UNDER PRESSURE:

Management of Neonatal Shock

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Neonatal Shock

- Discuss the pathophysiology that results in each type of shock
- Understand why many infants can have a combination of more than one type of shock
- Use pathophysiology to determine the appropriate combination of treatments for shock

Neonatal Shock

- Shock occurs when **oxygen delivery** is inadequate to meet oxygen demands resulting in organ failure.
- **Oxygen delivery** to the organs depends on **oxygen content and blood flow**

Oxygen Content and Blood Flow

- Oxygen content is determined by hemoglobin concentration and oxygen saturation
- Blood flow (tissue perfusion) is determined by **cardiac output**

Cardiac Output

Cardiac output = **Heart Rate** x **Stroke Volume**

Extremes in **Heart Rate** determines:

- High output failure - decreased cardiac output due to insufficient filling time (decreased stroke volume) from tachycardia (SVT, A-flutter)
- Low output failure – decreased cardiac output due to insufficient heart rate from bradycardic rhythms (heart block)

Stroke Volume

- Determined by:
- Preload – amount of blood returning to the heart
- Afterload – the resistance against which the heart must pump
- Contractility – how well the myocardium squeezes

Summary of Oxygen Delivery

O2 delivery = O2 content + Cardiac Output

O2 Content = Hemoglobin X O2 saturation

Cardiac Output = Stroke Volume x Heart Rate

Stroke Volume determined by:
Preload, contractility and afterload

Decrease in Stroke Volume

Caused by:

– Decreases in Preload

– Decreases in Contractility

– Alterations in Afterload

Decreased Preload – Hyovolemic Shock

- Major cause is hypovolemia
  - Intrapartum blood loss
    - Acute feto-maternal hemorrhage
    - Acute feto-placental hemorrhage (partial cord occlusion)
    - Abruption
    - Cord laceration
    - Acute twin to twin transfusion syndrome
  - Postnatal hemorrhage
    - Intraventricular hemorrhage
    - Pulmonary or gastrointestinal hemorrhage
    - Adrenal hemorrhage
    - DIC from significant in-utero stress or sepsis
    - Capillary leak from sepsis (loss of intravascular colloid)
- Minor cause – excessive positive pressure may reduce venous return

Recognition

- High risk of suspicion from prenatal history
- Sinus tachycardia
- Prolonged capillary refill
- Cool extremities
- Pale
- Weak pulses
- Decreased blood pressure

Treatment

- Volume
  - 2006, Dutch Study in Intensive Care Medicine
  - Initial treatment with isotonic saline bolus 10 ml/kg
    - Reevaluate frequently and repeat bolus as needed
  - May need PRBC
    - review emergency blood procedures in the delivery room
  - Cord blood in extreme emergencies
    - Increased risk of contamination
    - Increased risk of thrombi

Decrease in Stroke Volume

Caused by:

– Decreases in Preload

– Decreases in Contractility

– Alterations in Afterload

Decreased Contractility - Cardiogenic Shock

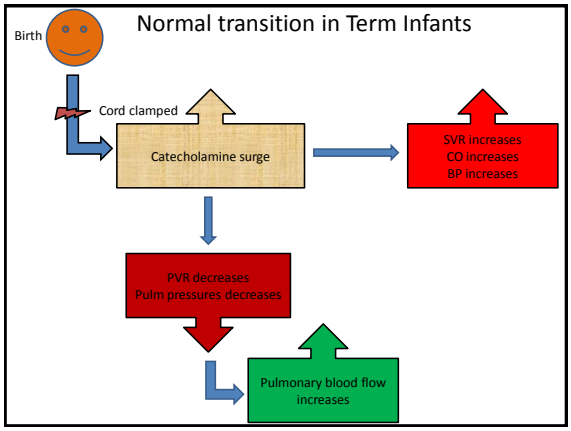
- Common Cause – hypoxic insult to the myocardium
  - Prenatal asphyxia
    - Intermittent cord compression
    - Chronic abruption
    - Fetal anemia
  - Intrapartum asphyxia
    - Acute abruption
    - Cord prolapse
    - Shoulder dystocia
    - Breech delivery with head entrapment
- Less common causes
  - Cardiomyopathy
  - Post viral myocarditis
  - Anomalous origin of the left coronary artery
  - Prematurity

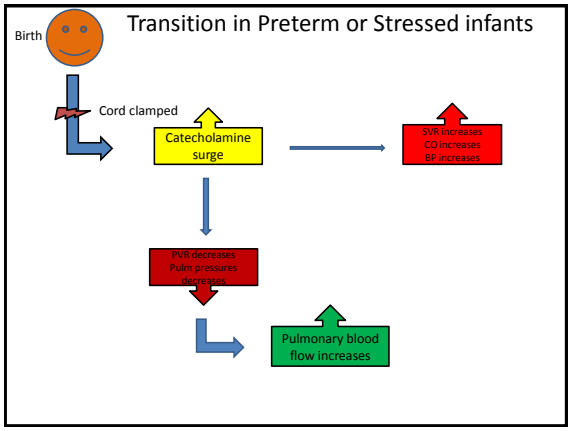
Decreased Contractility - Cardiogenic Shock

In neonates:

- LV functions at a higher baseline contractile state
- Relatively decreased LV muscle mass
- Increased ratio of type I collagen (tissue rigidity) to type II collagen (elasticity) – impaired LV diastolic function

Limits the neonates ability to increase stroke volume or myocardial contractility





Recognition

- Same signs and symptoms as in hypovolemic shock except
  - Can see less tachycardia or even bradycardia
  - Systolic murmur
    - Tricuspid regurgitation
  - Cardiac enzymes will be elevated
    - CPK-MB
    - Troponin-I
    - Brain Natriuretic Peptide – BNP

Brain Natriuretic Peptide - BNP

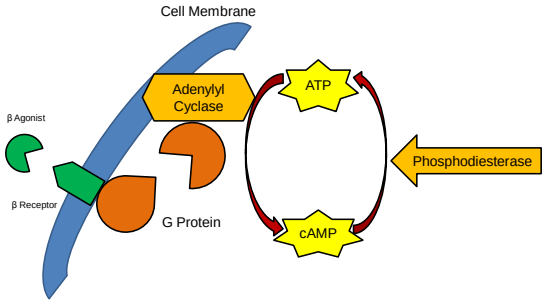
- Hormone secreted by the ventricular myocardium in response to:
  - Increase LV filling pressure
  - Myocardial wall stretch
  - Pressure load
- Actions include:
  - Diuresis
  - Natiuresis
  - Vascular smooth muscle dilatation
  - Antagonist of renin-angiotensin-aldosterone system

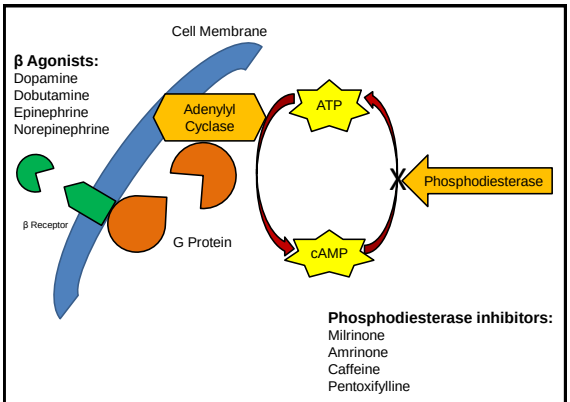
Brain Natriuretic Peptide - BNP

- Elevated in:
  - Congestive heart failure
  - Pulmonary hypertension
  - Various congenital heart diseases
  - Septic shock
- Values:
  - < 100 normal
  - 100-500 mildly high, repeat in 24 hours
  - 500-2000 cardiac dysfunction likely
  - > 2000 poor cardiac function

Treatment

- Volume as previously described unless hepatomegaly develops
- Inotropes:
  - Dopamine usual first choice
  - Consider Dobutamine – lower myocardial O2 consumption
  - Consider adding a vasodilator
    - Nitrosovasodilators
    - PDE inhibitors
    - Inhaled NO





Common Inotropes in Neonates

- Dopamine
  - Low dose – Dopaminergic receptors in the heart and kidney
  - Medium dose – Beta 2 agonist in the heart
  - High dose – alpha agonist in the peripheral circulation
- Dobutamine – combination of Epinephrine and Isoproteronol
  - Epinephrine – alpha and beta agonist
  - Isoproteronol – beta 1 agonist - vasodilatation
- Milrinone
  - Similar hemodynamic result to Dobutamine (inotropy and afterload reduction)
  - Different mechanism of action
- Epinephrine
  - Alpha agonist – vasoconstriction (increase afterload)
  - Beta 2 agonist in the heart

Treatment of Catecholamine Resistant Shock

- Arginine-vasopressin (AVP)
  - Synthesized in the hypothalamus
  - Release stimulated by hypovolemia and increased plasma osmolality
  - Acts via:
    - vascular V1 receptors - arterial vasoconstriction
    - renal tubular V2 receptors – renal free water re-absorption
  - Given as a continuous infusion
- Terlipressin – synthetic analogue of AVP
  - Similar pharmocodynamic profile
  - Longer half-life
    - Given as a bolus

Refractory Shock

- Hydrocortisone
- T3 – if suspecting hypothyroidism (primary or transient associated with prematurity)
- Pentoxifilline – used in VLBW infants (PDE inhibitor)
- Enoximone – PDE inhibitor mostly on beta 1 cAMP
- Levosimendan – increases Ca/actin/troponin complex binding sensitivity
- ECMO

Treatment of Catecholamine Resistant Shock

- Neonates have impaired cortisol production in response to stress
- Hydrocortisone:
  - Attenuates the downregulation of adrenergic receptors and second messenger systems
  - Mineralocorticoid-induced direct increase in myocardial and vascular smooth muscle cell contractility
  - Contribute to the maintenance of capillary integrity
  - Inhibit catecholamine metabolism and reuptake of norepinephrine into sympathetic nerve endings
  - Increase the expression of angiotensin type 2 receptors in the myocardium
  - Inhibit prostacyclin production
  - Inhibit the induction of inducible nitric-oxide synthase

Aids in sustaining the sensitivity of the cardiovascular system to catecholamines

Concerns with the use of Hydrocortisone

- Neurodevelopmental impairment
  - Safer than dexamethasone
  - Used for short course (3-5 days)
- Increased risk of intestinal perforation – do not use concurrently with indomethasin
- May primarily enhance the vasoconstrictive effects of dopamine or epinephrine compromising tissue perfusion despite normalizing blood pressure
- Unknown if it improves mortality or long-term outcome in patients with shock

Decrease in Stroke Volume

Caused by:

- Decreases in Preload
- Decreases in Contractility
- Alterations in Afterload

Alteration in Afterload in Neonates

- Neonates:
  - Left ventricular systolic performance is highly dependent on afterload
  - During transitional circulation neither ventricular output consistently reflects systemic blood flow due to shunts across the PDA and PFO
  - 1/3 < 30 weeks have a period of low systemic blood flow during the first 12 hours of life
  - This low-flow state can be predicted by gestational age
    - 70% < 26 weeks
    - 10% at 29 weeks
  - The peripheral circulation of the very preterm infant is balanced between overconstriction and overdilitation
    - Overconstriction dominates in the first 24 hours
    - Overdilitation dominates after 24 hours
  - Treatment needs to be tailored to the specific condition that exists

Septic Shock

Cold Shock	Warm Shock
• Well described in neonates	• Poorly understood in neonates
• Increased vascular tone	• Loss of vascular tone
• Low systemic blood flow	• Increased systemic blood flow
• Falling blood pressure	• Low blood pressure
• LV or RV dysfunction	

Septic Shock in Neonates

Complicated by:

- Limited ability to increase stroke volume or myocardial contractility
- Reopening of the PDA
- Development of PPHN – from cytokine elevation, acidosis and hypoxia

High morbidity and mortality (Pediatric Critical Care Medicine 2008 Vol 9, No 2)

Majority of deaths occurred in the first 72 hours

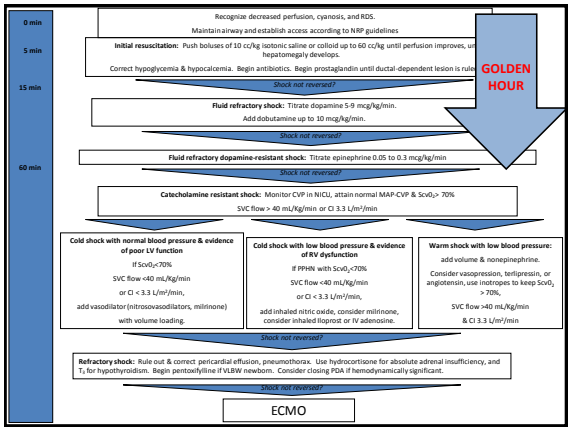
Highest risks for infants < 1000 grams

Highest mortality with gram negative sepsis

Neonatal Septic Shock

Critical Care Medicine
OFFICIAL JOURNAL OF THE SOCIETY OF CRITICAL CARE MEDICINE

Clinical practice parameters for hemodynamic support of pediatric and neonatal septic shock: 2007 update from the American College of Critical Care Medicine – **February 2009**, Volume 37, Issue 2



Treatment of Septic Shock

- Septic shock combination of decreased preload (capillary leak, DIC) decreased contractility, and changes in afterload
- Decreased preload – fluid resuscitation to maintain tissue perfusion.
  - Use caution in premature infants due to risk of IVH and myocardial failure or pulmonary edema
- Decreased contractility – Dopamine, Epinephrine and Milrinone most common
- Changes in afterload – vasoconstrictors for warm shock and vasodilators for cold shock

Summary

- Shock in the neonatal period is a major cause of morbidity and mortality
- Anticipation and early recognition is essential
  - Prenatal and postnatal risk factors
  - Clinical history
  - Physical exam
  - Adjunct blood tests
- Aggressive resuscitation and treatment can change the outcome in the neonate – the Golden Hour
  - Normal saline is recommended as initial fluid resuscitation
  - Dopamine, Dobutamine or Milrinone and then Epinephrine are recommended for inotropic support
  - AVP or Hydrocortisone can be used for catecholamine resistant shock
  - Despite algorithims, frequent reevaluation and tailoring treatment to the specific patient will impact outcome