Cardiovascular System –
Cardiovascular changes at birth

Dr Graeme Polglase
Transition at Birth
Contents

The cardiopulmonary circulatory transition.

- Fetal and adult physiology
- Mechanisms driving the transition

Stabilisation of the cardiopulmonary circulatory transition.

- New insights into the benefit of delayed cord clamping.
Adult vs. Fetal circulation

Fetus:
- Umbilical flow supports LVO and RVO.
- Ventricles pump in parallel
due to:
  - foramen ovale
  - ductus arteriosus
Driven by:
  - umbilical circulation

Newborn/Adult:
- Ventricles pump in series
1. Blood flows from high pressure to low pressure

If $P_1 > P_2 \& P_3$ ($P_2 = P_3$)
Blood will flow equally in both directions.

If $P_1$ and $P_2 > P_3$
Blood will flow down $P_3$. 
2. Blood flows along the path of least resistance.

If $R_1 = R_2$
Blood will flow equally through both

If $R_1 > R_2$
Blood will flow through $R_2$
Fetal Circulation

Pulmonary Circulation:
- High Pressure
- High Resistance
- Low Blood Flow

Systemic Circulation:
- Lower Pressure
- Low Resistance

Ductus Arteriosus:
- Right to Left Flow

PVR > SVR

PPA > PSA

Ductus Arteriosus (Placenta)
**Pulmonary circulation**

**Vasoconstricted during fetal life**
- high resistance & low blood flow
- pulmonary pressure > systemic pressure
- right-to-left shunt through the ductus arteriosus.

**Causes of vasoconstriction**
- not known
- High degree of fetal lung expansion.
- Low PO\textsubscript{2}
- Release of circulating vasoconstrictors.
Newborn Circulation

Pulmonary Circulation:
Low Pressure
Low Resistance
High Blood Flow

Systemic Circulation:
High Pressure
Higher Resistance

Ductus Arteriosus:
Left to Right Flow

\[ P_{PA} < P_{SA} \]
\[ PVR < SVR \]
Cardio-Pulmonary Transition at Birth

Newborn
100% of RVO enters the lung
PBF is high, PVR is low
Systemic arterial pressure > pulmonary arterial pressure
DA flow is left to right

Need to
1) Decrease pulmonary vascular resistance
2) Reverse pulmonary-systemic pressure gradient
1) Decrease in pulmonary vascular resistance at birth

Overall mechanism unknown

- $\uparrow$ blood PO$_2$
- release of vasodilators (?)
- An effect of ventilation (?)
- Reduction in lung volume caused by lung aeration

Aeration of the lung is the principal component!
Pulmonary blood flow changes at birth

Instability

Deliver
Clamp cord
Start Ventilation

FETUS
NEWBORN
Cardio-Pulmonary Transition at Birth

Need to
1) Decrease pulmonary vascular resistance
   Aerating the lung

2) Reverse pulmonary-systemic pressure gradient
Cardiovascular changes at birth

Reversing the pulmonary-systemic pressure gradient

Clamp umbilical cord
- lose 1/3 of fetal blood volume
  • Umbilical cord “milking”
- lose 50% of venous return
- ↑ Systemic blood pressure

Driven by removal of the
Cardiovascular changes at birth

Venous return from umbilical circ ↓ → ↓ right atrial filling
↓ right atrial pressure (RAP)
+ aeration of the lung

All happens within the first minutes of life.

Systemic arterial pressure > Pulmonary arterial pressure
(left to right ductus arteriosus flow)
LAP > RAP → reversal of flow through and closure of foramen ovale (FO)
Cardio-Pulmonary Transition at Birth

Need to

1) Decrease pulmonary vascular resistance
   Aerating the lung

2) Reverse pulmonary-systemic pressure gradient
   Remove the placental circulation
The cardiopulmonary transition

- **Left Heart**
- **Right Heart**
- **Lungs (Low PVR)**
- **Brain**
- **Body**
- **Placenta**

**Before Cord Occlusion**
- Umbilical cord occlusion
- Ventilation

**After Cord Occlusion**
- PPA > PSA, PPA < PSA
- Stabilises Left and Right Ventricular Output at Birth

50% of CVO
Contents

The cardiopulmonary circulatory transition.
  Fetal and adult physiology
  Mechanisms driving the transition
Stabilisation of the cardiopulmonary circulatory transition.
  New insights into the benefit of delayed cord clamping.
A Role for Neuroprotection?
Impaired Cerebral Autoregulation

Developmental immaturity can render the preterm neonate particularly susceptible to cerebral hemodynamic consequences in response to systemic disturbances.

Graph showing cerebral blood flow autosregulation in preterm and adult. 
- Preterm range: ~50 mmHg
- Adult range: 90-150 mmHg

Note: "develop the preterm susceptibility consequences disturbs"
Circulation Stabilisation – Delayed Cord Clamping

Does the timing of ventilation onset relative to umbilical cord clamping improve the stability of the circulatory transition at birth in a baby which is apnoeic?
Surgical Methods

Flow probes:
• Left pulmonary artery
• Ductus arteriosus
• Carotid artery

Catheters:
• Main pulmonary artery
• Main Carotid Artery
• Jugular Vein
Experimental timeline

(Clamp 1\textsuperscript{st} Vent 2\textsuperscript{nd})

(Vent 1\textsuperscript{st} Clamp 2\textsuperscript{nd})
Cardiovascular effects of cord clamping prior to ventilation.

Fetus

- Placenta
- Lower body
- Right Heart
- Left Heart
- Upper body
- Lungs
- Ductus arteriosus
- Foramen Ovale
- Pre-ductal arteries

Low resistance
50% of CO
What are the cardiovascular consequences of cord clamping prior to ventilation?
What are the cardiovascular consequences of cord clamping prior to ventilation?
Changes over the first 10 heart beats

Left Ventricular Output Critically Dependent Upon Increasing Pulmonary Blood flow
Effect of cord clamping followed by ventilation
Effect of cord clamping followed by ventilation
Delaying Cord Clamping until Ventilation Initiated

Lungs aerate

Placenta

Lower body

Lungs

50% ↓ Venous Return

Right Heart

Left Heart

Upper body

Foramen Ovale

Ductus arteriosus

MONASH University
Cardiovascular consequences of ventilating before cord clamping

**Unventilated (Clamp 1st)**

**Ventilated (Vent 1st)**
Changes over the first 10 heart beats

- **Carotid arterial pressure (mmHg)**
  - Clamp First
  - Ventilated

- **Carotid blood flow (mL/min/kg)**
  - Clamp First
  - Ventilate First
Ventilation before cord clamping stabilises the cardiovascular transition at birth

Improves Stability!
Benefits of delayed cord clamping until ventilation onset

- Decrease PVR and hence increase PBF before the cord is clamped
- PBF can immediately replace umbilical venous return as the primary source of preload for the LV
  - Stabilises LV output after birth
  - Potentially reduces risk of IVH
Delaying cord clamping until ventilation onset improves cardiovascular function at birth in preterm lambs

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4Department of Neonatal Medicine, Royal North Shore Hospital and University of Sydney, Sydney, New South Wales, 2065, Australia
5Department of Paediatrics, Leiden University Medical Centre, Leiden, The Netherlands
6Department of Newborn Research, The Royal Women’s Hospital, Melbourne, Australia

Key points
- Delayed cord clamping improves circulatory stability in preterm infants at birth, but the underlying reason is not known.
- In a new preterm lamb study we investigated whether delayed cord clamping until ventilation had been initiated improved pulmonary, cardiovascular and cerebral haemodynamic stability.
- We demonstrated that ventilation prior to cord clamping markedly improves cardiovascular function by increasing pulmonary blood flow before the cord is clamped, thus further stabilising the cerebral haemodynamic transition.
- These results show that delaying cord clamping until after ventilation onset leads to a smoother transition to newborn life, and probably underlies previously demonstrated benefits of delayed cord clamping.

Abstract

Delayed cord clamping improves circulatory stability in preterm infants at birth, but the underlying physiology is unclear. We investigated the effects of umbilical cord clamping, before and after ventilation onset, on cardiovascular function at birth. Prenatal surgery was performed on lambs (123 days) to implant catheters into the pulmonary and carotid arteries and probes to measure pulmonary (PBF), carotid (CA BF) and ductus arteriosus blood flows. Lambs were delivered at 126 ± 1 days and: (1) the umbilical cord was clamped at delivery and ventilation was delayed for about 2 min (Clamp 1st; n = 6), and (2) umbilical cord clamping was delayed for 3–4 min, until after ventilation was established (Vent 1st; n = 6). All lambs were subsequently ventilated for 30 min. In Clamp 1st lambs, cord clamping rapidly (within four heartbeats), but transiently, increased pulmonary and carotid arterial pressures (by ~30%) and CA BF (from 30.2 ± 5.6 to 40.1 ± 4.6 ml min⁻¹ kg⁻¹), which then decreased again within 30–60 s. Following ventilation onset, these parameters rapidly increased again. In Clamp 1st lambs, cord clamping reduced heart rate (by ~40%) and right ventricular output (RVO; from 114.6 ± 14.4 to 38.8 ± 9.7 ml min⁻¹ kg⁻¹), which were restored by ventilation. In Vent 1st lambs, cord clamping reduced RVO from 153.5 ± 3.8 to 119.2 ± 10.6 ml min⁻¹ kg⁻¹, did not affect heart rates and resulted in stable blood flows and pressures during transition. Delaying cord clamping for 3–4 min until after ventilation is established improves cardiovascular function by increasing
Acknowledgements

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Andrew Gill

Leiden University Medical Centre
Arjan te Pas

Beyond Retirement
Colin Morley
The magic minutes after birth – making the most of them

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Role of a sustained inflation at birth

Stuart Hooper
Should a liquid-filled lung be ventilated in the same way as an air-filled lung?

Will they behave the same?
Inflation Pressures drives airway liquid movement
Pressures generated by Inspiration drives airway liquid movement
Pressures generated by Inspiration drives airway liquid movement.
Pressures generated by Inspiration drives airway liquid movement
Partial airway liquid retention
non-uniform ventilation

Inspiration

$P = \text{pressure}$
Should a liquid-filled lung be ventilated in the same way as an air-filled lung?

Will they behave the same?
Ventilation: the basics

Inspiration
Exhalation

$CO_2$ $O_2$

When the lung is liquid-filled:
Inspiration - needed for airway liquid clearance
Expiration - superfluous as no gas exchange
Uniform Lung aeration
Sustained Inflations
What are the Unknowns??

- How long should the sustained inflation be?
- What Inflation pressure?
Physics of lung aeration

\[ R_T = R_1 + R_2 \]

\( R_1 \) = resistance to moving liquid through a tube
\( R_2 \) = resistance to moving liquid across alveolar wall

\[ R_1 \propto \frac{\text{viscosity} \times \text{length tube}}{(\text{radius tube})^4} \]

\( R_2 \) determined by epithelial barrier properties and surface area

**Smaller very preterm infants:**

Smaller airways + lower surface area = \( \uparrow \uparrow \) Resistance
2010 ILCOR Guidelines

Recommend inflation pressures of:

- 30 cmH₂O in term infants and
- 20 to 25 cm H₂O in preterm infants
  “occasionally higher pressures are required”.
Duration & Inflation pressure for a SI

\[ R_T = P \times \frac{T}{\Delta V} \]
Effect of age on SI starting pressure

![Bar chart showing the effect of age on SI starting pressure. The x-axis represents gestational age at delivery (days), and the y-axis represents starting pressure (cmH2O). The chart indicates that the starting pressure decreases with increasing gestational age.]
Effect of age SI duration and airway resistance
Sustained Inflations: where are we?

- Inflation Pressure and duration will differ between infants:
  - Airway size
  - Maturity of the distal airways
  - The volume of airway liquid present at birth

- Solution??
  - Target an inflation volume of 20mL/kg
Figure 1.8: Sequence of physiological events in animal models from multiple species involving complete total asphyxia. Note the prompt increase in heart rate as soon as resuscitation is begun.
Cardiopulmonary resuscitation

What do the guidelines say?

- HR <60 bpm (apneic, non-responsive infants)
  - Start chest compressions
  - IV epinephrine
- Respiratory support
  - ILCOR - No consensus
    “initiation of intermittent positive-pressure ventilation at birth can be accomplished with either shorter or longer inspiratory times”
  - European - 5x 3 sec inflations
Cardiopulmonary resuscitation

“Establishing pulmonary ventilation is the key”

How???

- Conventional 60 breaths/min
- 5x 3 sec inflations
- ????? 30 sec sustained inflation
Protocol

Deliver & Clamp cord
Start resuscitation
BP = 20-25 mmHg
Finish 30 min after Resuscitation start

Groups
1. Conventional 60 breaths/min
2. 5x 3 sec inflations
3. 30 sec sustained inflation

Outcomes
1. Restoration of HR >120 bpm
2. Restoration of BP > 40 mmHg
3. Respiratory mechanics
HR Changes

Resuscitation start

Heart rate (BPM)

Time from resuscitation onset (s)
Restoring cardiac function

[Graphs showing heart rate and carotid arterial pressure over time from onset of resuscitation.]
Why is a SI so effective?

- Better at aerating the lung
  - To increase $O_2$ uptake
  - To increase PBF and increase preload

- But is this a good thing??
  - Could the higher BP cause brain haemorrhage
Blood brain barrier

- Extravasation of serum indicates disruption to the blood brain barrier.

Extravasation
(Immunoreactive blood vessel)

No extravasation
Sheep serum extravasation - blood brain barrier disruption

<table>
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<tr>
<th>Groups</th>
<th>Number of animals with sheep serum extravasation</th>
</tr>
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<tr>
<td>No SI</td>
<td>4/6</td>
</tr>
<tr>
<td>Multiple SI</td>
<td>3/6</td>
</tr>
<tr>
<td>Single SI</td>
<td>6/6</td>
</tr>
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</table>
Blood brain barrier disruption

There were more animals showing BBB disruption after a 30 sec SI

Data presented as median (IQR)
Summary

- Sustained inflation is fantastic at increasing HR in severely asphyxic newborns
- But!! the return in circulation may be too quick and should be tempered to prevent brain haemorrhage
The magic minutes after birth – making the most of them

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Monitoring of the newborn infant in delivery room

Peter Davis
Melbourne
Australian Resuscitation Council
Neonatal Satellite Meeting
Evaluate respirations, heart rate and colour

The International Liaison Committee on Resuscitation (ILCOR) Consensus on Science With Treatment Recommendations for Pediatric and Neonatal Patients: Neonatal Resuscitation

The International Liaison Committee on Resuscitation

The authors have indicated they have no financial relationships relevant to this article to disclose.
Assessment in the DR

• Colour
• Heart rate
• Chest rise
• (tone and reflex irritability)
Can we use clinical assessment of colour?

- 3-5 minute clips from 20 videos of varying gestation requiring varying degrees of resuscitation (including none)
- 27 medical and nursing observers noted the time at which the infant turned pink
- Corresponding oxygen saturation from a masked oximeter noted
How well do 27 observers agree about colour?

SpO₂ (%) at which infants were perceived to turn pink
How well do 27 observers agree about colour?

- Median saturation at which babies thought to become pink was 69
- Range extended from 10 to 100!
Colour and oxygen

- Improvement in colour may take several minutes to achieve, even in uncompromised babies. Exposure of the newly born to hyperoxia is detrimental to many organs at cellular and functional level.

- Therefore, colour has been removed as an indicator of oxygenation or resuscitation efficacy

ILCOR guidelines
Can we use the colour of an infant’s tongue?

• The Giraffe study
## Infant characteristics

<table>
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<th>Characteristics</th>
<th>Study group:</th>
</tr>
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<tr>
<td></td>
<td><em>n</em> = 68</td>
</tr>
<tr>
<td>Gestational age, mean (SD), week</td>
<td>38 (2)</td>
</tr>
<tr>
<td>Birth weight, mean (SD), g</td>
<td>3214 (545)</td>
</tr>
<tr>
<td>Apgar score at 1 min, median (IQR)</td>
<td>9 (8-9)</td>
</tr>
<tr>
<td>Apgar score at 5 min, median (IQR)</td>
<td>9 (9-9)</td>
</tr>
<tr>
<td>Type of anaesthesia, <em>n</em> (%)</td>
<td></td>
</tr>
<tr>
<td>Spinal/epidural</td>
<td>66 (97)</td>
</tr>
<tr>
<td>General anaesthesia</td>
<td>2 (3)</td>
</tr>
<tr>
<td>Time to first data, median (IQR), sec</td>
<td>76 (67-91)</td>
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### Assessor characteristics

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<th>n</th>
<th>(%)</th>
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<tr>
<td>Midwives</td>
<td>38</td>
<td>(84)</td>
</tr>
<tr>
<td>Paediatricians</td>
<td>7</td>
<td>(16)</td>
</tr>
<tr>
<td>≤1 year of experience</td>
<td>14</td>
<td>(31)</td>
</tr>
<tr>
<td>&gt;1 year of experience</td>
<td>31</td>
<td>(69)</td>
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Results

• When the colour is pink, the baby has a saturation >70% and probably does not need supplemental oxygen
Measurement of Heart Rate (HR) in the delivery room

• Guidelines recommend auscultation or umbilical cord palpation (count for 6 seconds and multiply by 10)

• HR is an (the most?) important sign in determining need for and response to resuscitation

• How precise and accurate are clinical measurements?
Assessment of heart rate:
Auscultation & palpation v ECG

Kamlin CO, O'Donnell CP, Everest NJ, Davis PG, Morley CJ. Resuscitation. 2006
Assessment of heart rate

- Auscultation of the heart rate is more accurate than palpation of the cord. However, both are relatively insensitive.

- **Auscultation** of the heart rate should remain the primary means of assessing heart rate. There is a high likelihood of underestimating the heart rate with palpation of the umbilical pulse, but this is preferable to other palpation locations.

ILCOR guidelines
How should we judge ventilation?

• Chest movement?
• Manometer?
ILCOR guidelines: Initial breaths

- Avoid excessive chest wall movement during ventilation of preterm infants

- Monitoring of inflation pressures may help provide consistent inflations and avoid unnecessarily high pressures

Pediatrics, 2010;126(5):e1323.
Displayed PIP vs Expired tidal volume

Chest wall movement?

• Infants < 32 weeks gestation who received face mask PPV immediately after birth

• Estimate tidal volume (quantitative and qualitative)
  – head view
  – side view
  – experienced and inexperienced operators

• Hot-wire anemometer flow sensor to measure gas flow and tidal volume

Tidal volume

Expired tidal volume (VTe) in mL/kg for each operator measured VTe estimated VTe
Tidal volume

expired tidal volume (VTe) in mL/kg for each operator

measured VTe estimated VTe

measured VTe  estimated VTe
Tidal volume

expired tidal volume (VTe) in mL/kg for each operator

measured VTe
estimated VTe

Box plots showing the distribution of expired tidal volume (VTe) in mL/kg for each operator, with measured VTe in blue and estimated VTe in red.
Chest movement vs Expired tidal volume

Expired Tidal Volume (ml/kg)
Clinical signs of effective ventilation are imperfect

• Displayed PIP is a poor surrogate for tidal volume delivered

• Chest rise is an inaccurate, unreliable measure of adequacy of ventilation
Why might this be important?
Too much ventilation

• Björklund (Pediatric Research 1997)
  – 5 pairs of 127-128 day lambs (~28 weeks’)
• Six large manual inflations
  – reduced compliance
  – worse gas exchange
  – widespread lung injury
What can help us?

• Pulse oximetry
  – How to apply
  – How accurate?
  – Limitations

• Respiratory function monitoring
  – An introduction
Obtaining pulse oximetry data in neonates: a randomised crossover study of sensor application techniques

C P F O’Donnell, C O F Kamlin, P G Davis, C J Morley

Arch Dis Child Fetal Neonatal Ed 2004;000:1–2. doi: 10.1136/adc.2004.058925

Conclusion: Apply the sensor to the right hand and then to the patient cable
Feasibility of oximetry in the DR

Using optimal technique:
• 90% of infants have oximetry data in < 92 sec
• preterm infants are easier to monitor than term

How accurate is PO measurement of heart rate?
Accuracy of pulse oximetry measurement of heart rate of newly born infants in the delivery room. 
### Agreement between HR measurements

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<td><strong>Mean Difference</strong></td>
<td>-0.8 bpm</td>
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<td><strong>95% Limit of Agreement</strong></td>
<td>± 10.9 bpm</td>
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Bland-Altman plots showing the level of agreement between $HR_{ECG}$ and $HR_{Nellcor}$ (A) and between $HR_{ECG}$ and $HR_{Masimo}$ (B).
# Agreement between HR measurements

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**Bland-Altman plots**

A: Bland-Altman plot showing the level of agreement between $HR_{ECG}$ and $HR_{Nellcor}$.

B: Bland-Altman plot showing the level of agreement between $HR_{ECG}$ and $HR_{Masimo}$.

Bland-Altman plots showing the level of agreement between $HR_{ECG}$ and $HR_{Nellcor}$ (A) and between $HR_{ECG}$ and $HR_{Masimo}$ (B).
Heart rate in the delivery room: What is normal?
Heart rate in healthy term babies (no interventions)
Oxygen saturations in the delivery room: What is normal?
O₂ saturations in the first 10 mins

All babies no interventions in the delivery room

Don’t forget to look at the baby!
Measuring pressure and volume
Florian traces (200Hz) using Spectra software during ventilation
Summary (1)

- “Colour” is no longer recommended as a useful sign in the DR
- Clinical assessment systematically underestimates true heart rate
Summary (2)

• Pulse oximetry is a useful guide to assessment of oxygenation and heart rate in the DR but:
  – Know what is normal
  – Look at the baby

• Signs of effective ventilation are imperfect
  – Respiratory function monitoring helps us understand the problems
The magic minutes after birth – making the most of them

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