pulmonary endothelium. One randomised, controlled trial [71] reported that the prophylactic administration of 10 ppm iNO was associated with a significant reduction in pulmonary hypertensive events and a reduction in time to meeting extubation criteria. Mortality and length of ICU stay were, however, unaffected. Another similar, but smaller, study failed to demonstrate any benefit from prophylactic iNO [72]. The view of the consensus

# A starting point

prophylactic iNO [72]. The view of the consensus meeting experts was that data from other clinical trials was required before the routine prophylactic use of iNO could be recommended in children at risk of pulmonary hypertensive events after repair of congenital heart surgery. Inhaled NO has also been shown to improve the haemodynamic status in patients with elevated PVR after the Fontan operation [73] and in those with failing right ventricles [74]. There are no RCT's in this group of patients.

# A starting point

postoperative iNO in congenital heart patients at risk of pulmonary hypertension. The expert group felt that there is, however, sufficient evidence (from large case series) to support a trial of 20 ppm iNO for 10 min, increasing to 40 ppm if no response to the lower dose, in patients with clinically significant pulmonary hypertension complicating their perioperative course. In this setting it is recommended that iNO should only be continued if there is documented evidence of important haemodynamic improvement. After a 30-min trial of iNO at 20 ppm, increasing to 40 ppm, consideration should be given to discontinuing the drug if no clinically significant response has occurred.

# Renal

- Monitor Input and Output hourly
- Daily Weight

# FLUID OVERLOAD

## Fluid Overload in Infants Following Congenital Heart Surgery

Matthew A. Hazle, MD[1]; Robert J. Gajarski, MD[1]; Sunkyung Yu, MS[1]; Janet Donohue, MPH[1]; Neal B. Blatt, MD, PhD[2]

**Objective:** To describe postoperative fluid overload patterns and correlate degree of fluid overload with intensive care morbidity and mortality in infants undergoing congenital heart surgery.

**Design:** Prospective, observational study. Fluid overload (%) was calculated by two methods: 1) (Total fluid in – Total fluid out)/(Preoperative weight) × 100; and 2) (Current weight – Preoperative weight)/(Preoperative weight) × 100. Composite poor outcome included: need for renal replacement therapy, upper quartile time to extubation or intensive care length of stay (> 6.5 and 9.9 days, respectively), or death ≤ 30 days after surgery.

**Setting:** University hospital pediatric cardiac ICU.

**Patients:** Forty-nine infants < 6 months of age undergoing congenital heart surgery with cardiopulmonary bypass during the period of July 2009 to July 2010.

**Interventions:** None.

**Measurements and Main Results:** Patients had a median age of 53 days (21 neonates) and mean weight of 4.5 ± 1.3 kg. Forty-two patients (86%) developed acute kidney injury by meeting at least Acute Kidney Injury Network and Kidney Disease Improving Global Outcomes stage 1 criteria (serum creatinine rise of 50% or ≥ 0.3 mg/dL). The patients with adverse outcomes ($n = 17$, 35%) were younger (7 [5 – 10] vs. 98 [33 – 150] days, $p = 0.001$), had lower preoperative weight (3.7 ± 0.7 vs. 4.9 ± 1.4 kg, $p = 0.0002$), higher postoperative mean peak serum creatinine ($S_{Cr}$) (0.9 ± 0.3 vs. 0.6 ± 0.3 mg/dL, $p = 0.005$), and higher mean maximum fluid overload by both method 1 (12% ± 10% vs. 6% ± 4%, $p = 0.03$) and method 2 (24% ± 15% vs. 14% ± 8%, $p = 0.02$). Predictors of a poor outcome from multivariate analyses were cardiopulmonary bypass time, use of circulatory arrest, and increased vasoactive medication requirements postoperatively.

**Conclusions:** Early postoperative fluid overload is associated with suboptimal outcomes in infants following cardiac surgery. Because the majority of patients developed kidney injury without needing renal replacement therapy, fluid overload may be an important risk factor for adverse outcomes with all degrees of acute kidney injury. (*Pediatr Crit Care Med* 2013; 14:44–49)

**Key Words:** acute kidney injury; cardiopulmonary bypass; congenital heart disease; dialysis; fluid overload; infants

# Cardiopulmonary bypass and edema: physiology and pathophysiology

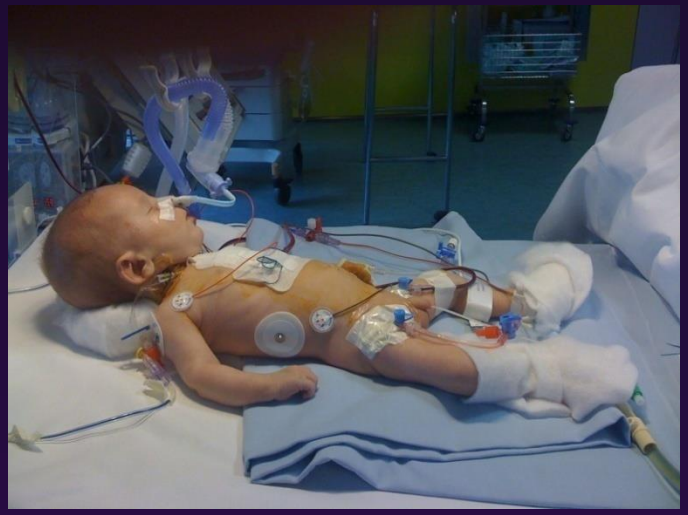
E Hirleman and DF Larson

*Sarver Heart Center, College of Medicine, The University of Arizona, Tucson, AZ, USA*

**Edema is a common morbidity following cardiopulmonary bypass (CPB) and can result in injury to many organs, including the heart, lungs, and brain. Generalized edema is also common and can lead to increased post-operative hospital stay and other morbidities. Pediatric patients are more susceptible to post-CPB edema and the consequences are more severe for this population. Hemodilution and systemic inflammatory responses are two suspected causes of CPB-related edema; however, the mechanisms involved are far from understood. Also, the common strategies to improve edema have not been completely successful and there is a need for new strategies at maintaining a fluid balance of patients as close to physiological as possible, especially for pediatric patients. An integrative approach to understanding edema is necessary as the forces involved in fluid homeostasis are dynamic and interdependent. Therefore, this review will focus on the physiology of fluid homeostasis and the pathologies of fluid shifts during CPB which lead to general edema as well as tissue-specific edema.** *Perfusion* (2008) 23, 311–322.

**Key words:** cardiopulmonary bypass; colloid; edema; inflammation; lymph; osmotic

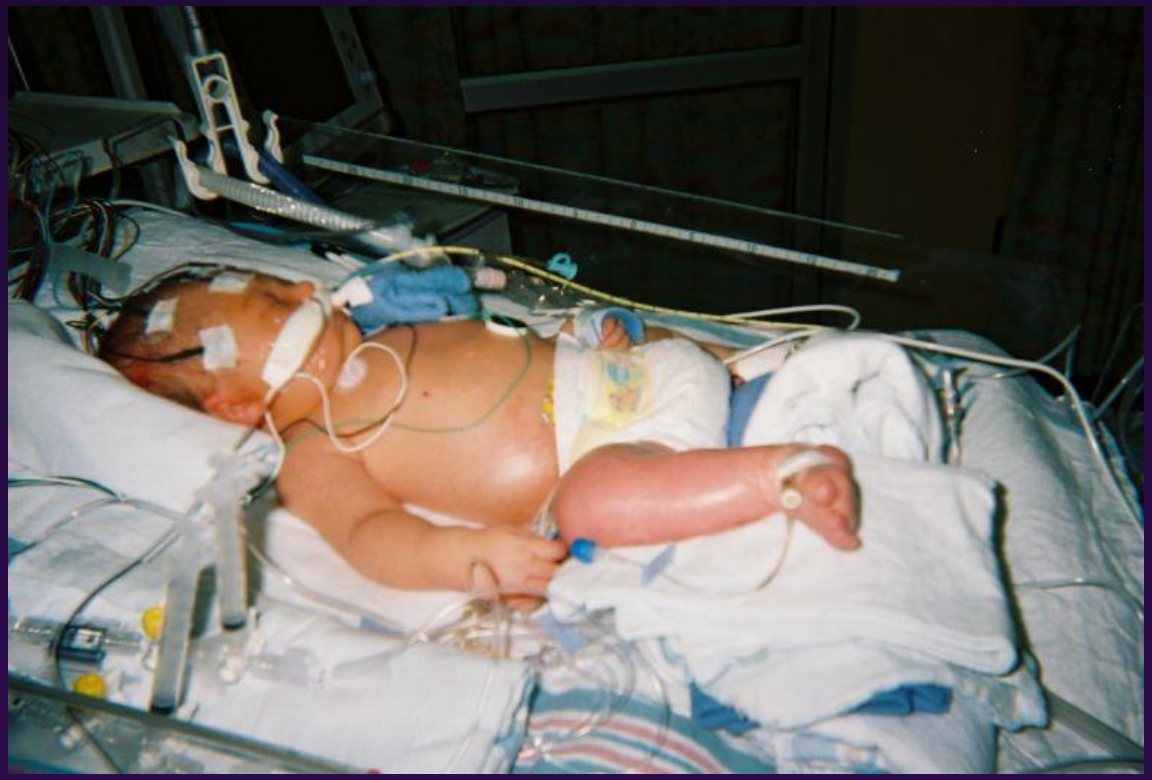
# PEDIATRIC CPB



- The CPB circuit is relatively much greater in small infants

- Longer CPB time at greater degrees of Hypotermia

# PEDIATRIC CPB



Propensity to Capillary Leak

Increase in total body water and tissue oedema

# Managment

- **Diuretic Therapy**
- **Inotropic Agents**
- **Renal Replacement Therapy**
  - **Peritoneal Dialysis**
  - **Hemofiltration**
  - **CVVH CVVHDF**

# Indication of RRT

**In general:**

- **1. Anuria or oliguria (<1ml/kg/h) > 4 hours despite intervention**
- **2. Creatinine > 75 μmol/L (0.85 mg/dL)**
- **3. Increased Creatinine level with:**
  - **Clinical signs of fluid overload**
  - **Hyperkalemia: Serum K+ > 5.5 mmol/L**
  - **Persistent acidosis**
  - **Low cardiac output syndrome**

# Survival and early initiation of RRT

**Table 3** Published reports of peritoneal dialysis after surgery for congenital heart disease (*NA* data not shown in the report)

| Study (ref) | Age | Weight | Time to peritoneal dialysis | Duration | Ultrafiltrate | Mortality |
|---|---|---|---|---|---|---|
| Sorof et al. (*n*=20) | 10 days (3–186) | 3.8 kg (2.7–6.8) | 22 h (5–40) | 50 h (13–92) | –93 ml/kg per 24 h (43–233) | 20% |
| Vricella et al. [13] (*n*=10) | 1–31 days | 2.9 kg | 59 h | 108 h | NA | 30% |
| Book et al. [10] (*n*=15) | 1 month to 14 years | NA | NA | 2–12 days | NA | 33% |
| Rigden et al. [1] (*n*=24) | 1 day to 5 years | 2.4–49 kg | 3–80 h | 1 h to 21 days | NA | 38% |
| Werner et al. [5] (*n*=32) | 22 months | 9.2 kg | 2.6 days | 7.1 days | –48 ml/kg per day | 47% |
| Giuffre et al. [12] (*n*=40) | 2 days to 15 years | 1.7–56 kg | NA | 12.2 days | NA | 57% |
| Fleming et al. [11] (*n*=21) | 7 days to 11 years | 6.7 kg (1.6–27 kg) | 2.5 days (1–6 days) | 136 h (4–360 h) | –9.2 ml/h (3.5–26 ml/h) | 62% |
| Reznik et al. [8] (*n*=19) | NA | NA | 9 days | NA | NA | 79% |

**Elahi MM, et al. *Early hemofiltration improves survival in post-cardiotomy patients with acute renal failure*. Eur J Cardiothorac Surg 2004;26:1027—31**

# Indications of PD

- 1. Anuria or oliguria despite intervention
- 2. Increased Creatinine level with:
  - Clinical signs of fluid overload
  - Hyperkalemia: Serum K+ > 5.5 mmol/L
  - Persistent acidosis
  - Low cardiac output syndrome

**Table 1. Cardiac Lesion of Prophylactic Peritoneal Dialysis Group (n = 186) Under One Year**

| Pathology | No. of Patients | *Risk Category |
|---|---|---|
| TGASimple dTGA (usual coronary artery pattern) Complex dTGA (abnormal coronary artery pattern, subpulmonary stenosis) | 7459 | 34 |
| TOF | 37 | 2 |
| APW*-IAA/IAA | 4*/6 | 4 |
| TAPVR | 5 | 4 |
| Truncus arteriosus | 2 | 4 |
| Coronary artery anomaly | 1 | 3 |
| Aortic stenosis | 2 | 4 |

TGA, Transposition of great arteries, TOF, tetralogy of Fallot; APW* -IAA, aorticopulmonary window associated with interrupted aortic arch; IAA, (total) interrupted aortic arch; TAPVR, total anomalous pulmonary venous return, coronary artery anomaly: LAD from RCA.

* Risk category according to Jenkins risk stratification for congenital heart surgery.20

- Fluid overload is associated to bad outcome and mortality
- Is mandatory to treat earlier FO
- Prevention of FO is possible and feasible (CPB prime, blood conservation, reduction CPB inflammatory response)

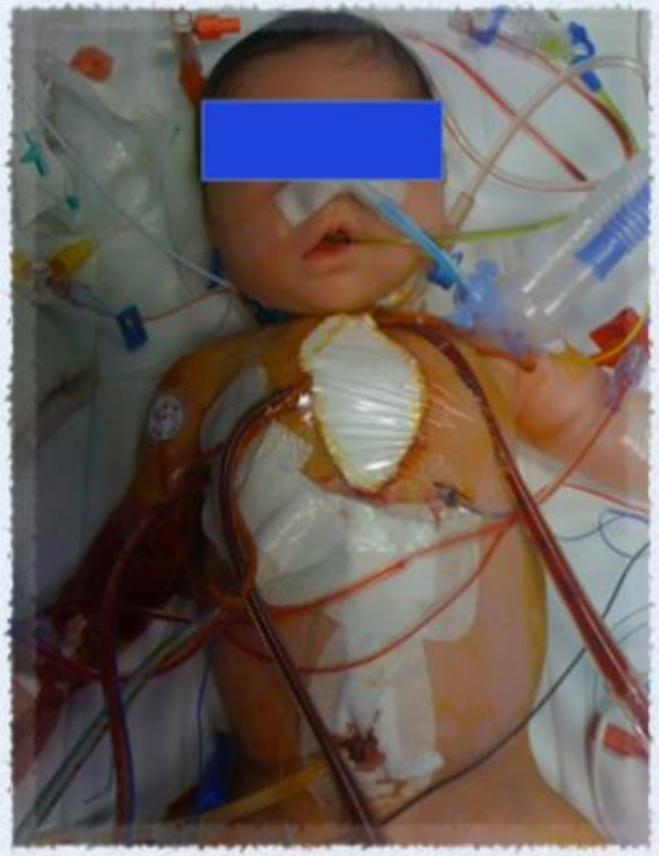
# 100% FLUIDI PARENTERALI

| Peso PZ | Fluidi Giornalieri | Fluidi Orari |
|---|---|---|
| < 10 Kg | 100 ml/kg | 4 ml/Kg/h |
| 10 - 20 Kg | 1000 ml + [50ml x (ogni Kg>10)] | + 2 ml(Kg/h |
| > 20 Kg | 1500 ml + [20 ml x (ogni Kg>20)] | + 1 ml/Kg/h |

# PZ CARDIOCHIRURGICI

## CIRCOLAZIONE EXTRACORPOREA

- 0 gg : 50% dei FLUIDI TOT
- 1 gg: 75% " "
- 2 gg: 85% " "
- 3 gg 100% " "



# PZ CARDIOCHIRURGICI

## SENZA CIRCOLAZIONE EXTRACORPOREA

- 0 gg : 75% dei FLUIDI TOT
- 1 gg: 85% " "
- 2 gg: 95% " "
- 3 gg 100% " "