Clinical Guidance

Neonatal Manual Chapter 2: Cardiovascular Problems

Summary
This manual contains clinical guidelines developed by the Neonatal Unit multidisciplinary team over recent years. This chapter contains guidelines on management of babies with various problems on the Postnatal Ward. It is linked to and should be used in conjunction with the completed neonatal manual details of which are contained in the introductory chapters.

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2. Cardiovascular Problems

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2.1 HEART MURMURS DETECTED AT ROUTINE NEWBORN EXAMINATION

• If a heart murmur is detected during routine newborn examination, complete a thorough clinical examination including looking for signs of dysmorphism and other congenital malformations. Check transcutaneous oxygen saturation using a pulse oximeter and do 4 limb BP’s.
• If the baby is unwell, has cyanosis, signs of cardiac failure, or decreased or absent femoral pulses admit to NICU for urgent assessment and referral to the Paediatric Cardiology team.
• If there is a family history of congenital heart disease, other congenital malformations, dysmorphism or an abnormal antenatal echocardiogram discuss with registrar or consultant.
• Ask registrar or consultant to review if baby is well but murmur significant i.e. ≥3/6, harsh, diastolic, pansystolic, continuous or associated with an ejection click or precordial hyperactivity. If registrar / consultant confirms signs, ensure that referral to Paediatric Cardiology has been made before discharge. In these circumstances, Paediatric Cardiology assessment (+/- echocardiogram) is likely to be necessary prior to discharge or in the Cardiology Rapid Access Clinic soon after discharge. Arrange follow-up as decided by Paediatric Cardiology team.
• If the baby is well with grade 1-2/6 murmur loudest at the left sternal edge, has normal pulses, no ejection clicks and no signs of respiratory distress then review before discharge. If still present then arrange for Neonatology OPD follow-up in 4 - 6 weeks (Discuss with consultant on for postnatal wards). Warn the parents about significant signs to observe for (poor feeding, lethargy, pallor, sweating, cyanosis, apnoea and breathlessness) and to seek medical advice early should there be any concerns. Ask registrar or consultant to review if there is any uncertainty. ECG and CXR are unnecessary. If the murmur is still present when baby is seen in the Neonatology OPD, referral to Paediatric Cardiology may be arranged by the Consultant Neonatologist for that clinic.
2.2 HYPOTENSION

Hypotension is usually a feature of uncompensated shock in neonates. Signs of compensated shock may precede hypotension and include mottling, mild tachycardia and reduced spontaneous movement. Signs of uncompensated shock include hypoperfusion with prolonged capillary refill time, widening of toe-core temperature difference, tachycardia, metabolic acidosis, raised lactate and reduced urine output.

Causes of shock

- **Hypovolaemia**
  - acute blood loss
  - fluid losses (diuresis, insensible etc.)
  - third spacing (hydrops, NEC, sepsis, postoperative)
- **Distributive (aberrant local regulation or generalised vasodilation)**
  - common in extreme preterm infants
  - sepsis
  - effect of maternal medications (drugs given to mother for hypertension prior to delivery).
- **Cardiogenic**
  - impaired venous return
    - hyperinflated lungs (more likely with HFO)
    - pneumothorax
    - abdominal distension
  - myocardial dysfunction
    - perinatal asphyxia
    - more common in SGA babies if placental function poor
    - congenital heart disease (e.g. hypoplastic left heart syndrome)
    - post cardiac surgery
    - cardiomyopathy
  - arrhythmias

Definition of hypotension

- This is difficult to define accurately. If the lower 95% confidence interval is used for mean blood pressure, this approximates the baby’s gestational age in weeks - i.e. if a 25 week gestation baby is 1 week old, the minimal accepted mean BP should be 26mmHg
- Markers of tissue hypoperfusion should also be considered when deciding on the threshold for intervention of circulatory support (see below)
- Babies with a PDA are likely to have a decreased mean BP due to the increased pulse pressure. It may be reasonable to consider a minimal accepted mean BP of up to 3mmHg below the baby’s corrected gestational age in these cases, in the absence of markers of tissue hypoperfusion

**Action:**
1. Confirm the BP reading is accurate and the transducer has been calibrated and positioned correctly. Continuous intra-arterial BP monitoring is preferable in any unstable baby
2. Look for signs of tissue hypoperfusion – e.g. prolonged capillary refill time, metabolic acidosis (likely to be with increased anion gap (>12mmol/L) and raised lactate (>2mmol/l) – see metabolic acidosis protocol), reduced urine output
3. Consider possible underlying causes as above
4. Echocardiogram – exclude congenital heart disease, assess PDA, assess markers of hypovolaemia (underfilled left ventricle, ‘collapsed’ IVC etc.), assess left ventricular function etc. Echo should be requested if there is uncertainty as to the underlying problem and/or baby is requiring escalating inotropic support.
5. Consider CVP monitoring. CVP <2-3mmHg suggests hypovolaemia, and serial measurements may be a useful guide to volume expansion

**Treatment**
Consider in this order:
1. **Volume expansion**
   - In preterm infants this should not be firstline management of hypotension unless there is clear evidence of hypovolaemia.
   - In term infants this should be used cautiously unless there is good evidence of hypovolaemia (i.e. recent blood/fluid loss, raised haematocrit +/- low CVP)
   - 10 mL/kg 0.9% saline IVI over 20-30 minutes
   - Packed red blood cells may be used if there is evidence of recent acute blood loss or if PCV is <0.35
   - Repeat boluses of fluid should only be given if there is good evidence of hypovolaemia
2. **Dopamine**
   - Start if no evidence of hypovolaemia or following lack of response to volume expansion
   - Give via central venous line if available
   - Start at dose of 2.5 micrograms/kg/min (preterm infants may be exquisitely sensitive to small amounts of dopamine; don’t be tempted to increase this to a higher dose or to purge the line; this can lead to big swings in blood pressure)
   - Increase by 2.5-5 micrograms/kg/min. every 15 minutes according to haemodynamic response to a maximum of 20 micrograms/kg/min.
   - N.B. Dopamine may not be the best initial choice of inotrope in certain situations – e.g. peripheral vasoconstriction, PPHN and some types of cardiomyopathy. If in doubt discuss with the consultant neonatologist.

3. **Dobutamine**
   - This may be useful to add if there is inadequate response to dopamine and/or volume expansion. It may be also be a good first choice inotrope if there is marked peripheral vasoconstriction, PPHN or some types of cardiomyopathy. It may exacerbate hypotension by causing peripheral vasodilatation. It can also cause significant tachycardia.
   - Give via central venous line if available
   - Start at dose of 5 micrograms/kg/min.
   - Increase by 5 micrograms/kg/min. every 15 minutes according to haemodynamic response to a maximum of 20 micrograms/kg/min.

4. **Hydrocortisone**
   - Relative adrenocortical insufficiency is a recognised cause of hypotension in preterm infants. Therefore consider hydrocortisone in hypotensive preterm infants failing to respond to the above.
   - Hydrocortisone can also increase the effect of dopaminergic drugs
   - Dose - 2.5mg/kg IV every 4 hours for 2 doses then 6 hourly.

5. **Phosphodiesterase inhibitors e.g. milrinone**
   - Discuss with consultant (+/- Paediatric Cardiology team) prior to use
   - Phosphodiesterase inhibitors inhibit NO breakdown (thereby increasing NO levels) and have inotropic and vasodilator activity
- Milrinone: loading dose 50 micrograms/kg/min. IV bolus, followed by 0.5 micrograms/kg/min. The dose may be increased thereafter but not >0.75 micrograms/kg/min.

6. **Epinephrine (adrenaline) and norepinephrine (noradrenaline)**
   - Discuss with consultant prior to use.
   - Should be used with a peripheral vasodilator such as dobutamine or milrinone.
   - Epinephrine - dose – 0.1 - 1.5 micrograms/kg/min. according to response. (doses up to 0.5 micrograms/kg/min. may be used – discuss higher doses with a consultant if necessary)
   - Consider using norepinephrine as an alternative in PPHN (or if there is marked peripheral vasoconstriction). Dose – 0.02 – 0.1 micrograms/kg/min. (doses up to 0.5 micrograms/kg/min. may be used – discuss higher doses with a consultant if necessary)

**Weaning inotropes**
- Decisions about weaning of inotropes should usually be made on ward rounds
- Usually wean in reverse order that inotropes were started
- Wean one inotrope at a time
- Avoid hypertension
2.3 ARTERIAL OCCLUSION / THROMBOSIS
(see separate *Paediatric Thrombosis Guideline*)

- Loss of the peripheral pulses after arterial cannulation (including after cardiac catheterisation) with large catheters may be due to:
  - Vessel spasm - usually combined with some thrombus formation.
  - Occlusive thrombus at the puncture site - less commonly.
  - Vessel dissection - very rarely.
- Heparin is used to prevent propagation of thrombus while natural thrombolysis and relaxation of the spasm takes place.
- Pulses that can only be found on Doppler may be due to collateral flow when the major limb artery is occluded.
- Doppler ultrasound assessment of vascular occlusion may be helpful in the diagnosis and assessment after treatment. However, treatment should not be delayed by waiting for an ultrasound scan if circulation is compromised.

**Management**

1. Remove arterial catheter
2. If the limb is warm, normal colour and pulses are easily felt:
   - observe puncture site and peripheral pulses at least hourly.
3. If the limb is warm, normal colour but pulses are weak:
   - GTN patch – place half a 5mg patch over proximal part of affected limb
   - commence heparin (see separate *Paediatric Thrombosis Guideline*)
4. If the limb is cool, or colour pale or pulses absent:
   - give heparin bolus & infusion (as above) immediately.
   - start t-PA (see separate *Paediatric Thrombosis Guideline*)
2.4 PATENT DUCTUS ARTERIOSUS (PDA) IN PRETERM INFANTS

Clinically significant PDA occurs in 30-40% VLBW infants. It is associated with increased mortality, pulmonary haemorrhage, chronic lung disease, peri/intraventricular haemorrhage and NEC.

Diagnosis

- Clinical signs
  - Low-pitched, continuous murmur
  - Full pulses
  - Wide pulse pressure (i.e. >20-25mmHg)
  - Active precordium
  - Poor lower body perfusion (poor capillary refill, mottled skin)
  - Increased ventilatory requirements
  - Metabolic acidosis
  - Pulmonary haemorrhage

N.B. Absence of a murmur does not exclude PDA. If PDA suspected due to presence of other signs, investigate further and consider treatment

- CXR
  - May show cardiomegaly and pulmonary oedema

- Echocardiogram
  - This is useful if the diagnosis is in doubt, to confirm the presence of PDA prior to medical treatment or surgical ligation and to assess the degree of volume loading of the left atrium and ventricle.
  - An echocardiogram should always be performed prior to starting medical treatment for a PDA to rule out duct-dependant structural abnormalities.

Medical treatment

- Optimize oxygenation by appropriate ventilatory management. Use of higher PEEP (i.e. >6cmH₂O) may be beneficial to minimize the effects of pulmonary oedema and risk of pulmonary haemorrhage.
- Treat anaemia. Maintain Hgb >11-12g/dL
- Fluid restriction should only be necessary if there is clear evidence of fluid overload.
- Frusemide should be considered if there is evidence of pulmonary oedema or fluid overload
• **Ibuprofen**
  - Unless there are contraindications, ibuprofen should be started as early as possible in all VLBW infants with a clinically significant PDA in the first 2-3 weeks of life – i.e. those at greatest risk of increased mortality, pulmonary haemorrhage, chronic lung disease, peri/intraventricular haemorrhage and NEC.
  - For older VLBW infants and other infants with PDA, consideration of treatment with ibuprofen should be made on an individual basis.
  - Consideration should be given to stopping feeds or stopping any increase in feed volumes during treatment with ibuprofen because of its potential to reduce gut blood flow.

  - **Contraindications to ibuprofen:**
    - Renal failure – urine output <0.5-1.0ml/kg/hr. or creatinine >120 μmol/L and rising
    - Severe thrombocytopenia is not an absolute contraindication to ibuprofen treatment. Do not transfuse platelets prior to giving ibuprofen, unless evidence of significant bleeding or other clinical concerns.
    - Severe hyperbilirubinaemia (i.e. serum bilirubin above exchange transfusion level)
    - Evolving IVH
  - **Dose:** 3 IV doses 24 hours apart
    - 1st dose 10mg/kg
    - 2nd dose 5mg/kg
    - 3rd dose 5mg/kg
  - Doses of ibuprofen should be prescribed individually on the single dose part of the prescription chart so that an assessment is made for contraindications prior to each dose
  - Monitor urine output and document average 6 hourly. Check electrolytes, urea and creatinine and FBC once daily (or more frequently if indicated) during ibuprofen treatment.
  - If signs of PDA persist after 1st course of ibuprofen, consider a second course of ibuprofen, this can run straight on from the first course. (A repeat echocardiogram is not always necessary).
  - If signs of PDA persist after 2nd course of ibuprofen or if there are contraindications to treatment with ibuprofen, consider surgical ligation.
Surgical ligation

- Ensure echocardiogram has been done and discuss clinical details and echocardiogram findings with Paediatric Cardiology team
- Prior to surgery:
  - Check platelet count and clotting times are within normal limits
  - Maintain adequate haemoglobin as per anaemia guideline
  - Ensure 2 group and save samples in Blood Transfusion - it is not necessary to cross match packed red cells pre-operatively
  - Check written parental consent has been obtained (to be done by Cardiothoracic Surgery team)
  - Check blood gas immediately prior to transfer to operating theatre
  - If there is significant cardiorespiratory instability, consider inserting a peripheral arterial line prior to theatre
  - Follow guidelines as set out in transfer to theatre document.
  - Baby should have a nasal swab, followed by nasal bactroban and Octenisan wash prior to transfer to theatre.

- Post-operatively
  - Check ventilation and (arterial) blood gas, FBC, serum electrolytes, urea and creatinine and CXR immediately after return from operating theatre
  - Respiratory function frequently worsens immediately post-operatively and it is likely that increased ventilatory pressures will be required. Monitor tidal volumes.
  - Ensure adequate analgesia – regime needs to be individualized but IVI morphine at 10 micrograms/kg/hour is suggested for the 1st 12-24 hours post-operatively
  - Monitor urine output 6 hourly and fluid restrict as appropriate total fluids usually 80-100mL/kg/24 hours for 24-48 hours post-op)
  - Request a post-operative echocardiogram from the Paediatric cardiology team

Ex utero referrals for PDA ligation

- All requests for PDA ligations from other hospitals should be directed to the registrar covering NICU. Babies >2kg may be referred to PICU only if a NICU cot is unavailable.
- The NICU team will liaise with the referring hospital to arrange transfer to St.Thomas’ Hospital NICU as soon as a cot and theatre slot is available.
- NICU consultant or SpR or NICU nurse in charge will liaise with Paediatric Cardiology case manager, bleep 0159.
- Once baby has been admitted to St.Thomas’ Hospital NICU, NICU team will assess the baby clinically and carry out routine pre-op blood tests – FBC and film, full neonatal
profile, 2 samples for blood group, CXR and request Cardiology team to perform an echocardiogram.

- Ensure parents available for consent to be done by cardiothoracic surgical team.
- The NICU team will arrange transfer back to the referring hospital. Babies referred from other hospitals for PDA ligation only should be transferred back within 24-48 hours unless they are too unstable to transport.
- Ensure a post-op echocardiogram is performed by the Paediatric Cardiology team prior to transfer back to the local hospital
- Ensure any X-rays from admission are on CD-ROM to be transferred back with the baby to the local hospital or arrange for a direct PACS transfer.
- The NICU team will arrange transfer back to the referring hospital
2.5 HYDROPS FETALIS

Hydrops fetalis is characterized by excess fluid in 2 or more body compartments (ascites, pleural and pericardial effusions and subcutaneous oedema). Uneven distribution of excess fluid is common. Additional features noted in utero include polyhydramnios and placental thickening (>6cm). The pathophysiology involves conditions leading to abnormal transport of water between the capillary plasma and extravascular tissues including increased capillary hydrostatic pressure, decreased plasma colloid osmotic pressure, increased capillary permeability and decreased lymph flow.

Classification

- **Immune Hydrops**
  - Alloimmune haemolytic disease e.g. Rh isoimmunization
  - Aetiology for the majority of the cases prior to 1960’s but rare now

- **Non-immune Hydrops**
  - Currently ~75% of cases fall into this category
  - Incidence estimated to be 1 per 3000 deliveries

Non-immune hydrops fetalis: differential diagnosis

**Haematologic**

- Fetal alloimmune haemolytic anaemia
- α-Thalassemia
- Fetomaternal or twin-to-twin transfusion

**Congenital Infections**

- Cytomegalovirus
- Parvovirus B 19
- Toxoplasmosis
- Syphilis
- Chagas Disease

**Cardiovascular**

- Arrhythmias
- Cardiomyopathy
- Lesions that result in increased right atrial pressure and volume (usually with atrioventricular regurgitation e.g. Ebstein’s)
- Left-sided obstructive lesions
- Premature closure of the foramen ovale
- Absent ductus venosus
Premature closure of arterial duct
Intracardiac tumors (tuberous sclerosis)
Chorangioma of the placenta, chorionic or umbilical vessels
Haemangiomas (Hepatic, Klippel-Trenaunay-Weber syndrome)

Lymphatic Abnormalities
- Lymphangiectasia
- Cystic hygroma
- Turner’s syndrome
- Noonan’s syndrome

Pulmonary abnormalities
- Lymphangiectasia
- Chylothorax
- Cystic adenomatoid malformation
- Hypoplasia

Other
- Obstructive uropathy
- Congenital nephrotic syndrome
- Chromosomal abnormalities (trisomy 15, 18, 21, XX/XY)
- Neoplasms
- Storage diseases
- Idiopathic

Non immune hydrops fetalis: diagnosis

Antenatal history and investigation results -
- Has alloimmunization been excluded?
- Fetal medicine ultrasound / fetal echocardiography results
- Karyotype
- Maternal serology
- Maternal FBC, antibodies, Kleihauer test
- Amniotic fluid analysis with cultures/PCR
- Fetal cordocentesis – FBC, blood gp., DAT, haemoglobinopathy screen

Antenatal treatment -
- Fetal thoracocentesis/paracentesis
- Blood counts
- Intrauterine transfusion
- Pharmacological treatment through mother (e.g. arrhythmia)
Postnatal investigations -

- CXR / AXR
- ECG
- Ultrasound head, abdomen & chest
- Echocardiography
- Blood tests
  - Blood group and Coombs’ test (direct and indirect)
  - FBC and film
  - Kleihauer test (maternal blood)
  - Array CGH
  - Neonatal full profile
  - Haemoglobin electrophoresis
  - Bacterial and viral cultures / PCR
  - Serology for congenital infections (maternal and infant)
  - Diagnostic thoracocentesis and/or paracentesis
  - Placental anatomy and histology

Non-immune hydrops fetalis: treatment

- Cardiorespiratory stabilization
  - PPHN common, therefore aggressive ventilatory management often necessary including HFOV and iNO
  - Thoracocentesis, paracentesis and fluid and albumin replacement as needed
  - Inotropic support as indicated
  - Fluid restriction & diuretics
  - Specific therapy based on underlying aetiology

Nonimmune hydrops fetalis: prognosis

- Fetal death in ~50% of all cases diagnosed in utero
- ~50% survival in liveborn hydropic infants

Immune hydrops fetalis

Above principles of treatment apply but also note the following

- For hyperbilirubinaemia – refer to separate protocol with a low threshold for exchange transfusion
- Use irradiated blood for transfusion / exchange transfusion due to (small) risk of graft versus host disease if in utero transfusion has been performed
2.6 HYPERTENSION

Normal blood pressure
- Increases with gestational age, birth weight and post-natal age
- Blood pressure in preterm neonates at term corrected age is higher than term neonates at birth
- Blood pressure may increase by 10-20mmHg if stressed

Blood pressure should be measured by oscillometry (Dinamap) +/- an arterial line
- Cuff for Dinamap should be the largest that fits the arm or leg
- The mean BP from an arterial line is likely to be accurate even if the trace is damped

Definition of hypertension
This is difficult to define but the following graph should be used as a guideline to determine 95th centile mean BP according to birth weight and postnatal age.
Treatment for hypertension should be considered if the mean BP is greater than the appropriate value according to this graph on 3 separate occasions.

![95th centile mean BP by BW and postnatal age graph]
Causes of hypertension

- Renal
  - arterial or venous thrombosis
  - arterial stenosis
  - dysplastic kidneys
  - tumour (e.g. Wilm’s)
  - UTI
  - acute tubular or cortical necrosis
- Chronic lung disease
  - usually resolves by 6 months
- CVS
  - Coarctation
  - Aortic thrombus secondary to umbilical arterial catheter
  - middle aortic syndrome
- Endocrine
  - CAH
  - thyrotoxicosis
  - phaeochromocytoma
- Miscellaneous
  - IVH
  - Fluid overload
  - ECMO
  - Maternal cocaine (50% high normal or hypertension)
  - idiopathic
- Iatrogenic
  - dexamethasone (resolves within 2-14 days of stopping)
  - phenylephrine eye drops

Investigations

- Blood
  - FBC, neonatal full profile
  - renin, cortisol, 17αOHprogesterone, catecholamines
- Urine
  - MC&S
  - steroids, catecholamines
- Radiological
- renal u/s scan including Doppler assessment of renal vessels, IVC and aorta
- MCUG, DMSA, MAG3 (discuss with Paediatric Nephrology team before requesting these)
- Echocardiogram
- angiogram – Doppler assessment of renal vessels may be misleading, consider angiogram if high index of suspicion of renal artery stenosis

Clinical presentation
- Asymptomatic
- Cardiac failure mild to severe
- Encephalopathy
- Retinopathy
- Renal insufficiency

Treatment
- Treat underlying condition – discuss with Paediatric Renal and Cardiology teams
- Drugs
  1. Diuretics – chlorothiazide, frusemide, spironolactone
  2. Calcium channel blockers – nifedipine
  3. ACE inhibitors (neonates very sensitive) – Captopril - 0.01mg test dose, then 0.05 - 1.5mg/kg/dose tds
     Monitor BP every 15mins for an hour after a change of dose and check BP before each dose
     Monitor renal function, K⁺ and WBC
     N.B. captopril is contraindicated in renal artery stenosis
  4. β blockers – Propranolol
  5. Hydralazine

Treatment of hypertensive crisis
- Use labetalol or sodium nitroprusside IV
- May take more than 3 days to bring down to 95th percentile if longstanding

Outcome
Most causes resolve, but resolved neonatal hypertension may recur in later childhood
2.7 COARCTATION OF THE AORTA

Definition
Narrowing of the descending aorta, usually adjacent to the site of arterial duct insertion

Diagnosis
- This is usually a difficult diagnosis to make antenatally, therefore babies with suspected coarctation on antenatal fetal cardiology echocardiogram should be admitted to the Neonatal Unit immediately after birth for further investigation and management. Exclusion of coarctation is not usually possible until closure of the arterial duct has occurred.

Management of babies with suspected coarctation of the aorta
- Inform Paediatric Cardiology team if delivery anticipated following antenatal diagnosis. For a straightforward coarctation, there is no need to inform Cardiology until after delivery if the baby is being born in the middle of the night.
- Obtain antenatal Fetal Cardiology notes from Neonatal Unit antenatal file and file in the baby’s notes
- Resuscitate as normal, avoiding using oxygen unless the baby is cyanosed
- Examine the baby carefully, taking particular note of presence or absence of femoral pulses, blood pressure in all 4 limbs and any other congenital anomalies
- Admit to the Neonatal Unit. Heart rate and oxygen saturation should be monitored continuously and 4-limb blood pressure recorded 6 hourly. Examine femoral pulses 12 hourly and inform SpR / consultant if not easily felt.
- Check arterial blood gas and plasma lactate and repeat 12 hourly, or more frequently if concerns or if the baby is unwell. Discuss with SpR / Consultant if metabolic acidosis with increasing base deficit (or lactate) occurs.
- Insert 2 IV lines
- Take blood for karyotype including 22q deletion.
- Inform Paediatric Cardiology team (SpR / Fellow bleep 1344). Do not start Dinoprostone (Prostaglandin E2) unless advised to do so by the Paediatric Cardiology team. If Dinoprostone is required, monitor closely for apnoea and intubate and ventilate early if this occurs
- Feeding
  - If baby well, encourage breast feeding and avoid formula milk unless the mother does not want to breast feed.
- If baby unwell or surgery likely to be early, delay the onset of enteral feeds until baby is stable or post-op. Encourage mother to express breast milk early. Consider trophic feeds initially, followed by increasing to full feeds over a period of 48 hours or slower if there are concerns.
2.8 CYANOTIC CONGENITAL CARDIAC DISEASE

Cardiac causes of cyanosis in the early neonatal period
1. Transposition of the great arteries
2. Pulmonary atresia or critical pulmonary stenosis
3. Tetralogy of Fallot (if pulmonary stenosis severe)
4. Obstructed TAPVC
5. Ebsteins anomaly
6. Tricuspid atresia

Presentation
- Typically present with cyanosis on Day 1 to Day 3
- Presentation may be delayed in TGA if there is a VSD or ASD
- 20% of Fallot’s tetralogy present with cyanosis in the early newborn period and usually have a very narrow RVOT or pulmonary atresia
- Obstructed TAPVC leads to obstruction of the pulmonary veins and therefore marked respiratory distress as well as cyanosis that gets dramatically worse when the ductus closes.

Investigations
- The differential diagnosis will usually include other causes of sudden collapse in the early neonatal period i.e. infection, inborn errors of metabolism, respiratory disease – investigations should therefore cover these possible diagnoses
- CXR: oligaemia is typically seen except in TAPVC where there is marked pulmonary venous congestion
cardiomegaly is seen in Ebsteins
- ECG: may point to a specific diagnosis
- Echocardiography

Management
- Management should always be discussed with the Paediatric Cardiology team at the earliest possible opportunity
- General measures – admit to NICU, establish venous access, maintain temperature, avoid hypoglycaemia and ensure blood pressure is normal
- Arterial blood gas
- if this indicates respiratory failure or there are signs of significant respiratory distress, ventilate
- hypoxia alone is not an indication for ventilation in a baby with cyanotic cardiac disease
- metabolic acidosis:
  - consider possible underlying causes
  - use intravenous volume cautiously and only if there is clear evidence of hypovolaemia
  - if severe, worsening or associated with severe or worsening hypoxia, discuss management with Paediatric Cardiology team. Intubation and positive pressure ventilation, increasing the dose of prostaglandin E2 (PGE2) and/or inotropes may be required. In single ventricle physiology conditions, manoeuvres that balance pulmonary/systemic blood flow may be appropriate (see separate protocol). In other situations balloon atrial septostomy or emergency surgery may be the only options.

- **Prostaglandin E2 (PGE2)**
  - Only commence PGE2 after discussion with the Paediatric Cardiology team unless there is a clear indication that this should be commenced as soon as possible after birth in the Fetal Cardiology notes. Document clearly in the baby’s notes details of any discussions with the Paediatric Cardiology team.
  - Start 5ng/kg/min and increase in increments of 5ng/kg/min if indicated and only if suggested by the Paediatric Cardiology team
  - **Side-effects**: respiratory depression and apnoea – therefore ventilatory support may be required particularly if baby also preterm
  - In obstructed TAPVC where there is significant hypoxia and metabolic acidosis, PGE2 may cause a deterioration in the baby’s condition

- **Venous and arterial access**
  - In a patient with a duct dependent cardiac lesion on a IV PGE2 infusion it is vital to have good venous access. Therefore, the baby should either have a central venous line (i.e. UVC or longline line) or 2 peripheral lines.
  - Arterial access is desirable.
  - There are no contraindications to insertion of a UAC and UVC apart from in babies likely to need balloon atrial septostomy. Discuss with consultant before siting umbilical lines.
• Feeding
  - Use breast milk if available as this is likely to reduce the risk of NEC. If breast milk is available there is usually no contraindication to starting this early, but discuss with the consultant beforehand.
  - If no breast milk is available, consider donor breast milk and still start early otherwise delay the onset of formula feeds until at least day 3, then increase to full enteral feeds over 48 hours, or slower if there are any concerns.
• Diuretics may be helpful in obstructed TAPVC
• Other
  - Balloon atrial septostomy (BAS) or surgical septostomy may be performed in TGA or pulmonary atresia with intact ventricular septum. BAS is usually carried out on NICU or PICU. Babies for a BAS should be intubated, ventilated, paralysed and sedated prior to the procedure. Central venous access should be available or 2 good, working peripheral lines sited, as well as an arterial line. Umbilical lines should not be sited prior to a BAS being done.
  - Timing of surgery. Ensure that a clear plan for this has been documented in the baby’s notes and conveyed to the parents by the Paediatric Cardiology team. This is usually done following the Wednesday afternoon cardiology meeting, which should be attended by one of the Neonatology team.
2.9 ARRHYTHMIAS

Tachycardia
A tachyarrhythmia is suggested by a tachycardia out of proportion to the clinical status. The heart rate in SVT is usually >250/min. SVT is the most common and is often well tolerated. VT is very poorly tolerated and very rare in neonates. Fetal SVT may be managed in utero with maternal medication (usually digoxin or flecainide) and monitoring for heart rate and signs of hydrops.

Management of babies postnatally with fetal tachycardia (SVT)
- Neonatology SHO, registrar (and/or consultant) and NICU nurse to attend delivery
- Inform Paediatric Cardiology team prior to delivery. If baby is felt likely to be stable and in sinus rhythm at birth, the cardiologists do not need to be informed until after delivery.
- Ensure all equipment for extensive resuscitation is available including chest drains and cannulae suitable for paracentesis
- Rapid initial assessment and manage ABC as appropriate
- Manage hydrops according to separate protocol
- Manage SVT according to guidelines below and with advice of Paediatric Cardiology team
- Once initial stability has been achieved, admit to NICU and continue to monitor ECG, oxygen saturations and BP for at least 24 hours or longer if suggested by Paediatric Cardiology team
- If mother has been treated with anti-arrhythmic drugs during pregnancy, take blood for levels from baby as soon as possible after birth
- 12 lead ECG and rhythm strip (even if in sinus rhythm)
- Arrange 24 hour ECG as soon as possible as suggested by Paediatric Cardiology team
- Ensure Paediatric Cardiology follow-up is arranged prior to discharge
- Neonatology follow-up not necessary unless requested by Neonatology consultant

Management of acute SVT
- Rapid initial assessment and manage ABC as appropriate
- Perform 12 Lead ECG and rhythm strip
- Check electrolytes and treat any imbalance
- Ask for Paediatric Cardiology opinion (bleep 1344)
- Ice water immersion (and precipitation of the diving reflex) should be used as first line treatment.
• To perform Ice water immersion – Swaddle the child, place ice water in a bath and immerse the baby’s entire head, face first, for 5 seconds.

• Continue to record rhythm strip and give Adenosine: 50μg/kg rapid IV bolus initially, increasing by 50mcg/kg intervals up to 250μg/kg, every 2 minutes depending on response and according to formulary

• Eyeball pressure and other vagal stimulation manoeuvres apart from ice water immersion should not be attempted

• If unwell, compromised or resistant to adenosine → intubate and ventilate, sedate with IV morphine then synchronised DC cardioversion: 0.5 J/kg

• If resolves, further treatment with an antiarrhythmic (beta blocker or digoxin) may be considered. If using digoxin, loading dose may not be necessary if mother treated antenatally – discuss with Paediatric Cardiology team and refer to formulary.; maintenance dose 5microgram/kg BD. Propranolol (1mg/kg TDS) or other β-blockers may be considered as an alternative.

Congenital complete heart block
This is usually caused by maternal auto-antibodies (anti-Ro, anti-La). In-utero cardiac failure may occur leading to hydrops, particularly if the ventricular rate is <50/min.

• Management of delivery and initial resuscitation as above

• Admit to NICU

• Observe for signs of circulatory compromise: perfusion, BP, lactic acidosis

• 12 Lead ECG and rhythm strip

• Urgent Cardiology opinion – isoprenaline IVI may be considered. Dose 0.02μg/kg/min. increasing to a maximum of 0.5μg/kg/min. Pacing may be required.

• Check maternal auto-antibody screen for SLE if not done already

• Ensure Paediatric Cardiology follow-up is arranged prior to discharge

• Neonatology follow-up not necessary unless requested by Neonatology consultant
2.10 INVESTIGATIONS FOR CARDIOMYOPATHY

Dilated cardiomyopathy is the most common indication for paediatric cardiac transplantation and hypertrophic cardiomyopathy has important implications in view of the risk of sudden death in childhood or adolescence. Diagnosis is made by echocardiogram. Cardiomyopathy in a neonate may present with

- Cardiac Murmur
- Cardiac failure
- Persistent hypotension
- Cardiac arrhythmias
- Maternal diabetes
- Positive family history
- Dysmorphic features

History
- Check for maternal diabetes or administration of ritodrine
- Check if baby has received systemic steroids or insulin
- Check for any recent maternal viral illness +/- rash

Examination
- Look for dysmorphic features – Noonan syndrome, Leopard syndrome, mucopolysaccharidoses and consider review by Clinical Geneticist
- Check for gross hepatomegaly – Glycogen storage diseases and mucopolysaccharidoses
- Exclude hypertension

Investigations
- Echocardiography – confirms diagnosis and important to exclude congenital heart disease such as severe aortic stenosis or anomalous origin of left coronary artery from pulmonary artery (ALCAPA)
- ECG – look for ischaemic changes (ALCAPA), short PR interval (Pompe’s)
- Consider 24 hour ECG recording
- CXR
- Haematology – FBC, ESR, Blood film for vacuolated lymphocytes (EDTA sample)
- Blood culture
- Biochemistry – discuss with Paediatric Metabolic Consultant
• Neonatal full profile
• Plasma Amino acids
• Creatine Kinase – myocardial band (increased in X linked cardiomyopathy)
• Carnitine (decreased in primary carnitine deficiency) and acylcarnitine profile (fat oxidation defects)
• Cardiolipins (Barth Syndrome – if dilated cardiomyopathy and neutropaenia)
• Transferrin isoelectric focusing for congenital disorders of glycosylation, (may need repeating when older if normal)
• Thyroid function tests
• Blood glucose
• Lactate and pyruvate
• Selenium
• Thiamine
• Auto immune – antinuclear & anti DNA antibodies
• White cell Enzymes – if film positive for vacuolated lymphocytes (discuss with biochemical genetics)
• Virology
  - urine taken ASAP (but within 14 days) for CMV DEAFF/PCR
  - clotted blood for enterovirus (coxsackie, echovirus), adenovirus, rubella, EBV serology (order congenital/perinatal infection serology on EPR)
  - stool for electron microscopy
  - throat swab in virus transport medium for culture
• Urine for organic acid profile
• Urine for glycosaminoglycans (GAGs)
2.11 MANAGEMENT OF BABIES WITH SINGLE VENTRICLE PHYSIOLOGY CONDITIONS
(e.g. HYPOPLASTIC LEFT HEART)

Some babies are born with anatomy that means that instead of all blood passing through the lungs and then being pumped systemically, both the systemic and pulmonary circulation is provided by one side of the heart and there may be an imbalance between the flow to the lungs and to the systemic circulation. Typically there is an excess of blood flow into the lungs (Qp) and systemic hypotension, worsening over the first few days as pulmonary vascular resistance (PVR) falls. The extra strain on the heart leads to failure of the pumping chamber and hypotension worsens coronary perfusion, exacerbating the situation still more.

This is best illustrated when there is a single outflow tract e.g.
- hypoplastic left heart
- aortic atresia
- hypoplastic right heart
- pulmonary atresia
- truncus arteriosus

It may also be important to some extent with large VSD’s and AVSD’s, although the presence of separate outflow tracts eliminates the possibility of diastolic run-off into the pulmonary bed.

Presentation
- Initially – few signs, perhaps tachypnoea, increased recession, tachycardia etc. Oxygen saturations may increase as pulmonary blood flow increases. Blood pressure, perfusion, acid-base balance & lactate may remain stable. CXR – ‘wet’ lung fields
- Later – Worse tachypnoea and recession. Oxygen saturations still good, diastolic blood pressure falling, base excess becoming more negative, lactic acidosis develops. CXR – very ‘wet’.
- Very late – desaturation, hypotension, cardiorespiratory arrest.

Management
This is aimed at predicting those babies that will develop this problem and prevent progress into decompensation. There should be close involvement of the Paediatric Cardiology team. Most therapy is aimed at balancing the systemic and pulmonary blood flows.
- Give oxygen only for primary lung disease to minimise a fall in PVR. This is especially important when administering bag/mask ventilation. Oxygen saturations should be 75-85% depending on the baby.
• Cautious fluid restriction and use of diuretics after discussion with cardiologists. The CXR should be monitored for signs of excessive pulmonary blood flow.

• If decompensating, intubate and ventilate in air to maintain PCO2 approximately 7-8kPa. CO₂ dilates the systemic bed but is a pulmonary vasoconstrictor. This needs to be done with careful consideration as positive pressure ventilation can reduce the pulmonary vascular resistance and may make the situation worse. Non-invasive ventilation/CPAP may be useful when there is pulmonary overcirculation.

• Inotropes can be used to increase cardiac output, but will have the same effect on the systemic and pulmonary beds. The choice of inotrope should be discussed with the Paediatric Cardiology team. Inotropes are commonly required post-operatively or when septic.

• Hypoxic mixture – this involves increasing the nitrogen concentration of the inspired gases in order to decrease the oxygen concentration (down to 17%-19%) this will have the effect of increasing pulmonary vascular resistance and reducing pulmonary blood flow. The decision to use a hypoxic mixture should be made by the consultant, normally in discussion with the cardiologists. Help can be sought from the respiratory technicians and PICU. (See Hypoxic Mixture Setup guidelines).

• Single ventricle physiology is inherently unstable and should be resolved (e.g. PA banding) as soon as possible.
2.12 MANAGEMENT OF BABIES WITH 22Q DELETION

- This condition is defined by a chromosomal anomaly (22q11.1 deletion) and embraces children with a number of syndromes including velocardiofacial syndrome, Di George syndrome and other 3rd and 4th pharyngeal pouch syndromes.
- Deletions of the chromosome are detected using array CGH.
- These children may present with antenatal or postnatal diagnoses of cardiac anomalies (particularly aortic arch anomalies, tetralogy of Fallot, VSD), facial dysmorphism, cleft palate, feeding difficulties, scoliosis, hypospadias and later learning disability.

Physical examination
Check that there is clear documentation of a physical examination. Particular features to describe or exclude in this are as follows:
- dysmorphic features of face, skull or pelvis
- cleft palate
- scoliosis
- hypospadias

Investigations
- FBC and film (with manual differential)
- send blood to Clinical Genetics to check 22q status even if performed antenatally
- total CD4 count
- T-cell subsets (sample can be taken about 4 days after last blood transfusion)
- total IgE levels
- calcium and magnesium levels
- thyroid function tests
- CXR
- thymic ultrasound
- echocardiogram

Recommended referrals for further clinical investigations
- audiology assessment
- ophthalmological examination
- renal ultrasound (30% have structural renal abnormalities)
Medical treatment
Maintenance cotrimoxazole is recommended for those with low lymphocyte counts (<1.5 x 10^9/L), and regular intravenous immunoglobulin infusions may be instituted after several months.

Blood transfusions
All 22q deletion patients must receive CMV negative, irradiated blood until the child's immunological status is clarified. If blood is not irradiated, there is a risk of graft versus host disease developing.

Vaccinations
Children with any evidence of reduced T cell numbers should not receive live vaccines, but may be vaccinated according to routine with component or fixed vaccines.

Outpatient follow-up
Consider outpatient appointments for the following as necessary:
- Local General Paediatrics
- Paediatric Cardiology
- Immunology: all babies should be seen in Immunology clinic (see below)
- Plastic Surgery (for cleft lip and palate)
- Speech and Language Therapy
- Community Paediatrics
- Clinical Genetics referral for family studies

Growth retardation, psychiatric and autoimmune problems are more frequent in this patient group so that long-term hospital or community-based Paediatric follow up is recommended.

Immunological follow-up
Early immunology advice is needed for any of the following
- low lymphocyte count (<1.5 x 10^9/L)
- low serum calcium levels
- absent thymus on imaging

All babies should be referred to Dr Esse Menson’s immunology clinic by sending a routine referral letter. Babies without the above problems will be seen around 3 months of age. In this clinic, samples are collected for T cell precursors, T cell responses to tetanus vaccination and decisions are made as to vaccination strategies and further treatments.
Parent help groups:
The 22q11 Group, PO Box 1302, Milton Keynes MK13 0LZ;
email: 22q11@vcfs.net; tel: 0161 485 5155 or 0190 832 0852
2.13 PROBLEMS WITH LATERALITY

Laterality is determined in the early embryo in association with the establishment of the midline. Problems with laterality and of midline structures may therefore be found together.

Causes
- Most sporadic but some evidence for genetic basis – consanguinity↑; also a few families with apparent autosomal dominant inheritance; X-linked syndromes with laterality abnormalities.
- 50% Primary Ciliary Dyskinesia (PCD) have situs inversus (SI); +/-20% SI have PCD (Kartagener’s syndrome). Respiratory problems may present in the neonatal period (cough, rhinitis, unexplained respiratory distress).
- Maternal diabetes mellitus
- Twins
- Association with midline abnormalities

Definitions
- **Situs solitus** = normal situs
- **Situs inversus (SI)** = complete reversal of situs
  - 1:10,000
  - usually otherwise normal except +/- 5% cardiovascular abnormalities & PCD (as above)
- **Heterotaxy** (Situs ambiguus) – variable orientation of organs
  Is either isomerism sequence (bilateral right or left sidedness – usually cardiac, +/- abdominal or thoracic organs) or random
  - less common than SI
  - abnormal laterality of atrial appendages, +/- bronchi, lungs or liver
  - complex cardiac malformations and malrotation (or non-rotation) of intestine common
  - +/- asplenia / polysplenia
  - +/- other congenital abnormalities (particularly midline)

Isomerism sequences
- 1:24,000 at least
- Mortality RAI >LAI
• All cases of asplenia have RAI but polysplenia may occur without LAI

Right atrial isomerism sequence (RAI)
• Complex cardiac malformations in 100% with bilateral morphologically R atrial appendages
  – single atrium, AVSD, pulmonary stenosis / atresia, TAPVD, DORV
• Bilateral morphologically R bronchi +/- bilateral trilobed lungs
• Asplenia in most
• Malrotation of intestine (in 70%)
• +/- midline liver

Left atrial isomerism sequence (LAI)
• Complex cardiac malformations in most with bilateral morphologically L atrial appendages
  – single atrium, single ventricle, AVSD, pulmonary stenosis/atresia, interrupted IVC with azygos continuation
• Bilateral morphologically L bronchi +/- bilateral bilobed lungs
• Polysplenia in most, +/- biliary atresia and absent gallbladder (10% biliary atresia have LAI)
• Malrotation of intestine
• +/- midline liver

Investigations
In all cases of SI and heterotaxy:
• Paediatric Cardiology opinion – likely to need echocardiogram
• Abdominal u/s for aorta / IVC and mesenteric vessel orientation, spleen and liver
• Conjugated bilirubin (LAI)
• Blood film (but Howell-Jolly bodies unreliable for diagnosing asplenia)
• Upper gastrointestinal contrast study.
• Chest x-ray for bronchial anatomy (high voltage beam)
• Cranial u/s for midline defects
• Chromosome analysis

Management
• If malrotation present refer to Paediatric Surgery team as elective Ladd’s procedure may be indicated
- Paediatric Cardiology team will advise on any cardiac intervention required.
- Refer to Clinical Genetics
- If asplenia or polysplenia (both may be functionally asplenic)
  - prophylactic penicillin – (62.5mg 12hrly PO)
  - pneumococcal vaccine (see vaccination protocol)
  - all other vaccinations should be given as routine