Pulse Oximetry Screening
(?for Congenital Heart Disease)

Martin Kluckow
MBBS FRACP PhD CCPU
Associate Professor
Royal North Shore Hospital &
University of Sydney, Australia

Universal Pulse Oximetry
Measurement in the newborn
A new approach

Martin Kluckow
MBBS FRACP PhD CCPU
Associate Professor
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University of Sydney, Australia

Pulse oximetry in the well newborn
Screening test or documenting a vital sign?

- All children/adults have pulse oximetry documented on admission to hospital
- There is a requirement to document “color” in the neonatal care plan – in other areas pulse ox has replaced this (eg Resuscitation)
- Part of routine care in infants admitted to a nursery or via accident and emergency department
- Equipment is often (but not always) readily available – no extra cost to perform
- Minimally invasive, no calibration, familiar to patients and staff

AAP Guidelines

Pulse Ox screening
5th vital sign vs test for CCHD

Need for consent
Normal vs Extra test
CCHD screen
Need for ECHO
Parental Anxiety
Timing
False Positives

Background (CCHD)
Why worry?

- Congenital heart disease (CHD) = 9 in 1000 live births (excludes trivial disease – small ASD/VSD, bicuspid AV)
- 20-30% of these have critical CHD (i.e. requiring intervention in the 1st month of life)
- Evidence that delay in diagnosis associated with increased cardiovascular compromise and end-organ dysfunction, particularly if ductal dependent
- Kuehl and colleagues reported that 1.7% of children with any form of CHD died before identification of heart disease (incl 3-6% dTGA)
- Some UK studies have suggested that 25% of infants with CCHD were not diagnosed until after D/C with a median age of 6 weeks
Trends in congenital heart disease
Incidence 3-15/1000 births
62 reports on incidence of CHD

Differences in detecting and reporting/classification of CHD

Hoffman J Am Coll Card 2002

Trends in congenital heart disease
Lesions seen
Incidence of significant/major CHD

ALL significant/major CHD approx 2.5 / 1000

Hoffman J Am Coll Card 2002

Trends in congenital heart disease
Most deaths are in the first year

United States 1999–2006
Annual age-standardized mortality
Age at Death

Gilboa Circ 2010, Padley HLC 2011

Neurodevelopment in congenital heart disease — risk increased if collapsed
Weighted mean BSD-II outcome scores at 1 year of age in approx. 700 patients with any CHD (mild to severe) without chromosomal abnormalities

Snookes Ped 2010

Pulse oximetry screening in newborn infants

- 13 eligible studies, data from 229,421 newborns
- 9 studies excluded babies with antenatal diagnosis
- Pulse ox at <24 hrs in 6 studies
- 60% used the foot alone (post-ductal) vs pre and post-ductal screen

Pulse oximetry screening in newborn infants

Thangaratinam Lancet 2012
Pulse oximetry screening in newborn infants

- Overall for CCHD
  - 99.9% specificity
  - 76.5% sensitivity
  - 0.14% (1/1000) FP rate overall
  - FP >24 hrs 0.05% vs 0.50% at <24 hrs but sensitivity no different

Barriers to implementation of pulse ox screening

- Early postnatal discharge/Home births
- Not a good enough pick up rate
- Antenatal ultrasound and newborn examination are adequate
- False positives
- Need for neonatal admission and echocardiography
- Cost implications

Pulse oximetry screening in newborn infants – subsequent large studies

- Large prospective multicentre study in China – 122,738 infants
  - Overall for CCHD
    - 99.7% specificity
    - 83.6% sensitivity
    - Sensitivity increased from 77.4% for clinical exam alone to 93.2% adding pulse ox screen
    - FP rate of 0.3% (3/1000) of Clinical assessment
    - FP rate of 2.7% of these FP needed care
    - FP >24hrs 0.29% vs 0.55% at <24 hrs with sensitivity 78% vs 88% at <24hrs

“W” ultrasound

<table>
<thead>
<tr>
<th></th>
<th>Fetal diagnosis</th>
<th>IG ultrasound</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td></td>
</tr>
<tr>
<td>FSV</td>
<td>25 (83.3)</td>
<td>20 (60.0)</td>
</tr>
<tr>
<td>VSD</td>
<td>7 (16.7)</td>
<td>1 (3.0)</td>
</tr>
<tr>
<td>AVSD</td>
<td>5 (33.3)</td>
<td>1 (3.0)</td>
</tr>
<tr>
<td>Coarct</td>
<td>4 (33.3)</td>
<td>3 (9.0)</td>
</tr>
<tr>
<td>Complex coarct</td>
<td>4 (57.1)</td>
<td>3 (9.0)</td>
</tr>
<tr>
<td>Int Arch</td>
<td>1 (25.0)</td>
<td>3 (9.0)</td>
</tr>
<tr>
<td>Truncus</td>
<td>5 (100.0)</td>
<td>3 (9.0)</td>
</tr>
<tr>
<td>TGA*</td>
<td>10 (52.6)</td>
<td>5 (15.0)</td>
</tr>
<tr>
<td>TAPVR</td>
<td>0 (0.0)</td>
<td>1 (3.0)</td>
</tr>
<tr>
<td>PAVS</td>
<td>7 (77.8)</td>
<td>5 (15.0)</td>
</tr>
<tr>
<td>ASD/PSA</td>
<td>2 (28.6)</td>
<td>1 (3.0)</td>
</tr>
<tr>
<td>Isolated vascular</td>
<td>0 (0.0)</td>
<td>1 (3.0)</td>
</tr>
<tr>
<td>Rhythm</td>
<td>1 (50.0)</td>
<td>1 (3.0)</td>
</tr>
<tr>
<td>Other</td>
<td>2 (66.7)</td>
<td>1 (3.0)</td>
</tr>
<tr>
<td>Total</td>
<td>85 (43.6%)</td>
<td>25 (83.3%)</td>
</tr>
</tbody>
</table>

Reasons for not screening “We will pick CHD on the newborn examination”

- Postnatal clinical examination in the first few days of life
- Absence of murmur in 50% of CHD– CoAo, TGA, HLHS, Interrupted arch, TAPVD
- Detection of cyanosis visually (SaO2 <80%) - ?validity. Morley studies...
- Some estimates that newborn examination for CCHD gives up to 10 x false positive rate cf. pulse ox screen

Lesions found on screening

- Reviews suggest that about 30% (Range 13-48%) of infants with critical CHD leave hospital undiagnosed
- Types of critical CHD found by screening

Types of critical CHD

<table>
<thead>
<tr>
<th>Critical CHD</th>
<th>Number of Infants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coarct</td>
<td>25 (83.3)</td>
</tr>
<tr>
<td>TGA</td>
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Hoffman Neonatology 2011
Can adding pulse oximetry screening help with this?

<table>
<thead>
<tr>
<th></th>
<th>Physical exam alone</th>
<th>Physical exam + SpO2</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 39,521 babies *</td>
<td>63%</td>
<td>83%</td>
</tr>
<tr>
<td>Sensitivity for CCHD Detection</td>
<td>98%</td>
<td>98%</td>
</tr>
</tbody>
</table>

*Pre & Post ductal screen prior to physical examination
*Abnormal if SpO2 < 91%, x3 <95% or difference >3%

N = 122,211 babies *  
Sensitivity for CCHD Detection  
Physical exam alone 77.4%  
Physical exam + SpO2 93.2%

*Recently published large Chinese study


Screening technique

- Timing (False positives)
- One limb (post ductal) vs two limb (pre/post ductal)
- Saturation cut offs
- Response to positive screen

Timing of screen

- Time to reach SaO2 >95% is 20 mins in healthy babies (Range 3-90 minutes)
- Most investigators are using 24-48 hrs
- AAP guideline (2011) 24-48 hrs just before discharge
- Largest population based study (Meberg 2009) used a screen in first 24 hrs (50,000 babies)
- Balance
  - False positives due to TTN, RDS, sepsis and transitional circulation
  - Earlier diagnosis/prevent collapse, value of FP detection
  - Interference with discharge process

Timing of screen

![Graph showing age at development of significant physiological compromise](Schulze Pediatrics 2008)

Timing and False positives

<table>
<thead>
<tr>
<th>Age at 0-24 (m=24, n=450)</th>
<th>Age at 24-48 (m=450, n=450)</th>
<th>Age at 48-72 (m=450, n=450)</th>
</tr>
</thead>
<tbody>
<tr>
<td>False positive</td>
<td>62</td>
<td>48</td>
</tr>
<tr>
<td>False negative</td>
<td>38</td>
<td>52</td>
</tr>
<tr>
<td>False positives</td>
<td>120</td>
<td>167</td>
</tr>
<tr>
<td>Specificity (S)</td>
<td>98%</td>
<td>98%</td>
</tr>
<tr>
<td>Sensitivity (S)</td>
<td>98%</td>
<td>98%</td>
</tr>
</tbody>
</table>

Systematic review of the topic by the American Heart Association and American Academy of Pediatrics found the mean of false positives in studies was 0.87%

This falls much lower (to 0.035%) if screening done after 24hrs (0.5% vs 0.05% in latest meta-analysis)

Screening after 24 hrs may not fit with some models of care

False positives in first 24 hours for CHD may be of importance for other conditions

- Sepsis
- Metabolic
- Unrecognised respiratory conditions
### False positives

- **The AAP guideline states**
  
  *The work group recommended that screening not begin until 24 hours of life, or as late as possible if earlier discharge is planned, and be completed on the second day of life. Earlier screening can lead to false-positive results because of the transition from fetal to neonatal circulation.*

- **Are we delaying the documentation of SpO2 in our babies for the wrong reasons?**

- **Andy Ewer says**
  
  "A false positive is a hypoxaemic baby and a baby with undiagnosed GBS sepsis is just as likely to collapse/die as a baby with undiagnosed CCHD!"

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### Timing of screen

<table>
<thead>
<tr>
<th>Study</th>
<th>Timing</th>
<th>Total</th>
<th>FP with other pathology</th>
<th>Pathology found</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ewer</td>
<td>&lt;24h</td>
<td>50,083</td>
<td>27%</td>
<td>respiratory disorders, infection, mild CHD</td>
</tr>
<tr>
<td>Melang</td>
<td>&lt;24h</td>
<td>50,083</td>
<td>47% (133/351)</td>
<td>TTN, pneumonia, sepsis, CHD, other</td>
</tr>
<tr>
<td>Arlettaz</td>
<td>&lt;24h</td>
<td>3,242</td>
<td>62% (5/12)</td>
<td>PH, infection</td>
</tr>
<tr>
<td>Richmond</td>
<td>&lt;24h</td>
<td>5,626</td>
<td>47% (7/15)</td>
<td>TTN, pneumonia, PH, mild CHD, syndrome, brain bleed</td>
</tr>
<tr>
<td>Tursa</td>
<td>&lt;24h</td>
<td>3,242</td>
<td>42% (5/12)</td>
<td>PH</td>
</tr>
<tr>
<td>de Wahl</td>
<td>median 24h</td>
<td>50,083</td>
<td>60% (45/73)</td>
<td>TTN, respiratory disorders, PH, infection, mild CHD</td>
</tr>
<tr>
<td>Reisch</td>
<td>median 24h</td>
<td>2,314</td>
<td>100% (1/1)</td>
<td>TTN, pneumonia/sepsis, mild CHD</td>
</tr>
</tbody>
</table>

**TOTAL ~50%**

**TTN; transient tachypnea of newborn, PH; pulmonary hypertension**

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### What to screen – 1 (foot) or 2 limbs (foot and right hand (pre/post ductal))?**

- **Ewer study (UK 2011) used two limb screen**
  
  - SaO2 <95% in either limb OR more than 2% difference upper/lower
  - Use of just foot alone would have reduced FP by 84 babies (from 169), but missed 3 critical CHD (2 with HLHS identified antenatally and one with CoAo), one serious case (TA), 2 with significant CHD and 9 with respiratory problems

- **Granelli study (Sweden 2009) – used both <95% (post ductal) OR a difference of >3% as threshold -3% chosen as >2sd observer variability**
  
  - Use of just foot alone would have reduced FP by 61 but would have missed 1 critical, 1 serious, 1 significant and 13 respiratory
Left heart obstruction

N = 122,738 babies

<table>
<thead>
<tr>
<th>Condition</th>
<th>Total</th>
<th>Identified on screen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coarctation Aorta</td>
<td>7</td>
<td>3 (43%)</td>
</tr>
<tr>
<td>Interrupted arch</td>
<td>5</td>
<td>2 (40%)</td>
</tr>
</tbody>
</table>

*Pre & Post ductal screen prior to physical examination
*Abnormal if SPO2<91%, \( x^3 <95\% \) or difference>3%

What SaO2 cutoff to use?

- Norway – data from 1000 newborns
  - 2.5\textsuperscript{th} percentile for foot SaO2 is 95% - Meberg 2009
- Sweden 2.5\textsuperscript{th} percentile for foot SaO2 is 95%
- 3-4 other studies have also used this cut off
- AAP Guideline recommends <90% fail, or \( x^3 <95\% \) fail
- Difference between hand & foot of >3% considered abnormal
- AAP guideline recommends >3% difference
- <90% - definitely abnormal

Response to a positive screen/abnormal SpO2

“We don’t have a cardiologist available 24/7”

- Response to a member of the nursing staff reporting a “dusky” baby or a low saturation after an ad hoc pulse ox measure is done?
- Response to the finding of a murmur on the newborn examination?
- Response to a SaO2 of 89% on a screening test at 8 hrs?
- Is it any different? This is not a new problem – babies were always there – just not screened
- The referral pathways should already be in place

AAP/AHA Guidelines

“Any newborn with a positive screen result first requires a comprehensive evaluation for causes of hypoxemia. In the absence of other findings to explain hypoxemia, CCHD needs to be excluded on the basis of a diagnostic echocardiogram (which would involve an echocardiogram within the hospital or birthing center or transport to another institution) or through the use of telemedicine for remote evaluation.”

Response to a positive screen

- Expedited clinical examination (ECE)
- Observation in a nursery environment, repeat testing
- Investigations as needed from above
  - CXR
  - ECG
  - Exclude sepsis
  - Cardiology consultation/Echocardiogram only if indicated

Response to a positive screen

Suggested
Response to a positive screen
What is the pick up rate on ECHO?
- In the large Chinese study 3898 babies with a positive result from pulse ox or clinical assessment received a diagnostic ECHO
- 298 (7.5%) had a major CHD
- Only 147 (3.7%) had a CCHD
- Clinical assessment was responsible for most of the false positives
- Our local data shows that the number of ECHO’s required are significantly reduced with
  - Good antenatal surveillance
  - Early clinical diagnosis
  - Pulse Ox Screening at 24-48hrs

Summary courtesy K De Waal


True Negatives/False Negatives
- True Negatives
  - No costs beyond those of the primary screen
- False Negatives/Timing?
  - Not well studied – but quoted about 0.008%
    - Meberg <24h, (50,008 babies) FN 8
    - deWahl median >24h (39,821 babies) FN 10
    - Riede median >24h (41,442 babies) FN 4
    - Kawalec median >24h (27,200) babies FN 1

Real data – A 2 year audit from NSW

Summary
- 3.5 years of screening (18800 babies)
- 9 extra ECHO’s, 50% of which were abnormal. 6 further cases CCHD picked up via other routes (Antenatal, presented with symptoms before screen)
- 2 further infants with serious respiratory disease picked up
- False negatives – only one identified - VSD/PDA - needed surgery at 2 months of age
- FP for CHD = 26/18800(0.14%), but 15 normal with observation and 6 were respiratory.
- Real FP rate for pulse ox screen = 5/18800(0.03%) i.e. 1/3000 screened

Summary
- Simple, quick and painless
- Likely to be cost effective
- No increase in parental anxiety – even in false positive cases

Ewer AK Health Technology Assess 2012
Practicalities when introducing

- Guideline/Protocol
- Timing of screen / Measurement usually post ductal (foot), time to stability – up to 360 seconds (6 mins) recommended (Reich et al Ped Cardiology 2008)
- Suitable pulse oximeters - Radical Masimo – SET technology (motion resistance)
- Costs – reusable probes
- Up skilling midwives/postnatal ward staff
- Guidelines – not feeding/crying - to reduce true FP
- Documentation issues
- Response to failed pulse ox test
- Cardiology input
- Parental anxiety/Need for consent??

Technology may make this easier

- Masimo “Newborn screening mode”
- Algorithm more stable to allow more rapid identification of sat to record
- Simplified interface with algorithm built into it to allow rapid identification of a positive screen
- “Stereo” oximetry – two probes on one machine for simultaneous screening - ? More accurate, Faster
- ROOT screen (Check with Masimo)

Clear thinking is needed here!

- 1] Delink the pulse ox measure from CCHD - remove parental anxiety, perception that CCHD excluded by the test. Call this Pulse Ox screening NOT CCHD screening!
- 2] Consider pulse ox measure as a standard vital sign that needs to be documented in all newborns (as it is in all other hospital patients) and dealt with accordingly

Simplify your approach!

- 3] Measure in first 24 hrs (allow 4 hrs for transition). The so called false positives if done with an accurate pulse ox (Masimo) are actually babies we do want to know about (Respiratory, sepsis, PPHN). It makes no sense to delay a pulse ox measure based on the perception that an ECHO might be required in a false positive (for CCHD) baby.
- 4] Use existing assessment and referral pathways for blue baby, heart murmur, respiratory distress in your hospital to sort out a low pulse ox - medical assessment, observation and timely ECHO is part of the assessment but not mandated. We don’t have to develop a whole new system.

Reality check may be needed!

- 5] Positives (True & False) appear to be a lot less common in our setting (particularly Level 3 Units) than they are in the Lancet meta-analysis and studies
  - Babies identified antenatally
  - Babies identified and admitted before screen – reducing FP
- 6] Have a look at the current screening processes at your place (Antenatal ultrasound and newborn examination) - sensitivity and specificity. You are likely to find that they have much less precision than the reported results from pulse ox screen.