Recognition & Management of Neonatal Hypertension

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Factors Determining Blood Pressure

- Arterial Pressure is determined by:
  - Propulsion of blood by the heart
  - The resistance to flow of blood through the blood vessels

FLOW = Δ Pressure/resistance

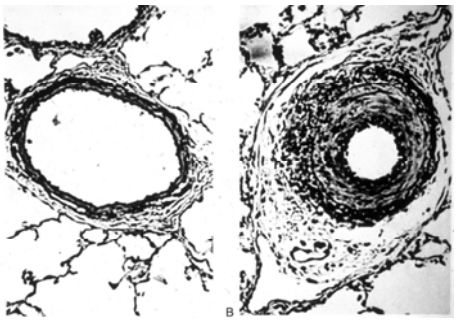
Δ PRESSURE = flow x resistance

Poiseuille's Law

$$Q\ [\text{Flow}] = \frac{\pi\,(Pi - Po)\,r^4}{8\eta l}$$

$$R\ [\text{Resistance}] = \frac{Pi - Po}{Q} = \frac{8\eta l}{\pi r^4}$$

Vascular Resistance in PPHN



Vascular Physiology: Limitations of BP Measurements

FLOW = Δ Pressure/resistance

Δ PRESSURE = flow x resistance

Significant changes in vascular resistance might result in changes in flow & thus tissue perfusion, without recognizable changes in BP

Control of Blood Pressure

- Neural regulation
  - Arterial baroreceptors
  - Autonomic nervous system
- Renin-angiotensin system
- Arginine vasopressin
- Blood volume, cardiac output

Clinical Events that Effect BP in the Newborn Infant

- Blood loss
- Route of delivery
- Asphyxia
- Patent ductus arteriosus
- Apnea
- Respiratory support
- Antenatal steroids
- Postnatal steroids

Blood Pressure Changes in the Newborn Infant

- Low systolic blood pressure at birth is secondary to low C.O. & peripheral resistance
- Systolic BP increases significantly in the first 5 days & continues over the next 6 months, then remains constant until 6 yrs, & then increases until 18 yrs
- Increase secondary to:
  - Increase in C.O. & peripheral vascular resistance

Blood Pressures Changes Over Time

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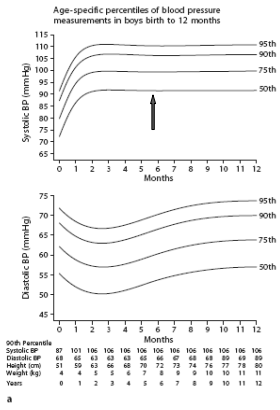

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What is Hypertension for the VLBW Infant?

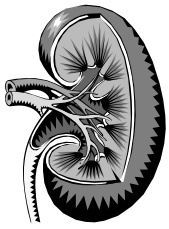
Systemic Hypertension in the Newborn Infant

- Hypertension = >95%
  - From adult data with essential hypertension
  - Lack of biological significance

- 1st Week of Life for Term Infant = >95 mmHg
- Incidence is 0.2 to 2.6%
- Usually related to renal or CV abnormalities

Neonatal Hypertension: Renal Causes

- Renovascular
  - Thromboembolism
  - Renal artery stenosis
  - Mid-aortic coarctation
  - Renal vein thrombosis

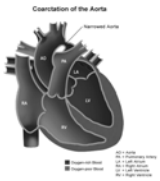


Neonatal Hypertension: Renal Causes

- Renal Parenchymal Disease
  - Polycystic kidney disease
  - Multicystic-dysplastic kidney disease
  - Tuberous sclerosis
  - Ureteropelvic junction obstruction
  - Renal hypoplasia, unilateral

Neonatal Hypertension: Other Causes

- Thoracic aortic coarctation
- BPD, Decadron use
- Congenital adrenal hyperplasia
- Hyperthyroidism
- Pain
- Seizures
- Adrenal hemorrhage
- ECMO

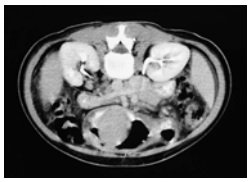


Diagnostic Test for Neonatal Hypertension

- Urine analysis (Culture)
- CBC, platelet count
- Electrolytes, Ca^{++}
- BUN, creatinine
- Plasma renin
- Chest x-ray
- Renal ultrasound with Doppler flow studies
- Cardiac echo

Diagnostic Test for Neonatal Hypertension – Additional Test

- Thyroid studies
- Nuclear scan
- Cortisol
- Aldosterone
- Urine VMA/HVA
- Renal angiogram
- Abdominal CT/MRI



Systemic Hypertension in the Newborn Infant - Treatment

- Hydralazine
  - Direct relaxation of arterial smooth muscle
- Sodium Nitroprusside
  - Nitric oxide donor
- Labetalol
  - Alpha/beta receptor blockage
- Propranolol
  - ß- adrenergic-receptor blockade
- Captopril & Enalapril
  - Angiotensin-converting enzyme (ACE) inhibitor

Neonatal Hypertension: IV Drugs for Acute Hypertension

Table 3 Intravenous agents for acute hypertension and hypertensive emergencies/urgencies (*ACE* angiotensin converting enzyme, *IV* intravenous, *BPD* bronchopulmonary dysplasia)

Drug	Class	Dose	Route	Comments
Diazoxide	Vasodilator (arteriolar)	2–5 mg/kg per dose	Rapid bolus injection	Slow injection ineffective; duration unpredictable; use with caution – may cause rapid hypotension
Enalaprilat	ACE inhibitor	15±5 μg/kg per dose Repeat Q 8–24 h	Injection over 5–10 min	May cause prolonged hypotension and acute renal insufficiency
Esmolol	β blocker	Drip: 100–300 μg/kg per min	IV infusion	Very short-acting – constant infusion necessary
Hydralazine	Vasodilator (arteriolar)	Bolus: 0.15–0.6 mg/kg per dose Drip: 0.75–5.0 μg/kg per min	IV bolus or infusion	Tachycardia frequent side-effect; must administer Q 4 h when given IV bolus
Labetalol	α & β blocker	0.20–1.0 mg/kg per dose 0.25–3.0 mg/kg per h	IV bolus or constant infusion	Heart failure, BPD relative contraindications
Nicardipine	Ca^{2+} channel blocker	1–3 μg/kg per min	Constant infusion	May cause reflex tachycardia
Sodium nitroprusside	Vasodilator (arteriolar & venous)	0.5–10 μg/kg per min	Constant infusion	Thiocyanate toxicity can occur with prolonged (>72 h) use or in renal failure

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Neonatal Hypertension: PO Drugs for Acute Hypertension

Table 4 Oral agents useful for hypertension in infants

Drug	Class	Dose	Interval	Comments
Captopril	ACE Inhibitor	<6 m: 0.01–0.5 mg/kg per dose Max 6 mg/kg per day	TID	Drug of choice for most neonatal HTN monitor serum creatinine and K^+
Clonidine	Central α agonist	0.05–0.1 mg per dose	BID–TID	Side effects include dry mouth & sedation; rebound hypertension with abrupt discontinuation
Hydralazine	Vasodilator (arteriolar)	0.25–1.0 mg/kg per dose Max 7.5 mg/kg per day	TID–QID	Suspension stable up to 1 week; tachycardia & fluid retention common side-effects; lupus-like syndrome may develop in slow acetylators
Isradipine	Ca^{2+} channel blocker	0.05–0.15 mg/kg per dose Max 0.8 mg/kg per day	QID	Suspension may be compounded; useful for both acute & chronic HTN
Amlodipine	Ca^{2+} channel blocker	0.1–0.3 mg/kg per dose Max 0.6 mg/kg per day	BID	Less likely to cause sudden hypotension than isradipine
Minoxidil	Vasodilator (arteriolar)	0.1–0.2 mg/kg per dose	BID–TID	Most potent oral vasodilator; excellent for refractory HTN
Propranolol	β – blocker	0.5–1.0 mg/kg per dose	TID	Maximal dose depends on heart rate; may go as high as 8–10 mg/kg per day if no bradycardia. Avoid in infants with BPD
Labetalol	α and β blocker	1.0 mg/kg per dose Max. 10 mg/kg per day	BID–TID	Monitor heart rate; avoid in infants with BPD
Spironolactone	Aldosterone antagonist	0.5–1.5 mg/kg per dose	BID	Potassium "sparing"; monitor electrolytes. Takes several days to see maximum effectiveness
Hydrochlorothiazide	Thiazide diuretic	1–3 mg/kg per dose	QID	Monitor electrolytes
Chlorothiazide	Thiazide diuretic	5–15 mg/kg per dose	BID	Monitor electrolytes

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Systemic Hypertension in the Newborn – Long-term Outcome

- Outcome related to cause
- Large percent come off medications by the first year of life
- Most come off medication by the 2nd year of life
- Chronic hypertension is usually related to congenital renal anomalies

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