PULMONARY HYPERTENSION: Acute pulmonary hypertension of the newborn (aPHN)

RECOGNITION AND ASSESSMENT

Definition

- Severe hypoxaemia due to failure of normal postnatal drop in pulmonary vascular resistance
- Can be primary (idiopathic) or secondary

Idiopathic persistent pulmonary hypertension of newborn (PPHN)

- Degree of hypoxia may be disproportionate to degree of hypercapnia
- no clear cause identified, but may be secondary to maternal drugs e.g. non-steroidal anti-inflammatory drugs or SSRIs
- Associated with polycythaemia

Secondary

- May be associated with:
- parenchymal lung disease e.g. meconium aspiration (MAS), surfactant deficiency, pneumonia/sepsis
- structural abnormalities: pulmonary hypoplasia, congenital diaphragmatic hernia (CDH), A-V malformations, congenital cystic adenomatoid malformation
- perinatal asphyxia or severe anaemia
- Rare causes: alveolar capillary dysplasia, surfactant protein B deficiency

CLINICAL FEATURES

Usually present in first 12 hr of life

- Hypoxia with/without hypercapnia, SpO_2 >10% difference in preductal (right hand) and postductal saturations (feet) (preductal saturations > postductal saturations)
- Mimics cyanotic heart disease
- CVS: tricuspid regurgitant murmur, right ventricular heave, loud second heart sound with/without systemic hypotension
- Idiopathic PPHN: minimal or no respiratory distress
- Secondary aPHN: moderate to significant respiratory distress

INVESTIGATIONS

- Blood gas shows hypoxaemia with rising oxygenation index
- Chest X-ray: variable findings depending on underling diagnosis (black lungs with normal or minimal changes in idiopathic PPHN)
- Echocardiogram (although not mandatory for initial diagnosis and management) is useful:
- to exclude cyanotic heart disease
- to assess pulmonary pressure
- to evaluate right and or left ventricular dysfunction
- Echocardiographic signs of aPHN in presence of normal cardiac anatomy:
- significant tricuspid regurgitation (TR) (may not always be present in right heart dysfunction)
- dilatation of right side of heart and/or hypertrophy of right ventricle
- right-to-left shunting across PFO and/or PDA
- pulmonary regurgitation
- bowing of interventricular septum to the left
- relatively small left ventricle (though apex forming)
- Pulmonary pressure is estimated from echocardiogram using: TR (systolic pulmonary pressure = 4 x $(VmaxTR)^2$ + usual right atrial pressure of 5 mmHg)

MANAGEMENT

- If suspicion of duct dependent congenital heart disease, start prostaglandin infusion IV (see **Prostaglandin infusion** guideline)
- Once aPHN suspected involve consultant neonatologist immediately
- Aims of management are to:

- decrease pulmonary vascular resistance
- maintain normal systemic blood pressure and end-organ perfusion
- treat underlying condition, if known

General measures
- Minimal handling and noise
- Secure arterial and central venous access, (see **Arterial line insertion** guideline or **Umbilical artery catheterisation and removal** and **Umbilical venous catheterisation and removal** guidelines)
- Maintain normal temperature, biochemistry and fluid balance
- Keep ionised calcium >1 mmol/L and Mg ≥1 mmol/L
- Keep Hb ≥120 g/L
- Give antibiotics (infection is difficult to exclude at onset of disease process) (see **Infection in first 72 hours of life** guideline)
- Surfactant therapy may be beneficial in parenchymal lung diseases, e.g. MAS, pneumonia, surfactant deficient lung disease – discuss with consultant
- Use sedation – may use muscle relaxation in babies with high ventilatory and oxygen requirements and/or ventilator asynchrony
- Refer babies with aPHN requiring iNO to NICU for ongoing management

Ventilation and oxygenation
- Aim for disease specific ventilatory strategies:
- lung recruitment in parenchymal lung disease
- discuss with consultant regarding surfactant therapy
- in black lung PPHN and CDH aim for gentle ventilation
- Commence with conventional ventilation (targeted tidal volume)
- High frequency oscillatory ventilation (HFOV) may be needed if requiring high pressures to deliver the set tidal volume [see **Ventilation: high frequency oscillatory ventilation (HFOV)** guideline]
- Aim for preductal SpO_2 91–95% kPa. Do not attempt to reduce pre and postductal saturation difference as long as postductal SpO_2 >70%
- Avoid intermittent desaturations (preductal) <85% or preductal SpO_2 >97%
- Aim for preductal PaO_2 7.3–10.6 (if right radial arterial line) (tolerable hypoxaemia)
- Monitor oxygenation index (OI)

$$OI = \frac{\text{mean airway pressure (cm } H_2O) \times \text{\% oxygen}}{\text{postductal } PaO_2 \text{ (kPa)} \times 7.5}$$

- If OI not available, consider oxygen saturation index (OSI)

$$OSI = MAP \times FiO2 \times SPO_2/100$$
$$OI = 0.0745 + (1.783 \times OSI)$$

- If umbilical arterial line OI will be higher as it is postductal OI and targeting lower postductal saturations
- Monitor OI trends
- Aim for $PaCO_2$ 6–8 kPa, avoid hypocapnia

Considerations for aPHN presentation in local neonatal unit (LNU)/special care unit (SCU)
- Refer to KIDS NTS for transfer to NICU and possible need for nitric oxide therapy, when:
- FiO_2 >0.5 and all reversible factors have been addressed, e.g. surfactant deficiency/DOPE/adequate ventilation (PiP ≤26 and mean airway pressure ≤16)

Pulmonary vasodilatation
- Use inhaled nitric oxide (NO) as a selective pulmonary vasodilator (see **Nitric oxide** guideline)
- Escalate to consultant and consider other pulmonary vasodilators (sildenafil, magnesium sulphate) while doing ECLS referral

Circulatory management
- Early echocardiogram recommended
- Aim for normal gestation specific blood pressure (see **Hypotension: Haemodynamic compromise** guideline, **Tables 2 and 3** for normal blood pressure values)
- Avoid supraphysiological blood pressure

- If hypotensive, one bolus of sodium chloride 10 mL/kg over 20–30 min
- If low pulse pressure (± LV dysfunction on echo), start beta dose adrenaline, if no adequate response add dobutamine
- If normal pulse pressure (± LV dysfunction on echo), start adrenaline (0.05–0.2 microgram/kg/min) and noradrenaline base (0.05–0.4 microgram/kg/min). If inadequate response, add dobutamine (5–10 microgram/kg/min)
- If hypotension with high pulse pressure (normal LV function), use vasopressin **and/or** noradrenaline
- Add prostin to support systemic circulation
- If normal blood pressure (RV dysfunctions), add milrinone – may need to add noradrenaline as milrinone may cause systemic vasodilatation
- If PDA restrictive or closing, add prostin to off load RV
- If no response to first-line inotrope, add hydrocortisone
- Monitor for side effects of treatment e.g. tachycardia, rising lactates
- Monitor urine output and UEs 4–6 hrly with vasopressin
- Avoid vasopressin in LV dysfunction

Severe and resistant aPHN not responding to conventional management in NICU

- Not responding or rising OI despite escalation of ventilation and iNO therapy
- Recurrent pulmonary hypertensive episodes
- Hypotensive despite inotropes or worsening side effects of inotropic therapy
- No significant progression in 2–3 days
- Discuss with KIDS NTS team (see **Transport and retrieval** guideline) and conference call with ECLS centre

Criteria for ECLS

- Baby born ≥34 weeks or ≥2 kg with aPHN
- If OI remains >25 despite starting above therapies — conference call with KIDS NTS and PICU to discuss management and ECLS criteria
- Reversible lung disease
- No lethal congenital malformation

Exclusion criteria (if in doubt, discuss with ECLS team)

- Major intracranial haemorrhage
- Lethal congenital or chromosomal anomalies
- Severe encephalopathy
- Major cardiac malformation

A baby accepted for transfer to ECLS centre will be retrieved by ECLS or PICU team

- ECLS centre will need:
  - cranial ultrasound scan
  - maternal blood for group and crossmatching (check with ECLS centre)
- Outreach ECLS
- ECLS team may decide to start outreach ECLS in NNU before transfer to ECLS unit. Check with ECLS team regarding diathermy unit and number of packed cell units needed for procedure

Referral for ECLS

- For West Midlands contact KIDS NTS team on 0300 200 1100
- KIDS NTS will liaise with ECLS centres to find a cot and/or give advice

aPHN (previously PPHN) 2025–28 Revised Sept25

Flowchart: Management of aPHN

Clinical evidence of aPHN OI >20
- Echocardiography to exclude cyanotic heart disease

Assessment
- BP, HR, CRT, urinary output and continuous pre- and post-ductal saturations
- BP (systolic, diastolic and mean) target >3rd centile for gestational age

Full response to iNO
- ↑SpO_2 >20, ↑PaO_2 >3, ↓FiO2 >0.2 on the same ventilator settings in 60 min

Partial response
- ↑SpO_2 10–20%, ↑PaO_2 2–3, ↓FiO2 ≥0.1

Monitoring
- BP every 15 min until stable, then hourly
- invasive BP recommended
- Monitor blood gas, lactate as clinically indicated
- If vasopressin used, U&Es and urinary output 4–6 hrly

Optimise lung recruitment, surfactant, Ca, Mg, sedation

Commence iNO at 20 ppm

Wean iNO as per guidelines

- If OI not available, consider oxygen saturation index
  OSI = MAP x FiO_2 x SpO_2/100
  [OI = 0.0745 + (1.783 x OSI)]

No/partial response

- Optimise ventilatory settings
- Early echo recommended

One fluid bolus 10 mL/kg over 20–30 min

↓ BP (narrow pulse pressure)
+/- echo: LV/biventricular dysfunction
- Beta dose adrenaline 0.05 microgram/kg/min Increase by 0.01–0.02 microgram/kg/min every 30–60 min (maximum 0.2 microgram/kg/min)
  or/add
- Dobutamine: 5 microgram/kg/min, increase by 5 microgram/kg/min every 30 min
  and
- If PDA closing start Prostin to support system circulation
- If no response to 1st line inotrope, add hydrocortisone 2.5 mg/kg 6-hrly

Caution: avoid vasopressin in LV dysfunction

↓ BP (normal pulse pressure)
+/- echo: LV/biventricular dysfunction
- Beta dose adrenaline 0.05 microgram/kg/min Increase by 0.01–0.02 microgram/kg/min every 30–60 min (maximum 0.2 microgram/kg/min)
  or/add
- Dobutamine: 5 microgram/kg/min, increase by 5 microgram/kg/min every 30 min
  and
- Noradrenaline base 0.05 microgram/kg/min increase by 0.05 microgram/kg/min every 30 min
  and
- If PDA closing start Prostin to support system circulation
- If no response to 1st line inotrope, add hydrocortisone 2.5 mg/kg 6-hrly

↓ BP (increased pulse pressure)
+/- echo: good biventricular function or only RV dysfunction, normal both COP
- Vasopressin 0.0003 units/kg/min, increased by 0.0001–0.0003 units/kg/min every 30 min
  or/add
- Noradrenaline base 0.05 microgram/kg/min increase by 0.05 microgram/kg/min every 30 min

RV dysfunction and low RV output, good LV function
- If BP normal: milrinone 0.25 microgram/kg/min, may increase up to 0.75 microgram/kg/min, no loading dose
- If hypotension: adrenaline 0.05 microgram/kg/min. Increase by 0.01-0.02 microgram/kg/min every 30–60 min (maximum 0.2 microgram/kg/min)
  or
- Dobutamine: 5 microgram/kg/min, increase by 5 microgram/kg/min every 30 min

- If no response to inotropes, pressors, pulmonary vasodilators and OI >25, discuss with ECLS centre
- Caution with milrinone, do not use unless blood pressure robust. Contraindication renal impairment