NRP 2018 Current Issues Seminar— Science behind NRP

Myra Wyckoff, MD, FAAP

Marya Strand, MD, MS, FAAP

American Academy of Pediatrics

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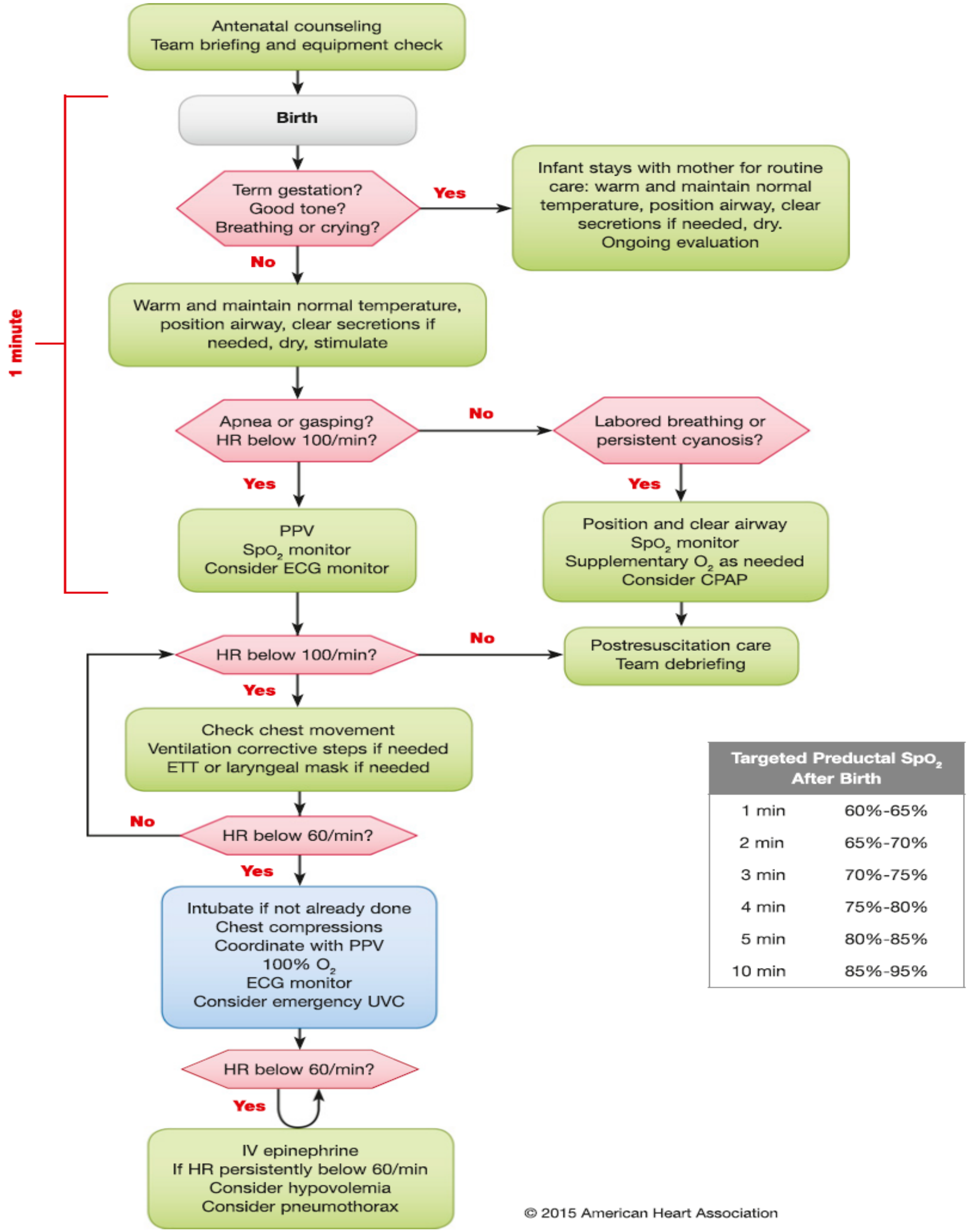
We do not intend to discuss an unapproved/investigative use of a commercial product/device in my presentation

Outline

- Review the transitional physiology that drives the NRP algorithm
- Discuss umbilical cord clamping and the effects in transition
- Review chest compressions and the role of epinephrine
- Save time for questions…

Current Algorithm For Neonatal Resuscitation for North America

- Adopted across the US and Canada on Jan 1, 2017



Key Physiology of Transition

The Role of the Fetal Lung *In Utero*

- The fetal lung is not involved in gas exchange
  - Gas exchange performed by the placenta
  - Lung is fluid filled
  - High pulmonary vascular resistance with only ~10% of the right cardiac output going to the lungs
- Primary role of the fetal lung is growth and development

Photo credit: http://ganeshabreizh.a.g.f.unblog.fr/files/2007/05/foetus15semaines.jpg

Pulmonary Transition at Birth

- Basic requirements for gas exchange
  - Ventilation
    - Rapid fluid clearance
    - Establishment of air-filled functional residual capacity
    - Spontaneous breathing
  - Perfusion
    - Rapid reduction in pulmonary vascular resistance
    - Adequate cardiac output with pulmonary perfusion
    - Delaying cord clamping until the lung is inflated may be an advantage in maintaining cardiac output

Photo credit: OB-GYN Dr. Aris Tsigris

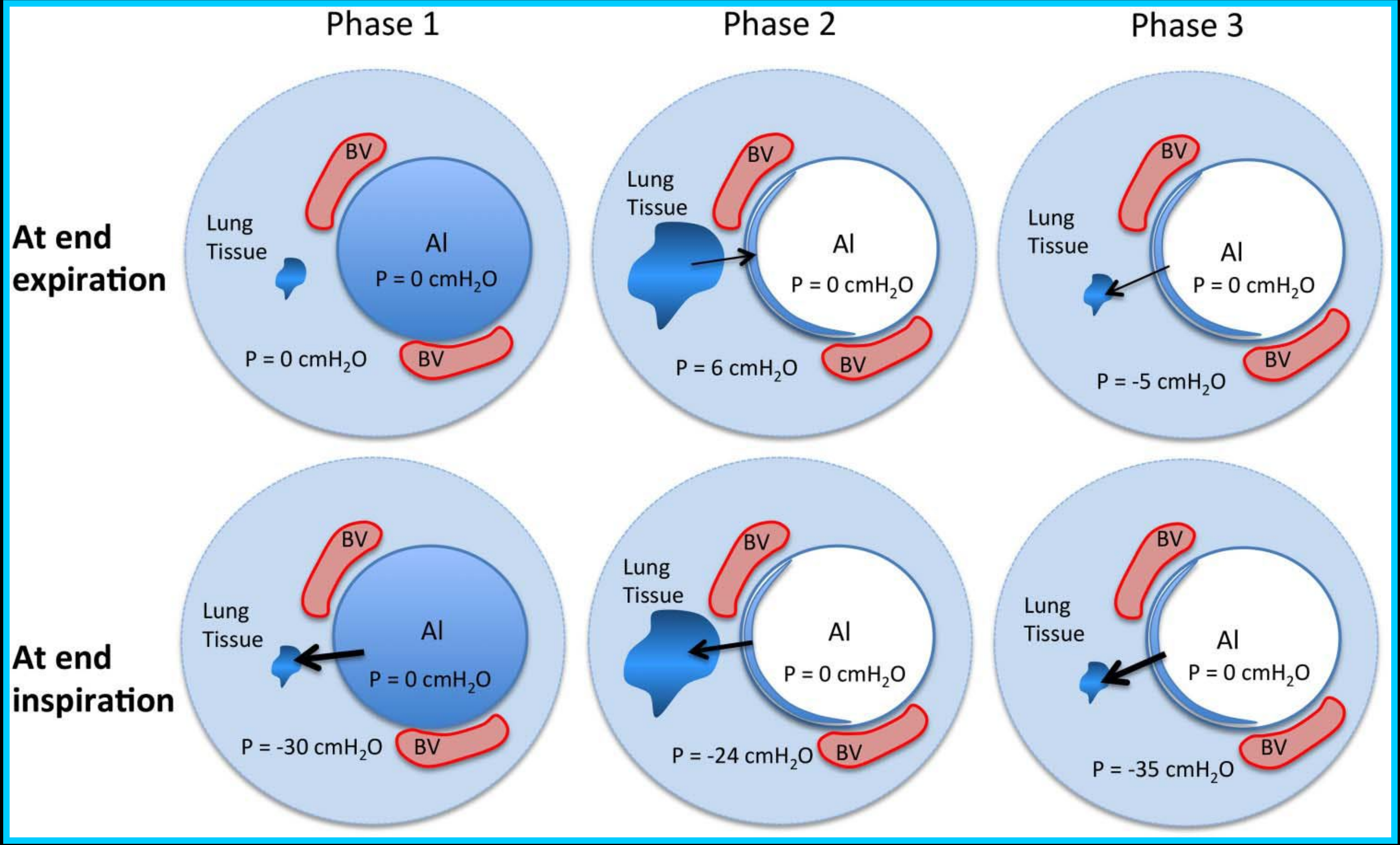
https://commons.wikimedia.org/w/index.php?title=File:HumanNewborn.JPG&oldid=291359275

Lung Aeration: THE Key to Successful Transition

- Lung Aeration
  - Not only critical for gas exchange
  - Also responsible for initiating the cardiovascular changes at birth
- THE critical central step that initiates the sequence of interdependent physiologic changes that enable the infant to transition to life independent of the placenta after birth

AAP-NRP Photo

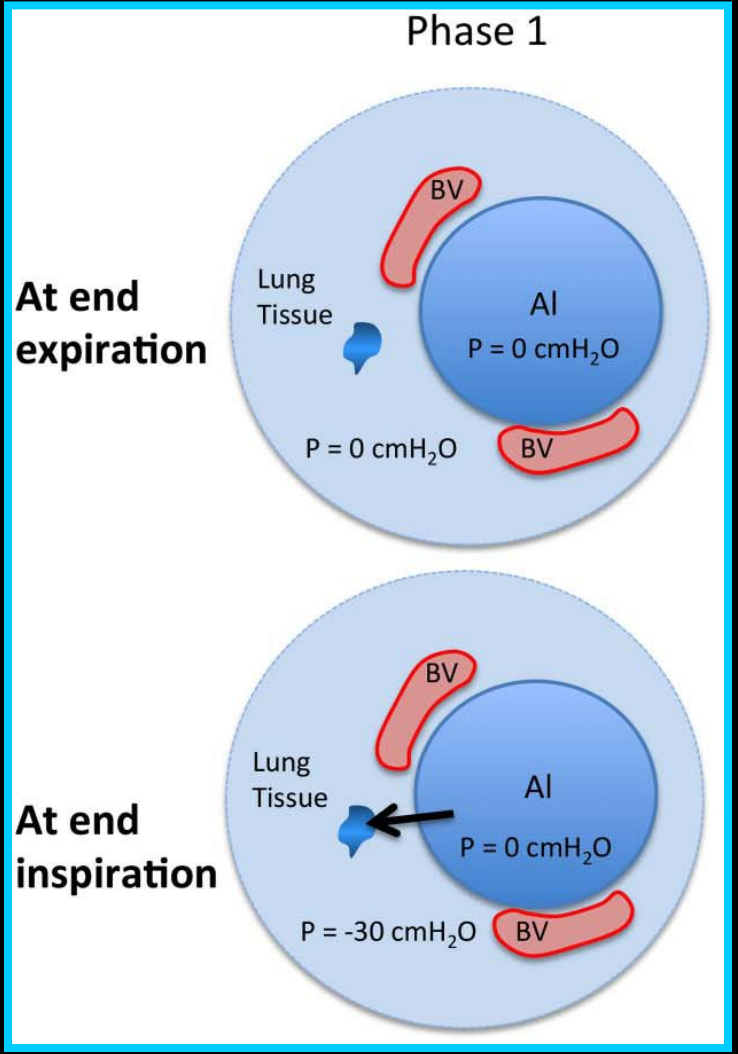
Respiratory Transition at Birth: A Three-Phase Process



- Phase 1: Airway Liquid Clearance
- Phase 2: Liquid Accumulation within the lung's interstitial tissue
- Phase 3: Respiratory Gas Exchange and Metabolic Homeostasis

Hooper et al. ADC F&N ed. 2016;101:F266-F271

Phase 1: Airway Liquid Clearance



Hooper et al ADC F&N

- Movement of liquid through airways and across the distal alveolar wall (secs-mins)
- Gas exchange is not possible during much of this phase
- Occurs through variety of different mechanisms
- The mechanism that contributes most will differ depending on timing (gestational age) and mode of delivery (vaginal vs cesarean)

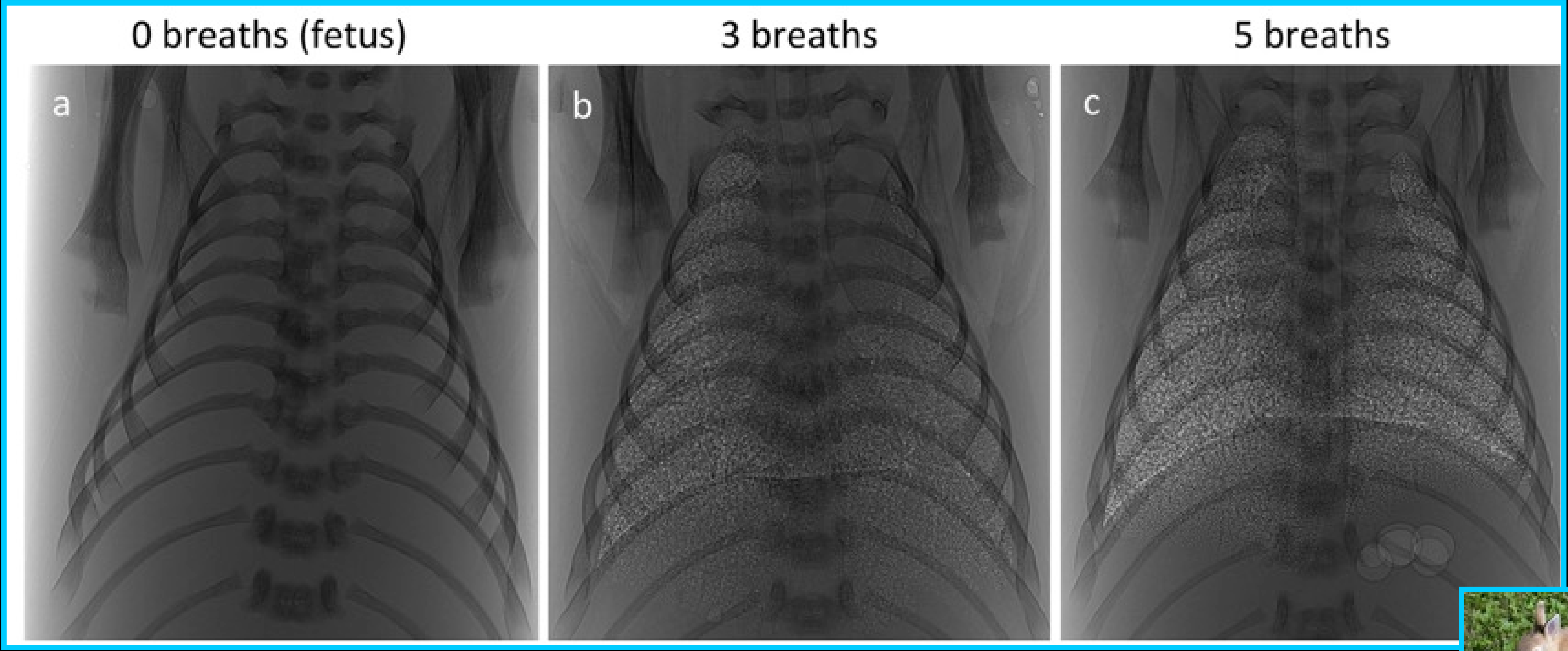
Phase 1: Airway Liquid Clearance

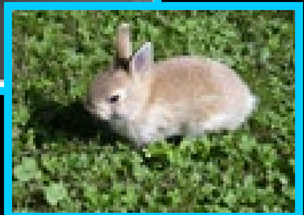
- Before birth-little contribution
- During birth
  - Fetal postural changes-increase fetal spinal flexion during vaginal delivery that helps force out liquid via the nose and mouth following delivery of the head
  - Na reabsorption via increased ENaC channel expression
    - Likely only a minor role during transition
    - Reverses the osmotic gradient leading to airway liquid reabsorption
    - Stimulated by increased circulating adrenaline and vasopressin released in response to labor
    - Blockade of ENaC channels delays but does not prevent liquid clearance

Phase 1: Airway Liquid Clearance

- After Birth-a significant amount of liquid must be cleared
  - Particularly from distal airways
  - Respiratory activity has THE most significant role in liquid clearance

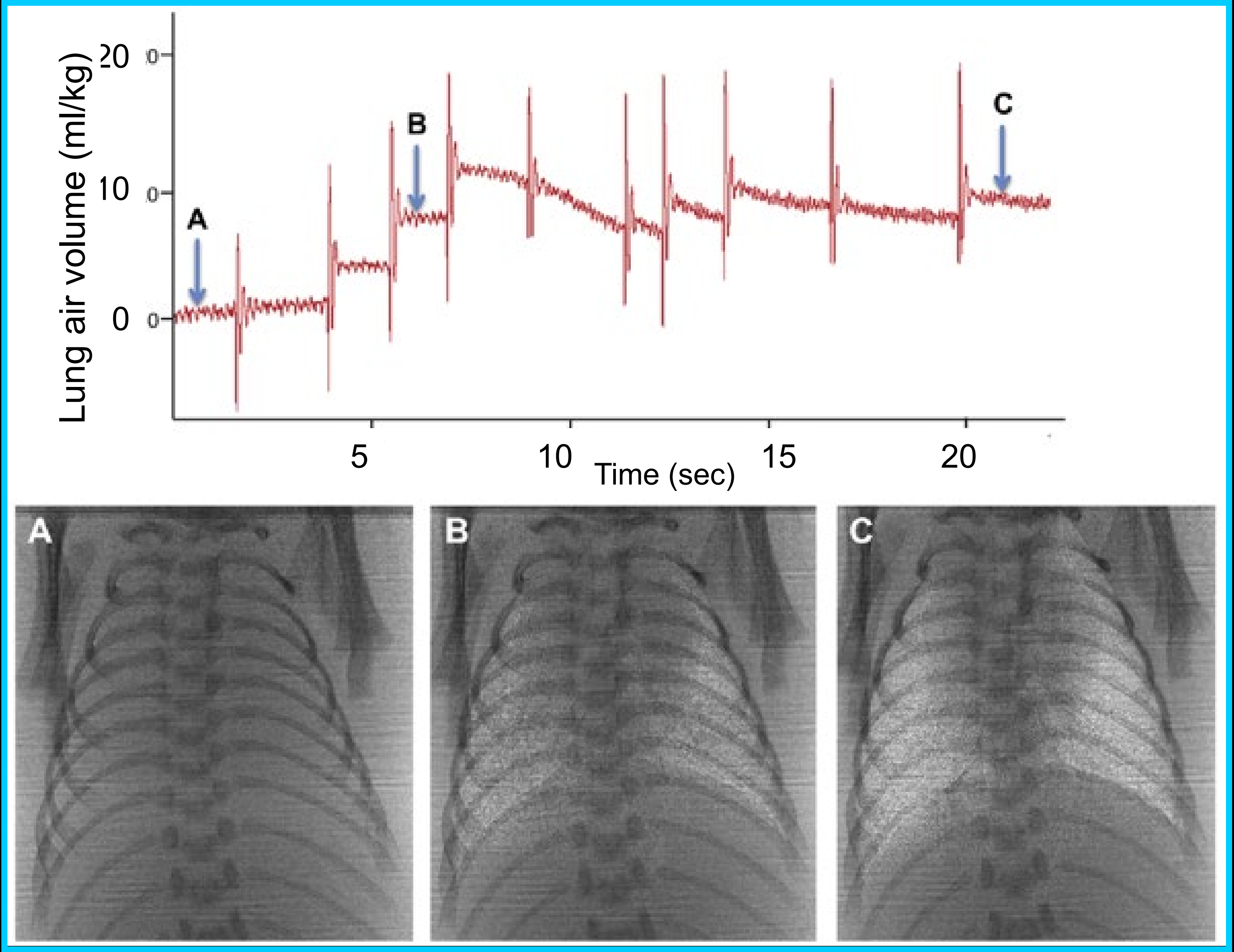
Phase Contract Radiograph Images of Term Newborn Spontaneously Breathing Rabbit Pups





Hooper et al. Neoreviews 2010;11:e474

Establishing Functional Residual Capacity

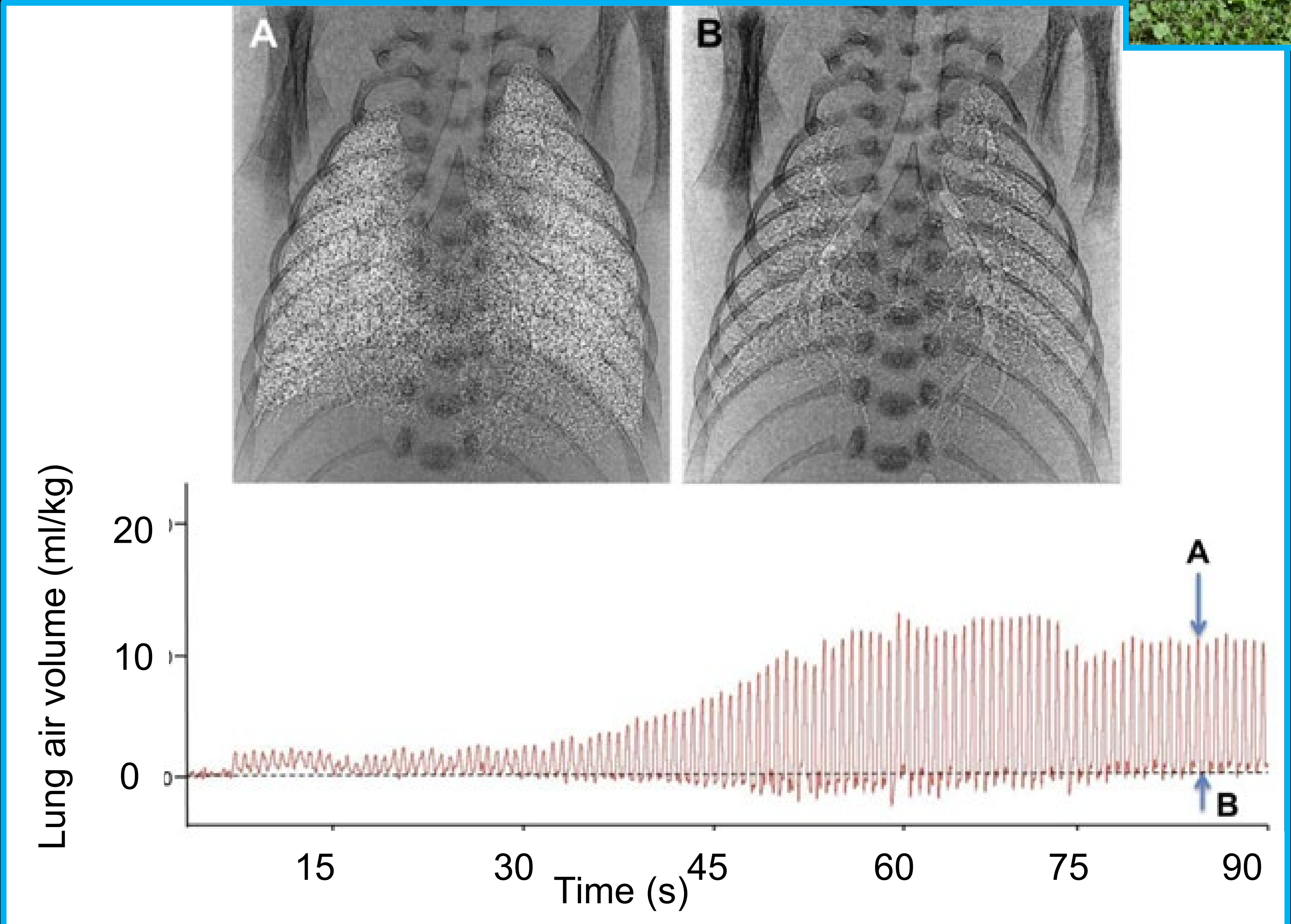


Adapted from Hooper et al. Semin Fetal Neonatal Med 2013;18:336-343

Phase 1: Airway Liquid Clearance When Resuscitation is Needed

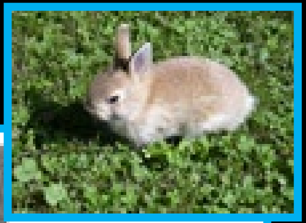
- What if the newly born infant is not spontaneously breathing?
  - Viscosity of liquid is much higher than air so airway resistance is ~100 times greater in liquid filled lung than air filled lung
  - Due to the high resistance of moving liquid through the airways relative to air, PPV with either higher pressures or longer inflation times are required to move the same volume of liquid compared with air
  - In the newborn rabbit model
    - use of PPV with PEEP compared to no PEEP helped clear fluid and establish an FRC
    - An initial sustained inflation seemed to helped clear fluid and establish an FRC

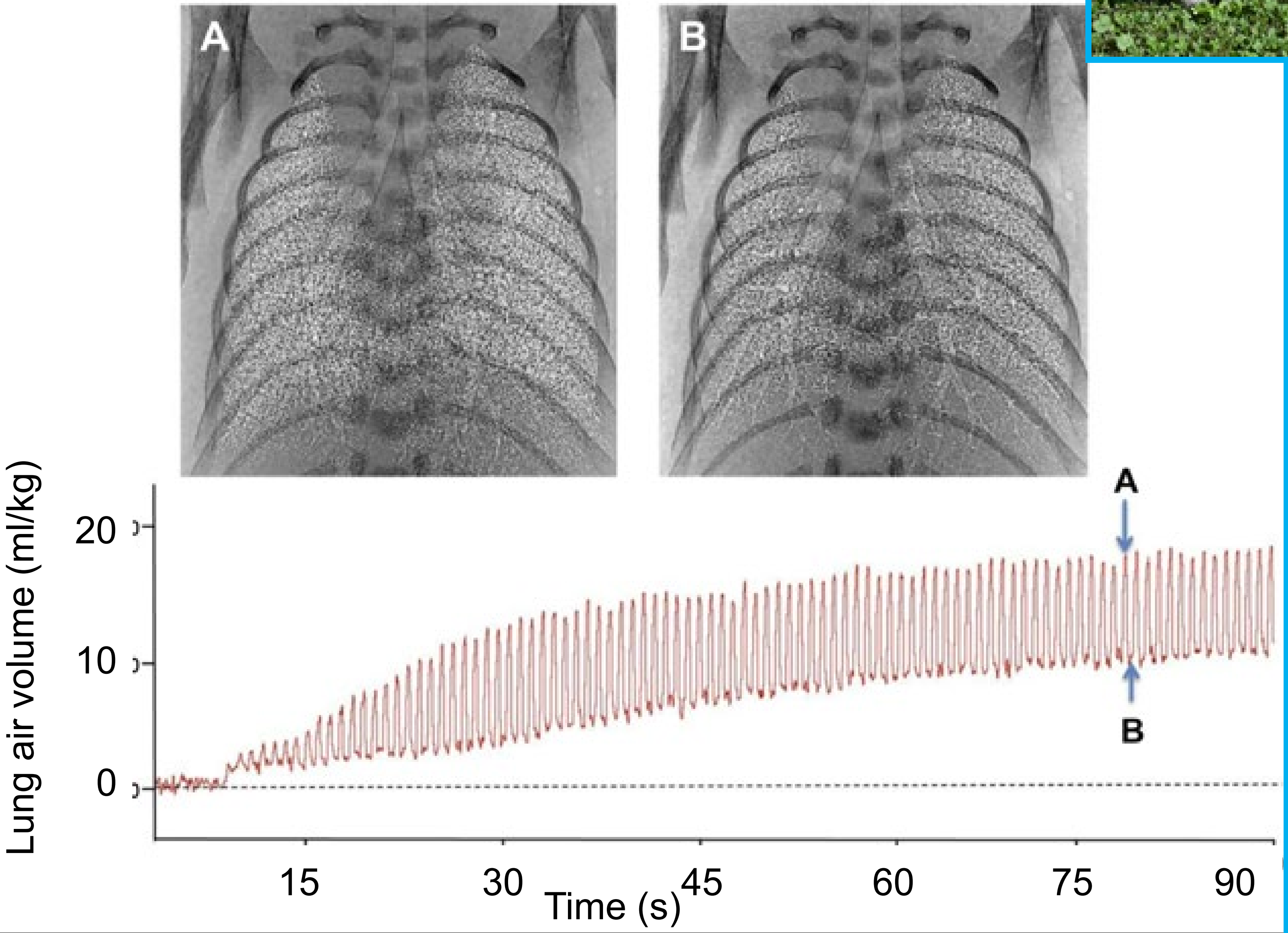
Establishing FRC <u>without</u> PEEP when no Spontaneous Effort in Preterm Rabbits



Adapted from Hooper et al. Semin Fetal Neonatal Med 2013;18:336-343

Establishing FRC with PEEP when no Spontaneous Effort in Preterm Rabbits

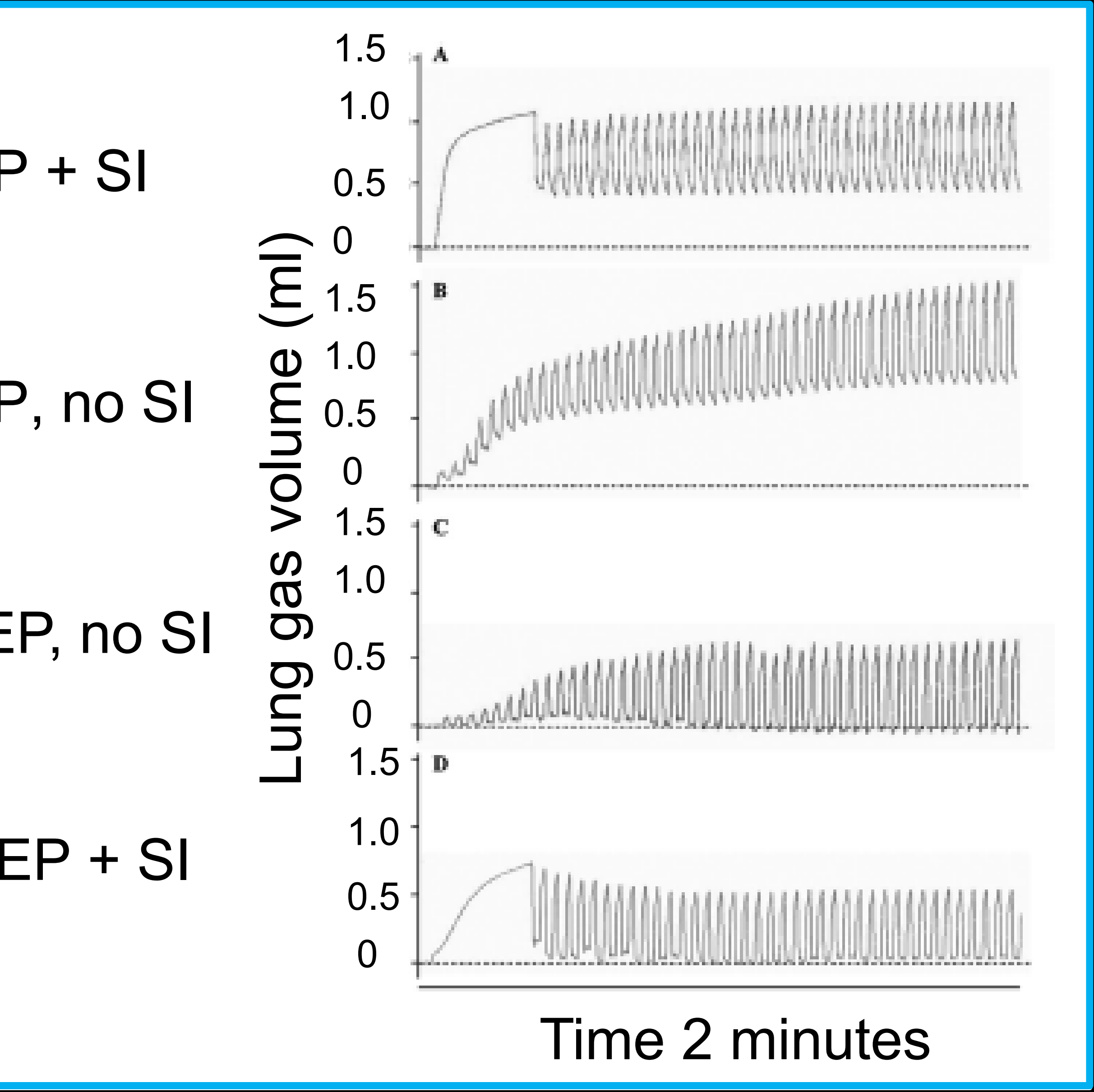




Adapted from Hooper et al. Semin Fetal Neonatal Med 2013;18:336-343

Establishing FRC with PPV ± PEEP ± Sustained Inflation

- Effects of PEEP (5 cmH2O) and SI (35 cmH2O; 20s) were additive
- Combining SI and PEEP improved FRC formation and uniformity of lung aeration
- <u>BUT</u> PEEP had the greatest influence



Adapted from Te Pas et al. Pediatr Res 2009;65:537

Does this physiology translate into clinical experience?

Sustained Inflation vs. Positive Pressure Ventilation at Birth: a Systematic Review and Meta-analysis

- 4 RCT

Mechanical ventilation <72 after birth

Study or Subgroup	SI Events	SI Total	IPPV Events	IPPV Total	Weight	Risk Ratio M-H, Random, 95% CI
Harling 2005	22	26	24	26	33.7%	0.92 [0.75, 1.12]
Lindner 2005	19	31	21	30	9.9%	0.88 [0.61, 1.26]
Lista 2014	88	148	97	143	43.3%	0.88 [0.74, 1.04]
te Pas 2007	38	104	52	103	13.1%	0.72 [0.53, 0.99]
Total (95% CI)		**309**		**302**	**100.0%**	**0.87 [0.77, 0.97]**
Total events	167		194			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.86$, df = 3 (P = 0.60); $I^2 = 0\%$
Test for overall effect: Z = 2.42 (P = 0.02)

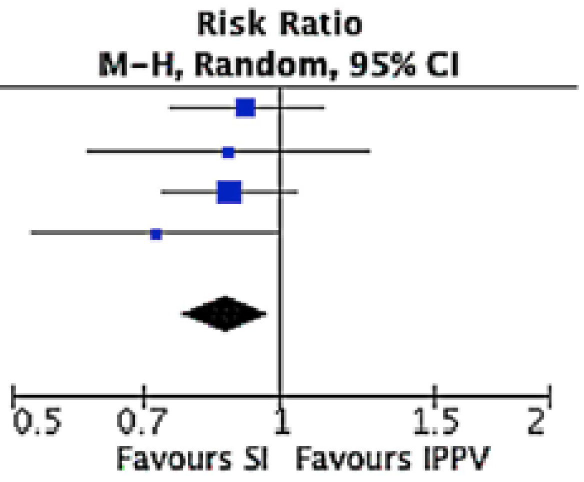


Figure 3 Outcome of mechanical ventilation <72 h after birth. IPPV, intermittent positive pressure ventilation; SI, sustained inflation.

Schmölzer et al. Arch Dis Child Fetal Neonatal Ed. 2015; 100:F361

Cochrane Library

Cochrane Database of Systematic Reviews

Cochrane Database of Systematic Reviews 2017, Issue 7. Art. No.: CD004953.
DOI: 10.1002/14651858.CD004953.pub3.

Sustained versus standard inflations during neonatal resuscitation to prevent mortality and improve respiratory outcomes (Review)

Bruschettini M, O'Donnell CPF, Davis PG, Morley CJ, Moja L, Zappettini S, Calevo MG

- 8 RCTs enrolling 941 infants
- Mostly VLBW and some ELBW infants

Figure 4. Forest plot of comparison: 1 Use of initial sustained inflation vs standard inflations in newborns receiving resuscitation with no chest compressions, outcome: 1.1 Death.

Study or Subgroup	SLI Events	SLI Total	control Events	control Total	Weight	Risk Ratio M-H, Fixed, 95% CI	A	B	C	D	E	F	G
1.1.1 Death in the delivery room													
El-Chimi 2017	0	57	0	55		Not estimable	-	-	-	?	-	-	+
Lindner 2005	0	31	0	30		Not estimable	?	+	-	?	+	+	-
Mercadante 2016	0	93	0	92		Not estimable	?	+	-	+	+	-	+
Schwaberger 2015	0	20	0	20		Not estimable	+	+	-	?	+	+	+
Jiravisitkul 2017	1	43	0	38	100.0%	2.66 [0.11, 63.40]	+	+	-	?	?	?	?
Subtotal (95% CI)		**244**		**235**	**100.0%**	**2.66 [0.11, 63.40]**							
Total events	1		0										
Heterogeneity: Not applicable													
Test for overall effect: Z = 0.60 (P = 0.55)													
1.1.2 Death before discharge													
Schwaberger 2015	0	20	0	20		Not estimable	+	+	-	?	+	+	+
Mercadante 2016	0	93	0	92		Not estimable	?	+	-	+	+	-	+
El-Chimi 2017	12	57	19	55	49.8%	0.61 [0.33, 1.13]	-	-	-	?	-	-	+
Jiravisitkul 2017	2	43	2	38	5.5%	0.88 [0.13, 5.97]	+	+	-	?	?	?	?
Ngan 2017	5	76	5	86	12.1%	1.13 [0.34, 3.76]	+	?	-	+	-	+	?
Lista 2015	17	148	12	143	31.4%	1.37 [0.68, 2.76]	?	+	-	+	+	+	+
Lindner 2005	3	31	0	30	1.3%	6.78 [0.37, 125.95]	?	+	-	?	+	+	-
Subtotal (95% CI)		**468**		**464**	**100.0%**	**1.01 [0.67, 1.51]**							
Total events	39		38										
Heterogeneity: Chi² = 4.94, df = 4 (P = 0.29); I² = 19%													
Test for overall effect: Z = 0.03 (P = 0.97)													

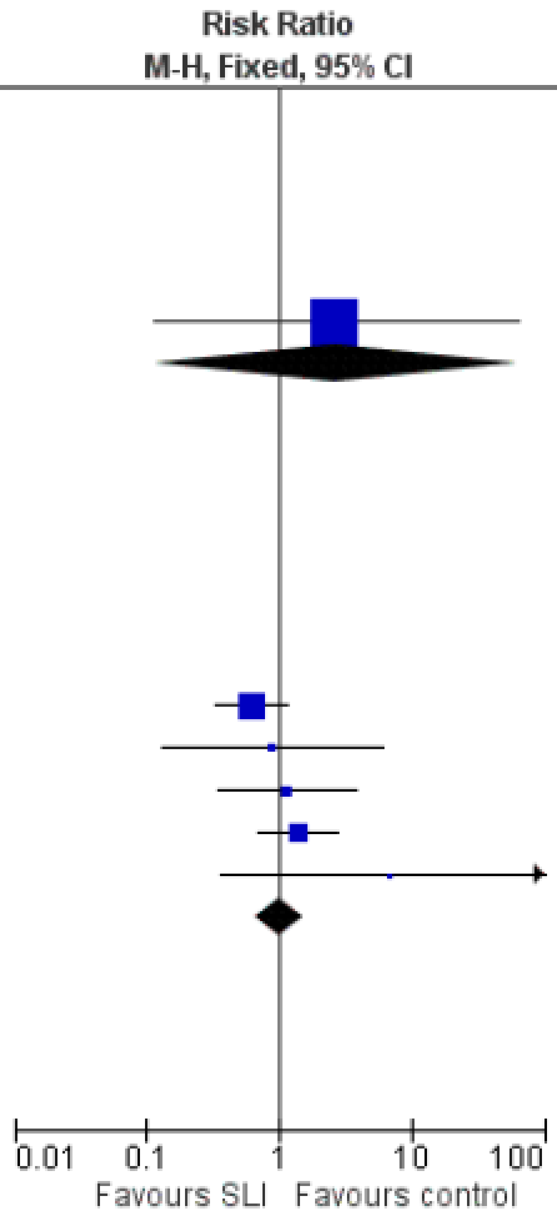
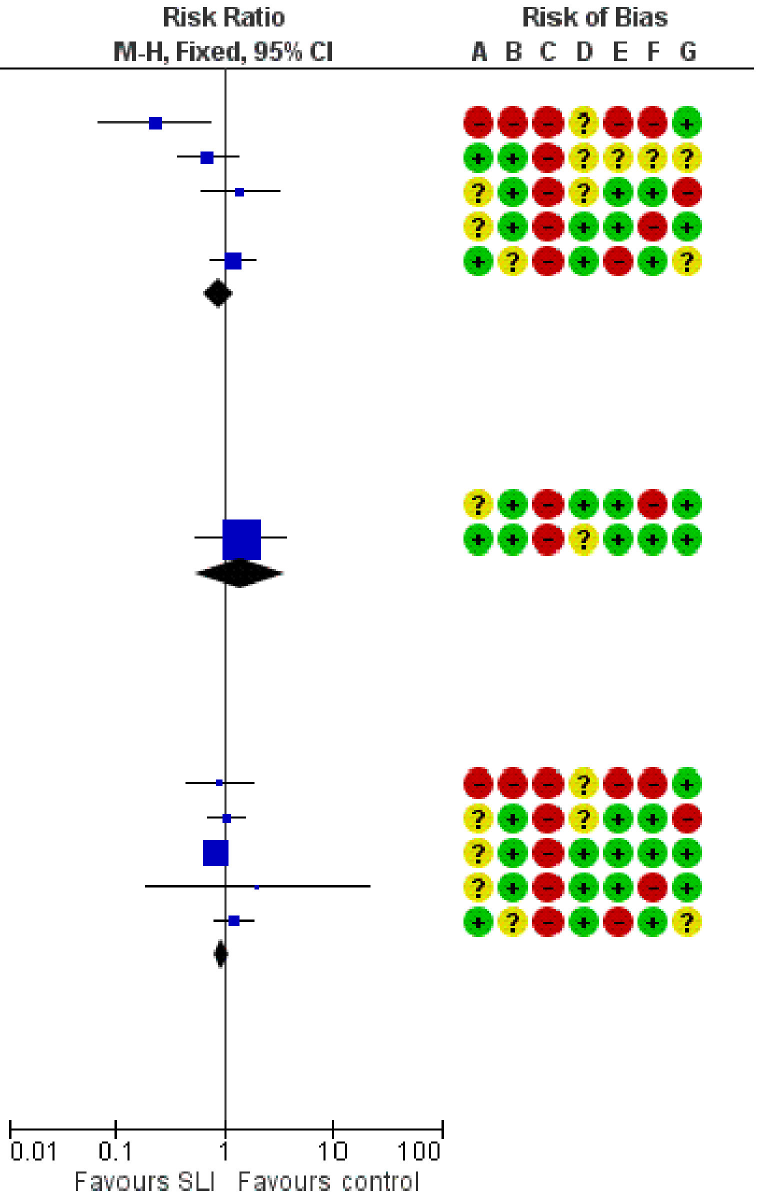
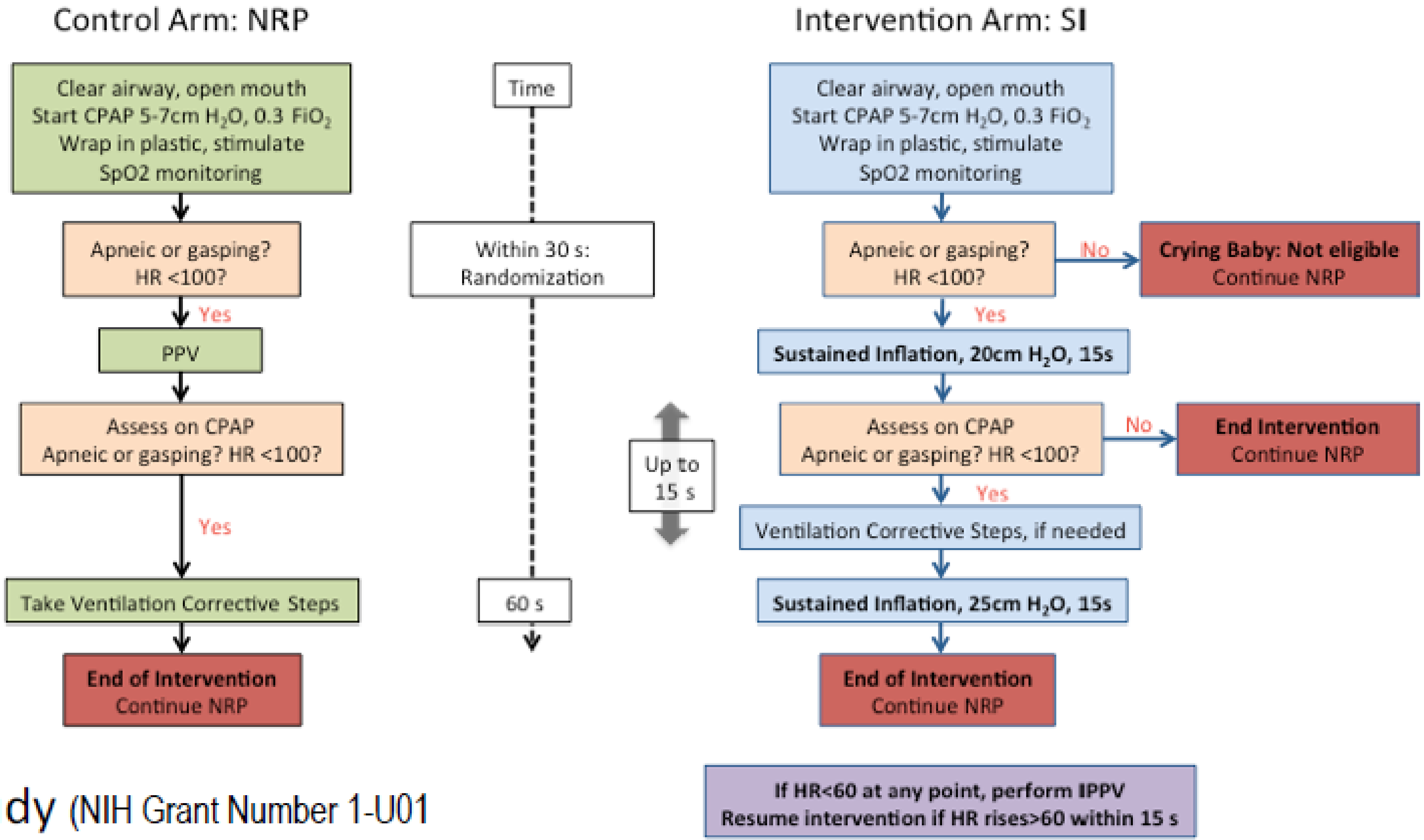


Figure 5. Forest plot of comparison: 1 Use of initial sustained inflation vs standard inflations in newborns receiving resuscitation with no chest compressions, outcome: 1.4 Endotracheal intubation.

Study or Subgroup	Favours SLI Events	Favours SLI Total	Standard inflations Events	Standard inflations Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.4.1 Endotracheal intubation in the delivery room						
El-Chimi 2017	3	57	13	55	22.9%	0.22 [0.07, 0.74]
Jiravisitkul 2017	11	43	14	38	25.7%	0.69 [0.36, 1.34]
Lindner 2005	10	31	7	30	12.3%	1.38 [0.61, 3.16]
Mercadante 2016	0	93	0	92		Not estimable
Ngan 2017	25	76	24	86	39.0%	1.18 [0.74, 1.88]
Subtotal (95% CI)		**300**		**301**	**100.0%**	**0.86 [0.62, 1.19]**
Total events	49		58			
Heterogeneity: Chi² = 8.30, df = 3 (P = 0.04); I² = 64%						
Test for overall effect: Z = 0.91 (P = 0.36)						
1.4.2 Endotracheal intubation within 24 hours						
Mercadante 2016	0	93	0	92		Not estimable
Schwaberger 2015	7	20	5	20	100.0%	1.40 [0.53, 3.68]
Subtotal (95% CI)		**113**		**112**	**100.0%**	**1.40 [0.53, 3.68]**
Total events	7		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.68 (P = 0.49)						
1.4.3 Endotracheal intubation by 72 hours of age						
El-Chimi 2017	11	57	12	55	8.0%	0.88 [0.43, 1.83]
Lindner 2005	19	31	18	30	12.0%	1.02 [0.68, 1.53]
Lista 2015	79	148	93	143	62.1%	0.82 [0.68, 1.00]
Mercadante 2016	2	93	1	92	0.7%	1.98 [0.18, 21.44]
Ngan 2017	30	76	28	86	17.2%	1.21 [0.80, 1.83]
Subtotal (95% CI)		**405**		**406**	**100.0%**	**0.93 [0.79, 1.09]**
Total events	141		152			
Heterogeneity: Chi² = 3.77, df = 4 (P = 0.44); I² = 0%						
Test for overall effect: Z = 0.95 (P = 0.34)						



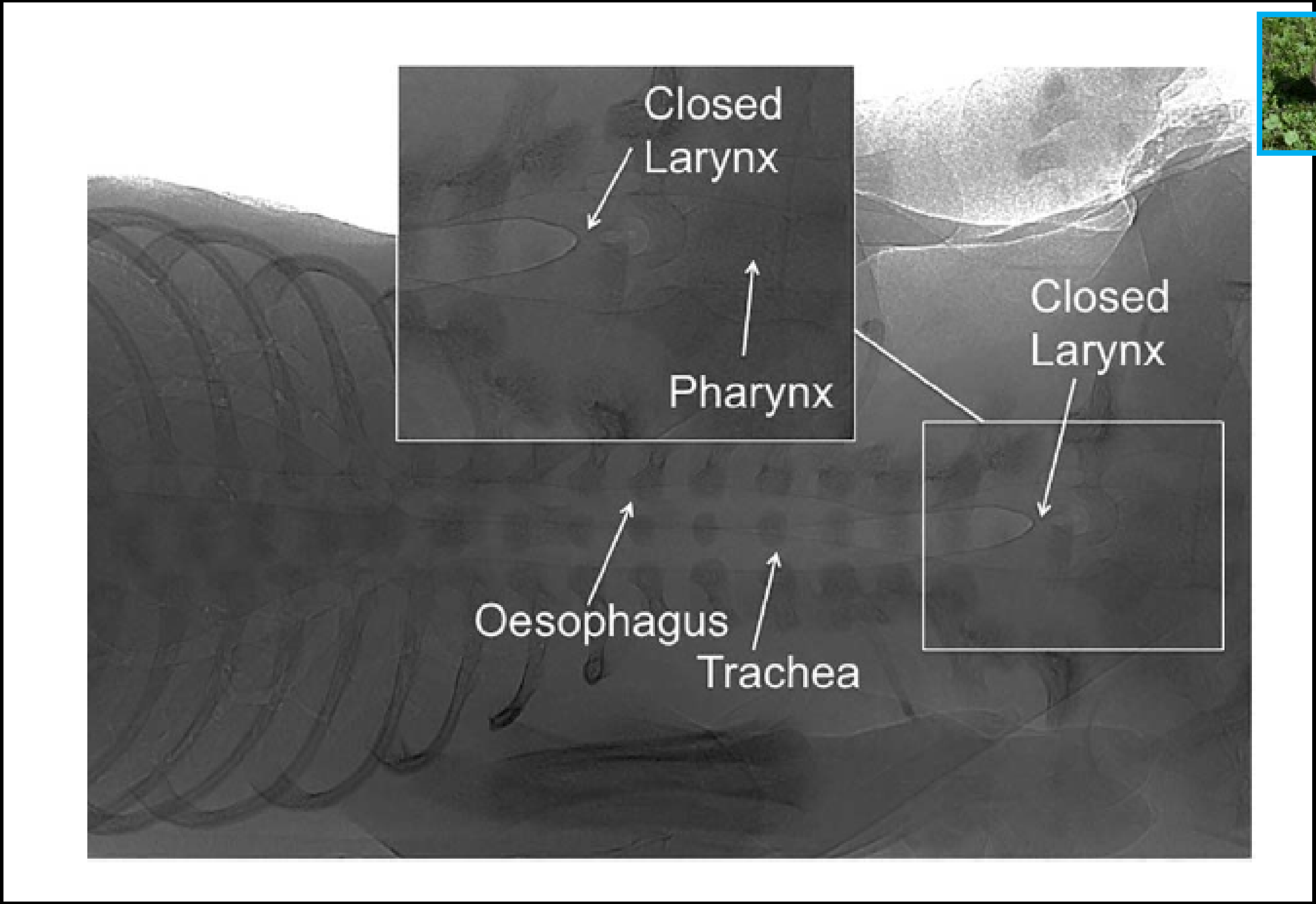


SAIL-Study (NIH Grant Number 1-U01 HD072906-01A1; PI: H. Kirpalani)

- 23-26 wks, n= 600 infants
- 14 sites in US, Canada, Europe
- Trial halted early by DSMB due to harm in the treatment arm

So Why Didn't Sustained Inflation Work in Clinical Practice?

- Method of application in animal models compared to humans is different
  - All animals were intubated
  - Human studies had SI applied with a facemask
- Analysis of the airflow and gas volumes during sustained inflation in humans
  - Air flow into the lung is greatly restricted unless the infant takes a breath, indicating obstruction
  - Could be consequence of poor head or mask position
  - More likely the glottis is actively closed

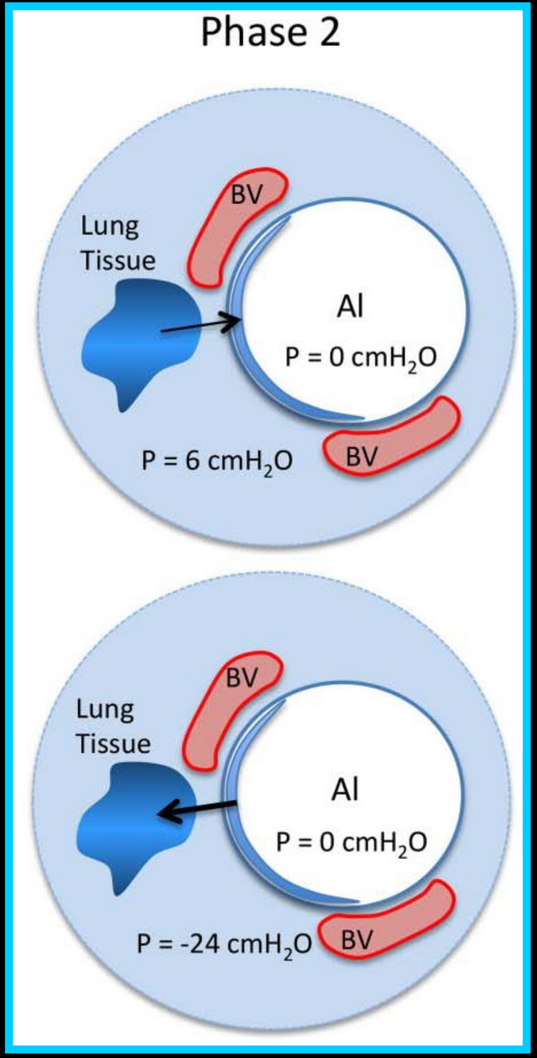


Adapted from Hooper et al. Semin Fetal Neonatal Med 2013;18:336-343

Knowledge Gaps

- Is there a role for Sustained Inflation during initial transition
  - If there is a role-what is the optimal length and pressure to use?
- ILCOR will complete a new systematic review once the SAIL trial results are officially published
- What is the optimal starting CPAP or PEEP to aid transition?

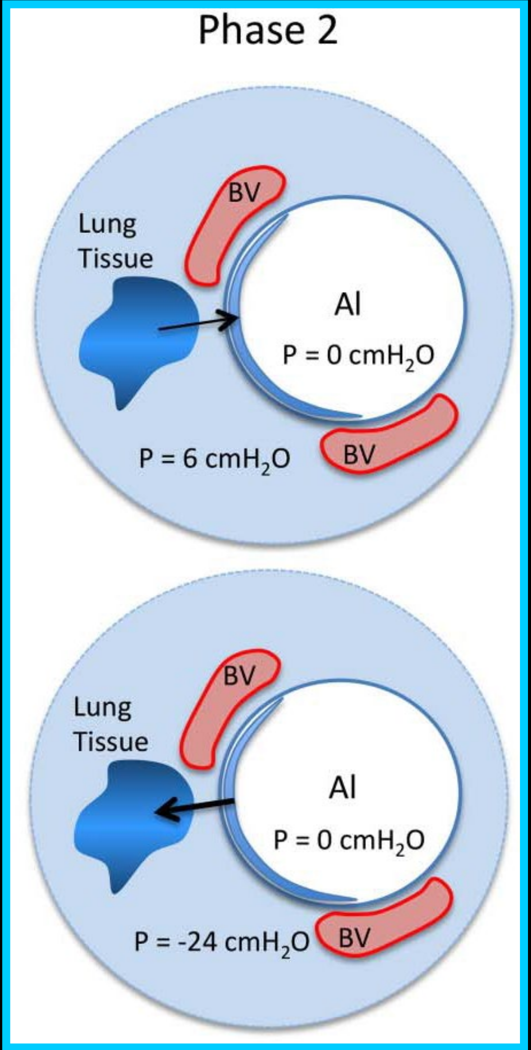
Phase 2: Liquid Accumulation within the Lung's Interstitial Tissue Compartment



- Clearance of the liquid from the lung tissue via the lymphatics and blood vessels takes considerably longer (4-6 hours)
- As a result, significant amounts of liquid reside whin the interstitial tissue compartment for the first 4-6 hours, essentially resulting in pulmonary edema
- As fluid accumulates in the tissue, the hydrostatic pressure increases which can lead to liquid re-entering the airways
- A continuous cycle of clearance and re-entry until the excess liquid is cleared by the lymphatics and vessels

Adapted from Hooper et al ADC F&N

Phase 2: Liquid Accumulation within the Lung's Interstitial Tissue Compartment



Adapted from Hooper et al

- The hydrostatic pressure generated during inspiration (20-80 cm H2O) is much greater than the reverse gradiant during expiration (6 cm H2O)
- Thus the potential to clear liquid during inspiration is considerably greater than the potential for airway liquid re-entry
- CPAP in the spontaneously breathing preterm infant is so critical
  - Assists the compliant chest wall in opposing lung recoil
  - Reduces the hydrostatic pressure gradient for liquid to move back into the airways
- Grunting after birth works the same way for newborns

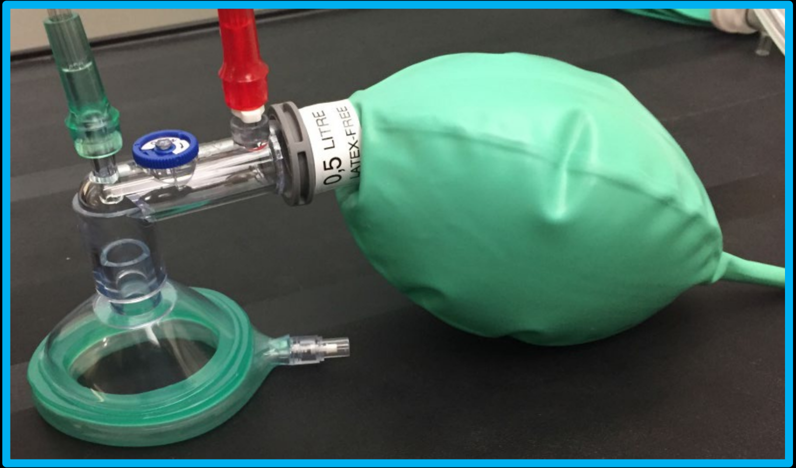
Does this physiology translate into clinical experience?

CPAP vs Intubation for Preterm Newborns in the Delivery Room

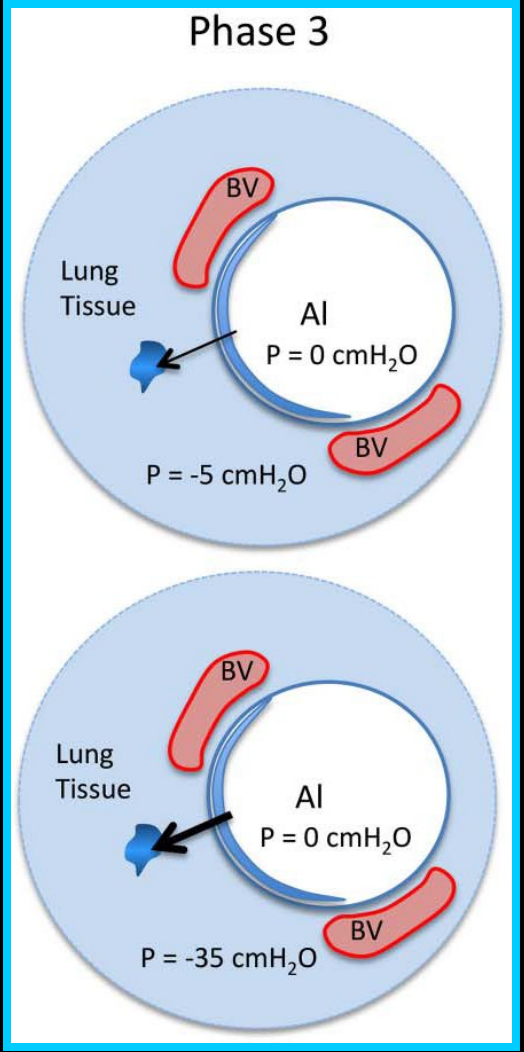
- 3 RCTs (n=2358)
- Potential benefit for reducing death or BPD (RR, 0.91; 95% CI, 0.83–1.00)
- No advantage for death alone, BPD alone, air leak, severe IVH, NEC, ROP
- Tx Recommendation: For spontaneously breathing preterm infants with respiratory distress requiring respiratory support in the delivery room, we suggest initial use of CPAP rather than intubation and PPV

Role of CPAP in the Delivery Room

- If heart rate and respiratory effort are adequate but there is increased work of breathing or a perception of cyanosis then CPAP can be considered
- CPAP helps establish functional residual capacity
  —CPAP can be delivered with a flow-inflating bag or a T-piece resuscitator, but NOT a self-inflating bag.

Phase 3: Respiratory Gas Exchange and Metabolic Homeostasis



Adapted from Hooper et al

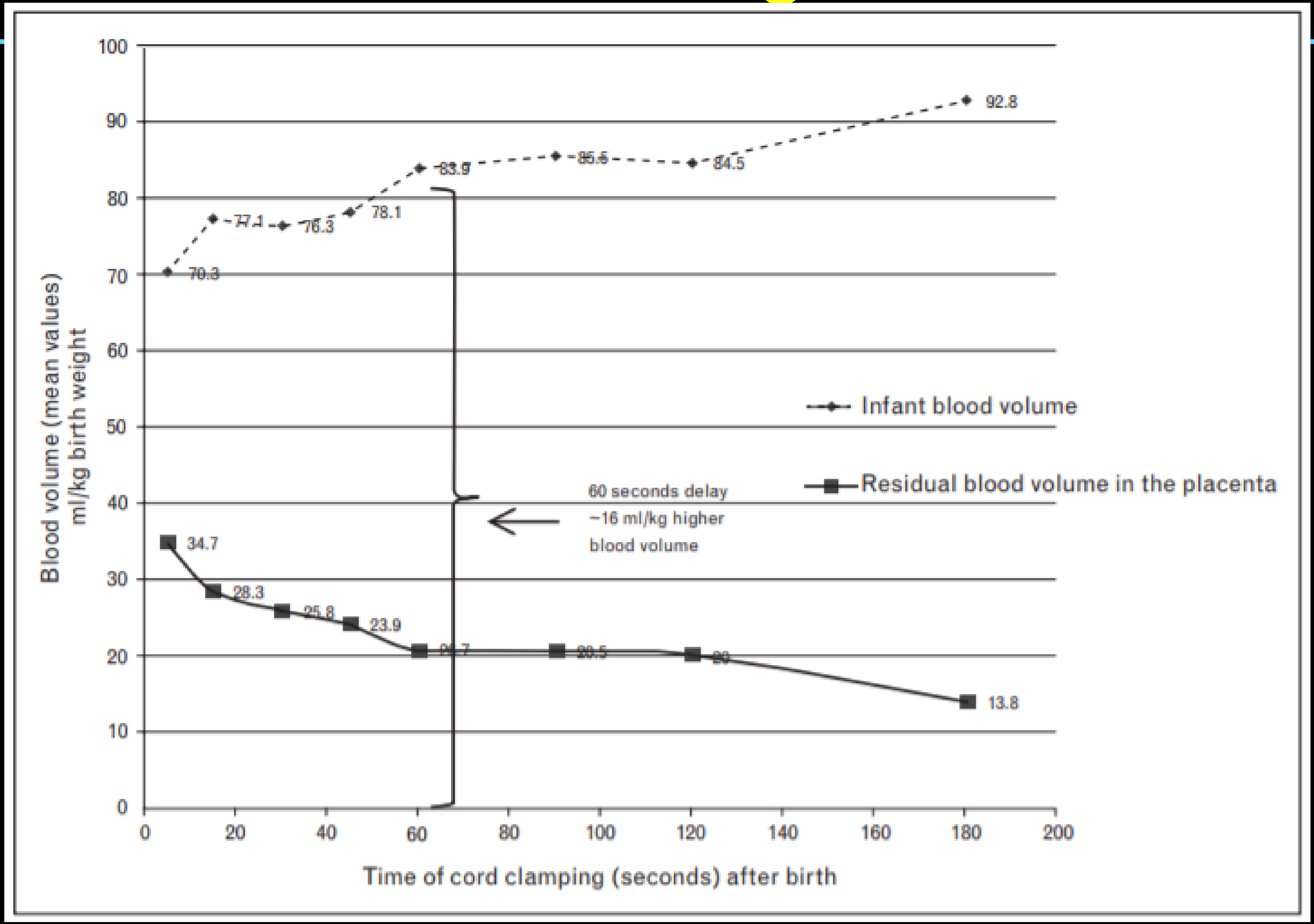
- Following lung aeration and clearance of liquid from the tissue, the infant has passed through the immediate birth transition phase
- Ventilation can be more focused towards gas exchange and maintaining respiratory gas homeostasis
- Success will depend on overcoming the structural and functional deficiencies of the lung
  - Surfactant deficiency
  - Immaturity of respiratory muscles
  - High compliance of the chest wall

Knowledge Gaps

- Are there other types of PPV devices that aid transition optimally?
  - Upright resuscitator bag
- Is there a role for less invasive surfactant administration in the delivery room?

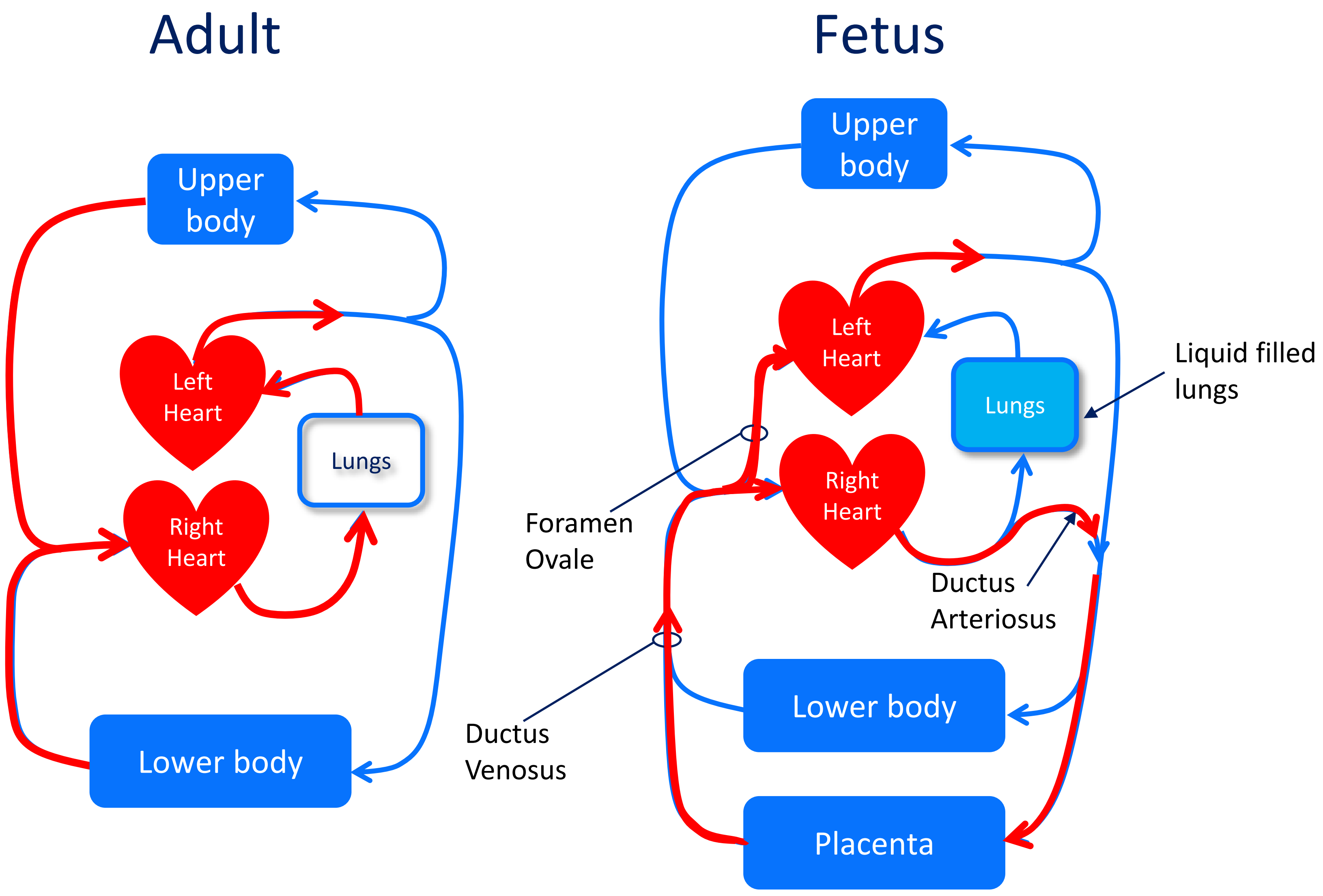
Cord Clamping and Placental Transfusion

Intact Cord during Transition



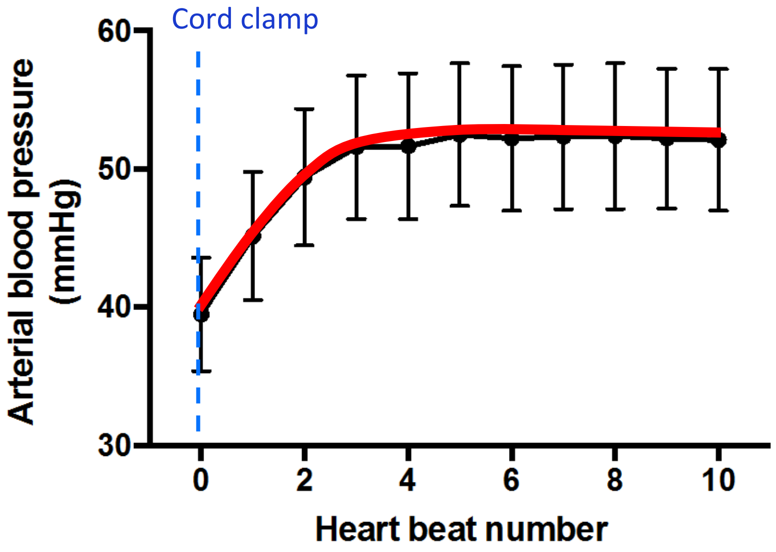
Raju Curr Opin Pediatr 2013, 25:180–187

Fetal and Adult circulations

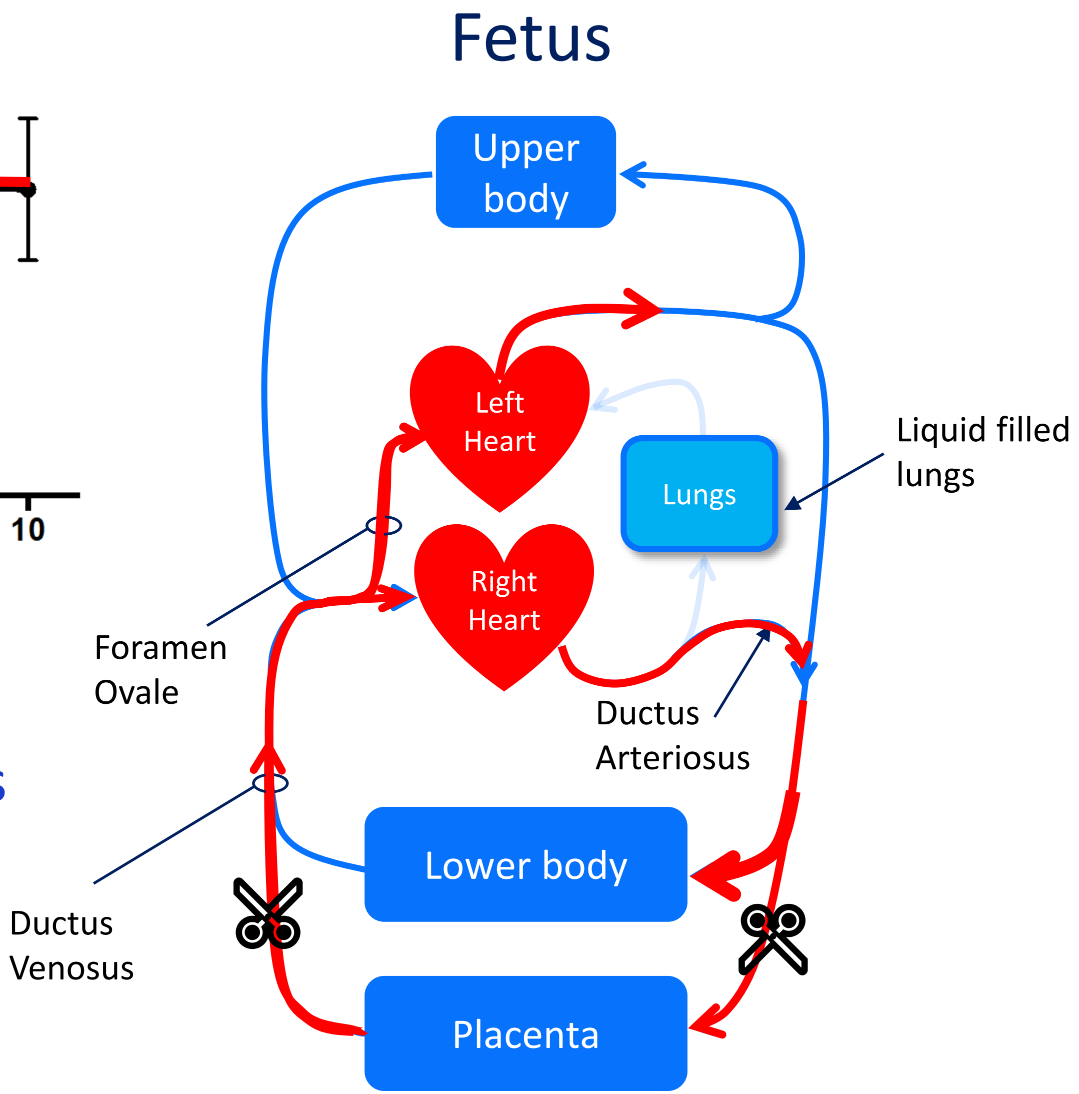


Courtesy of Stuart Hooper

Consequences of Umbilical cord clamping



Blood pressure increases by 30% in 4 heart beats



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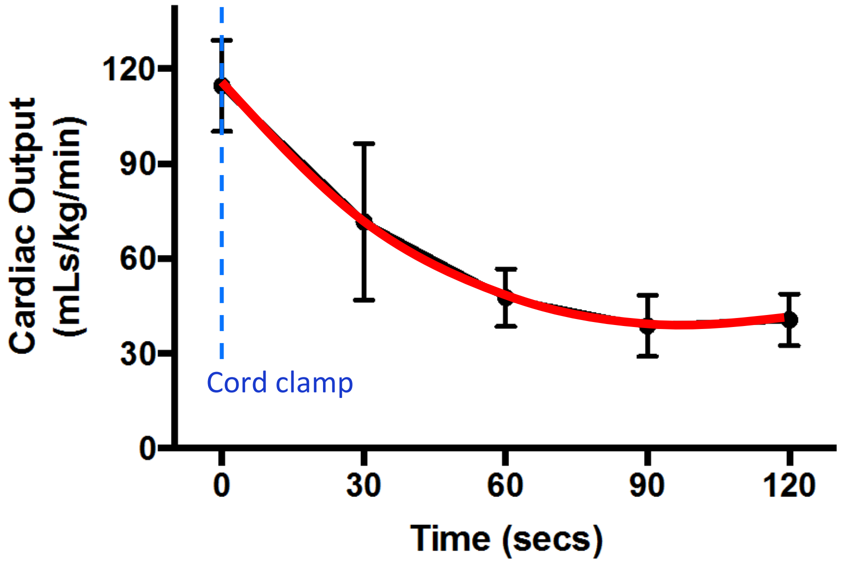
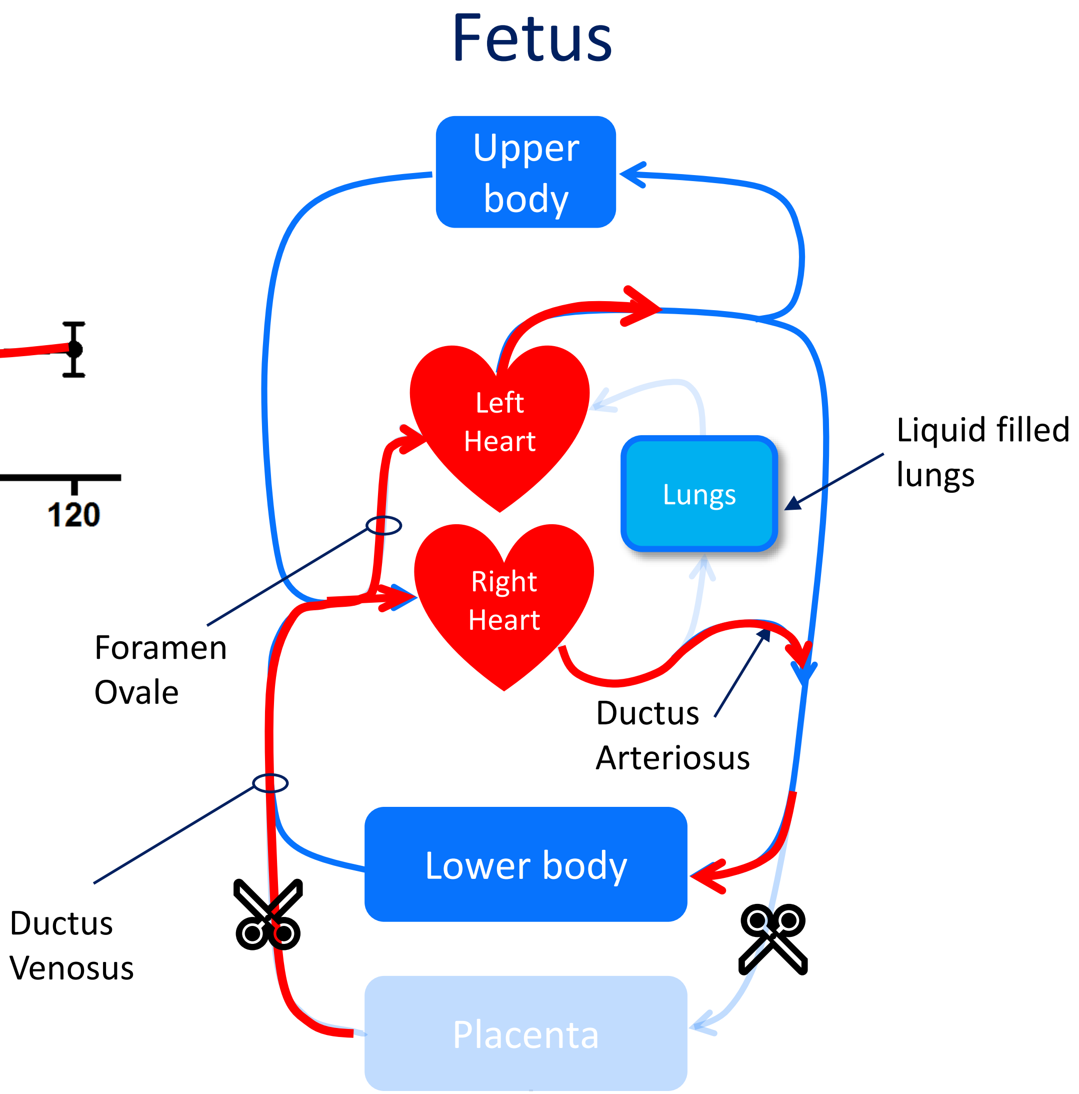
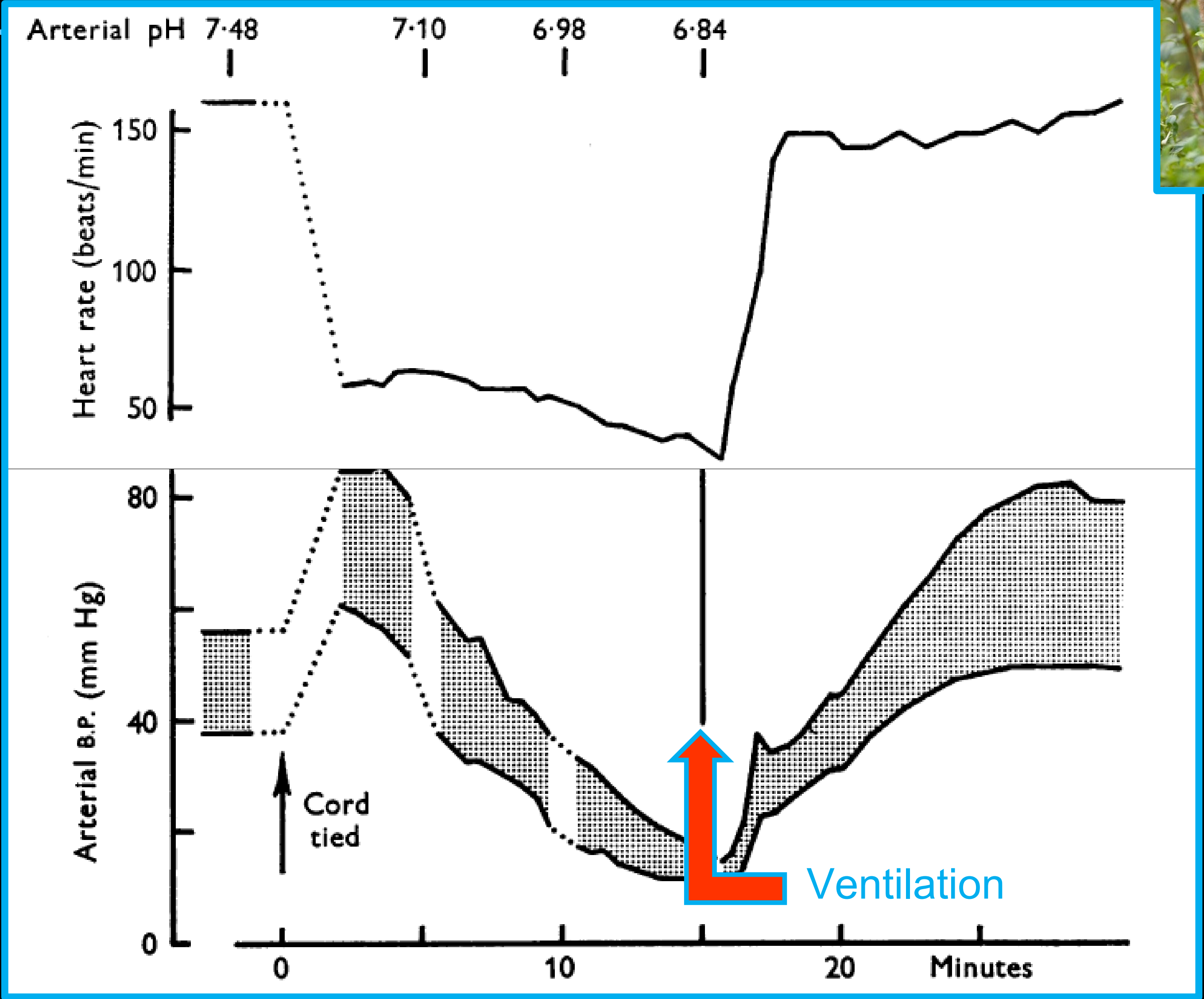


Cardiac Output decreases by up to 50% in 60 seconds



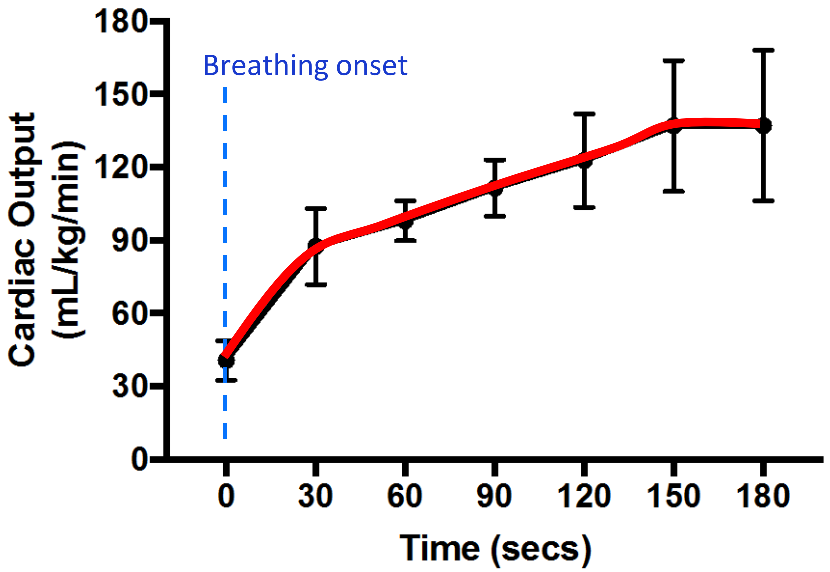
Courtesy of Stuart Hooper

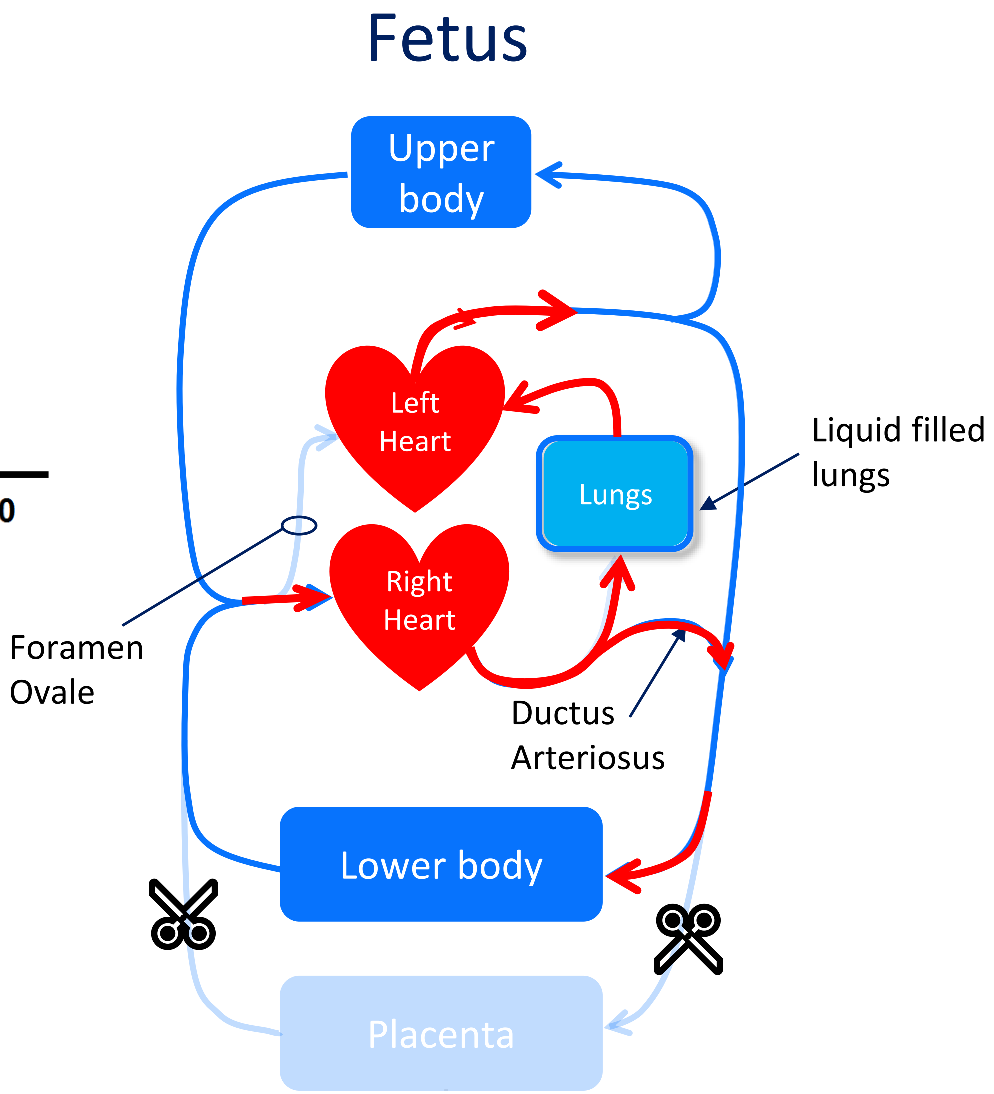
Cardiac Output



Dawes, J. Physiol. (1963), 169, pp. 167-184

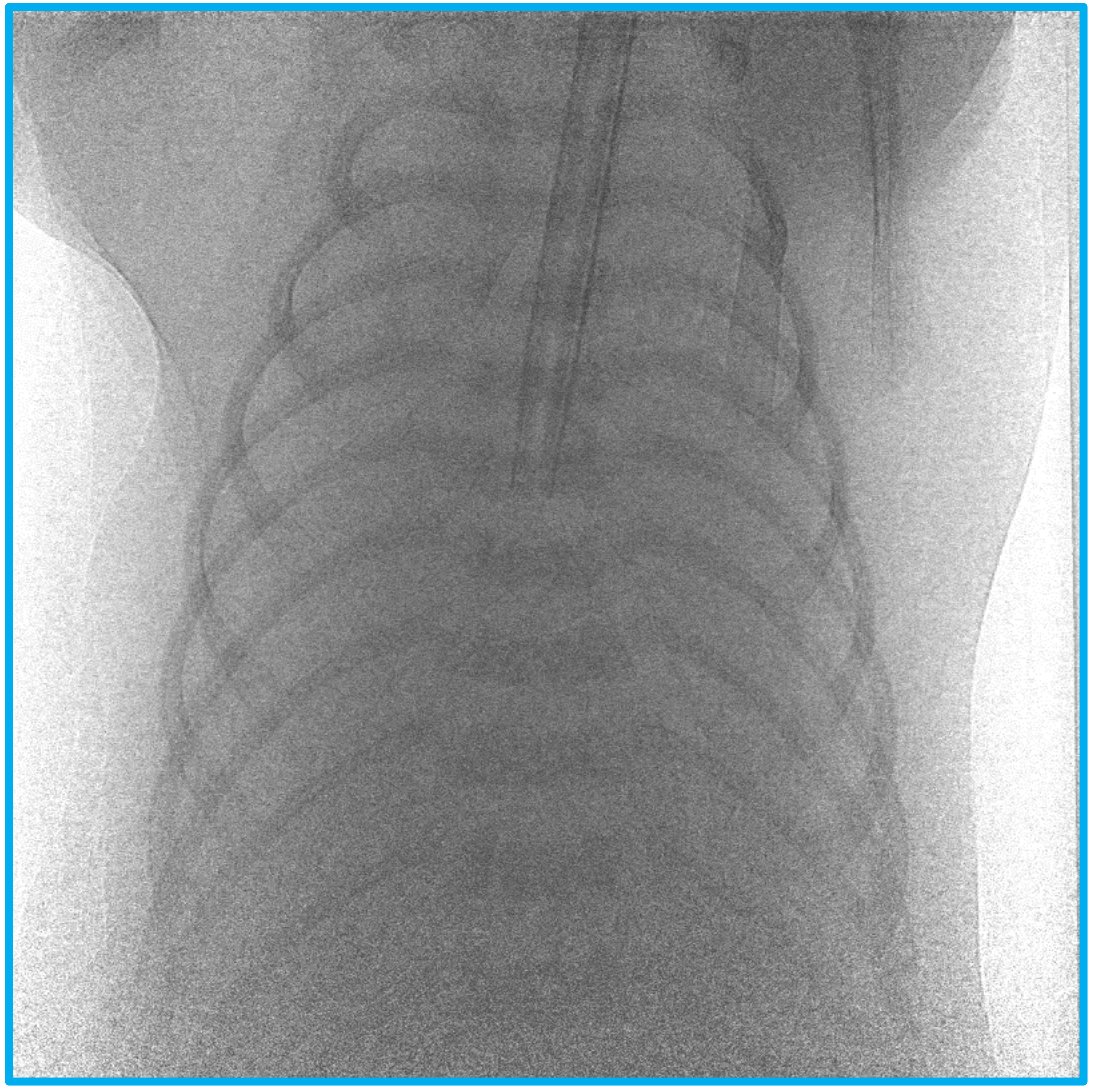
Lung aeration restores cardiac output





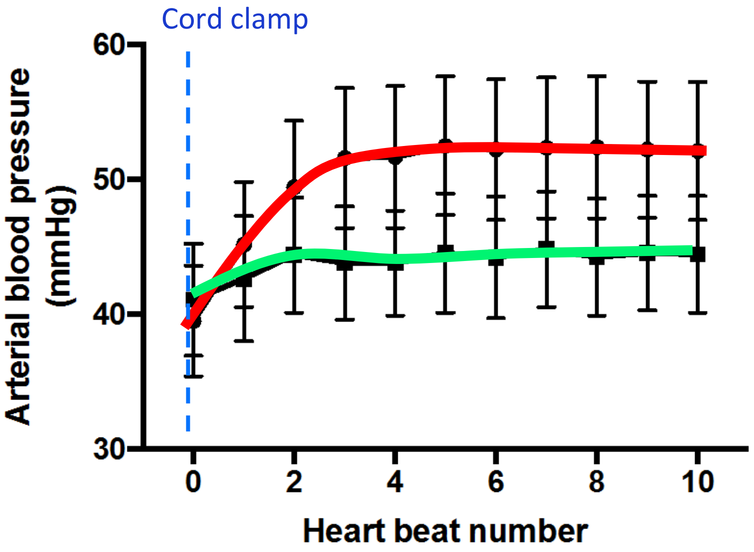
Lung aeration increases pulmonary blood flow which restores cardiac output

Courtesy of Stuart Hooper



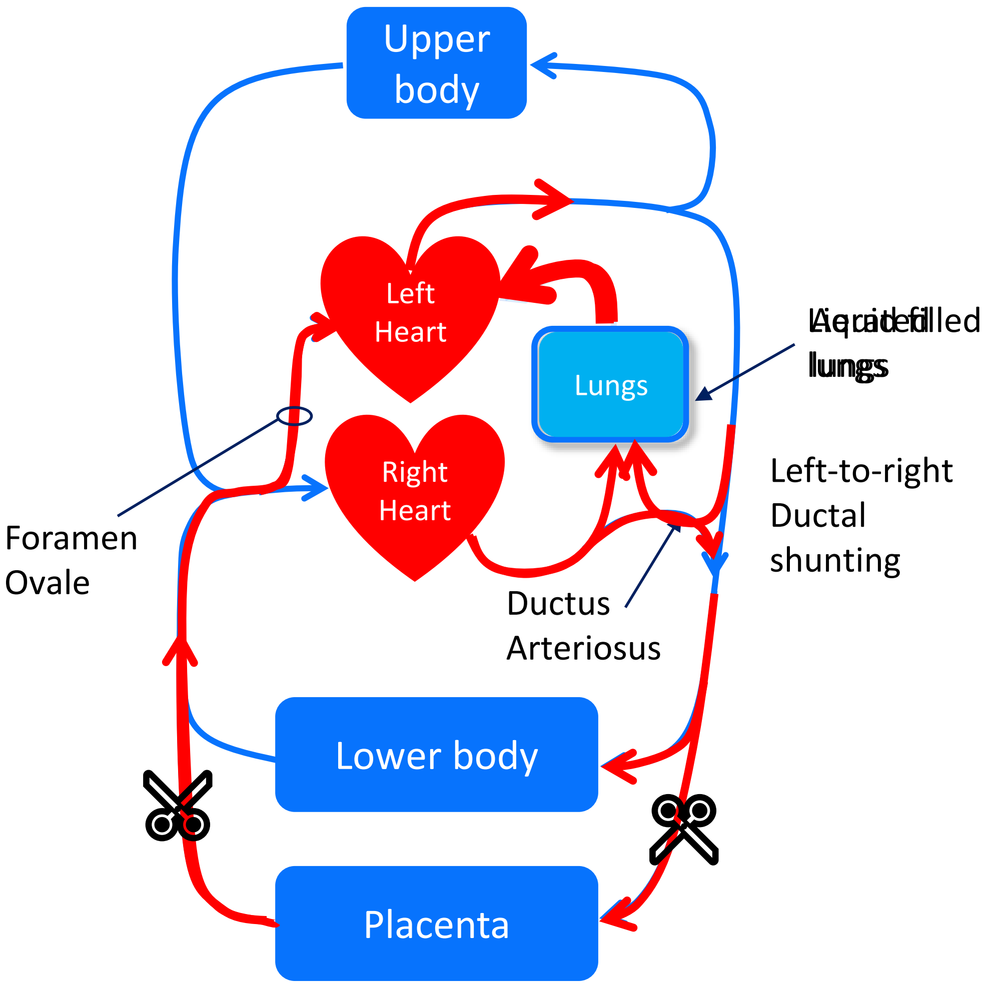
Courtesy of Stuart Hooper

Breathing onset before cord clamping



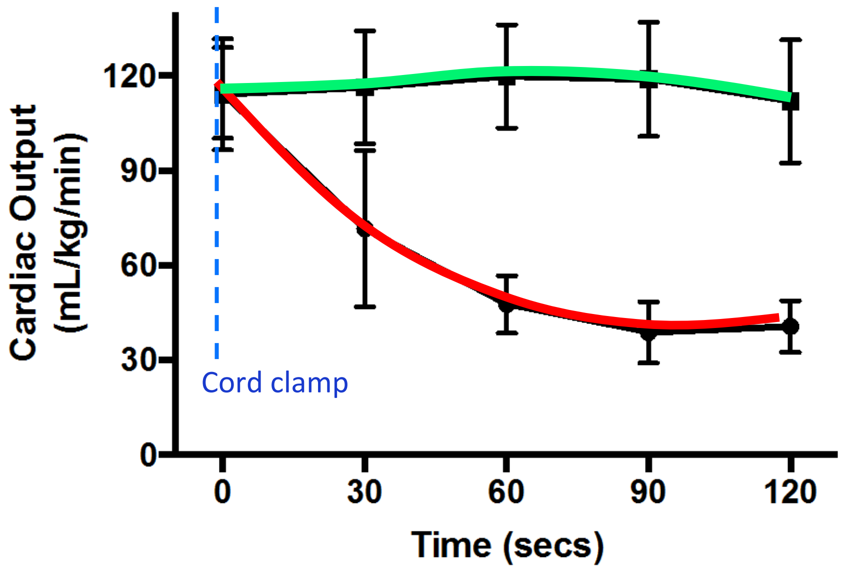
Avoid the increase in
Blood pressure

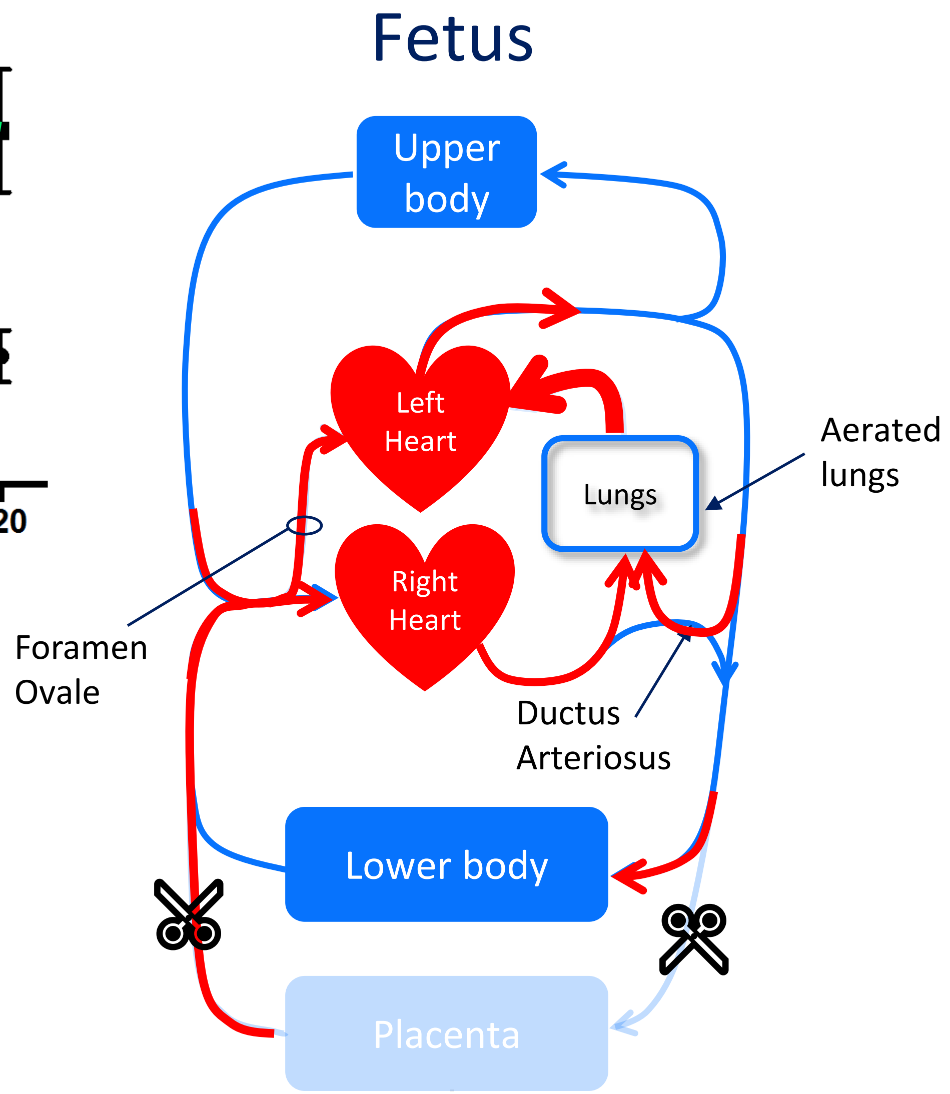
Fetus



Courtesy of Stuart Hooper

Breathing onset before cord clamping

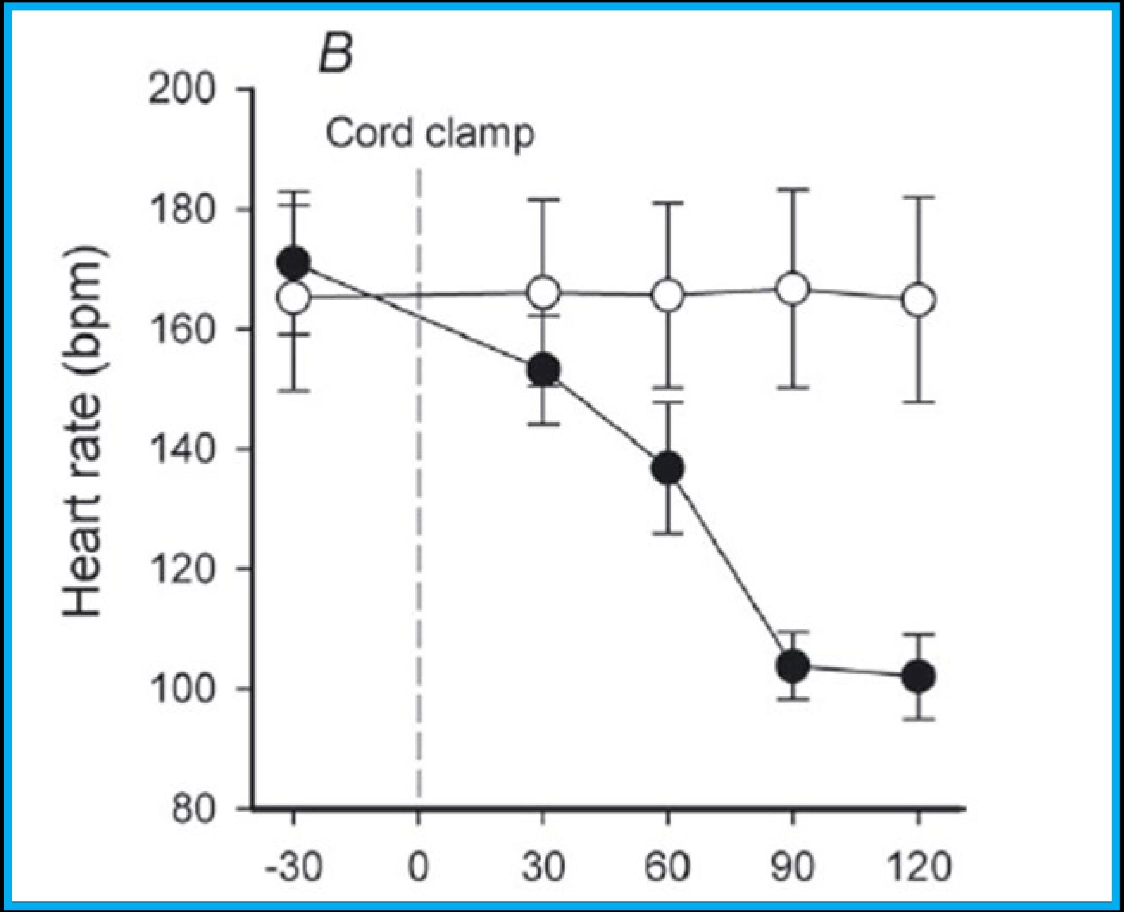


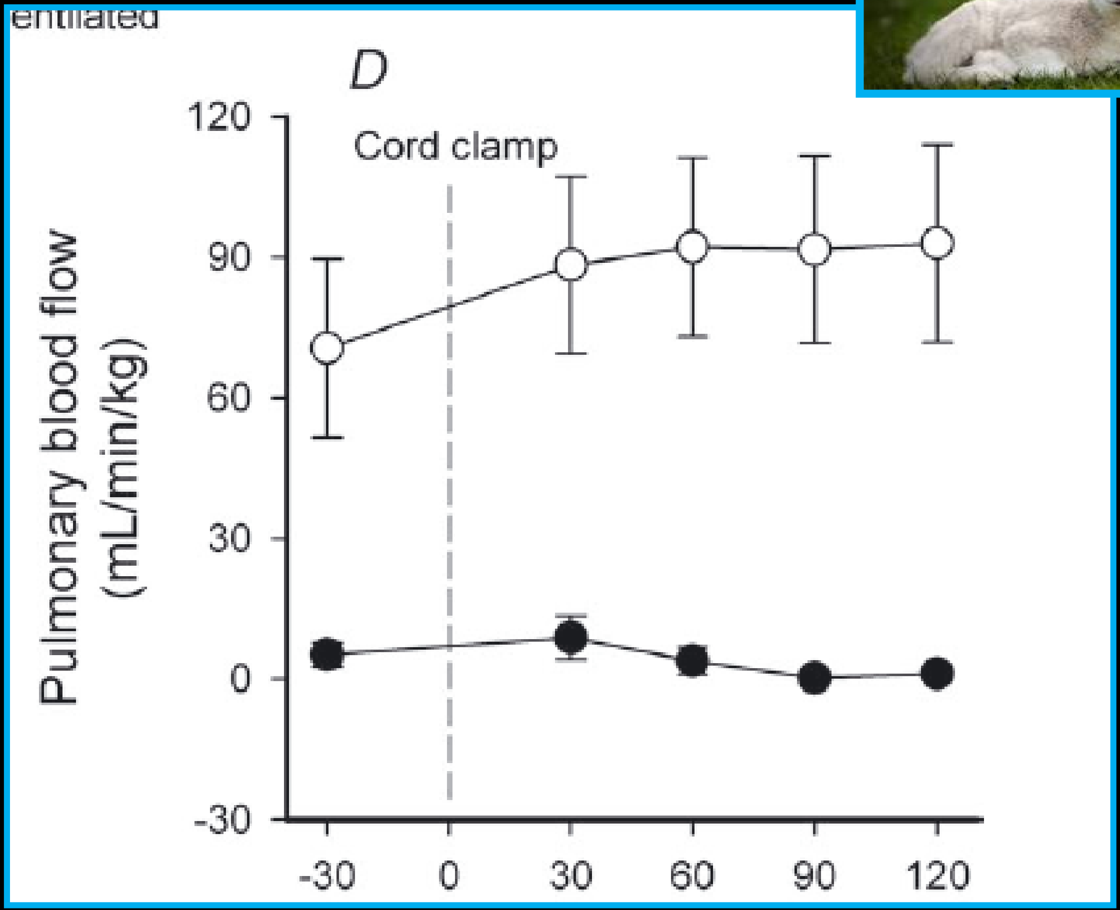


Cardiac Output is sustained

Courtesy of Stuart Hooper

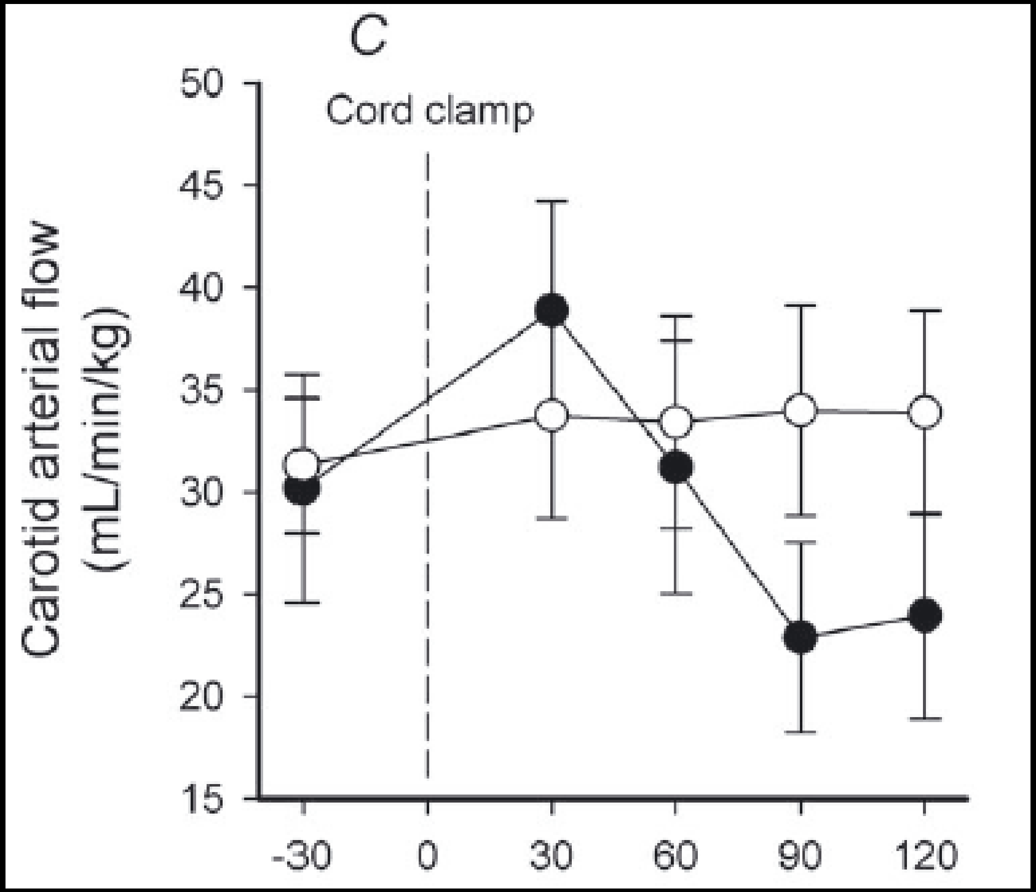
Ventilation prior to cord clamping

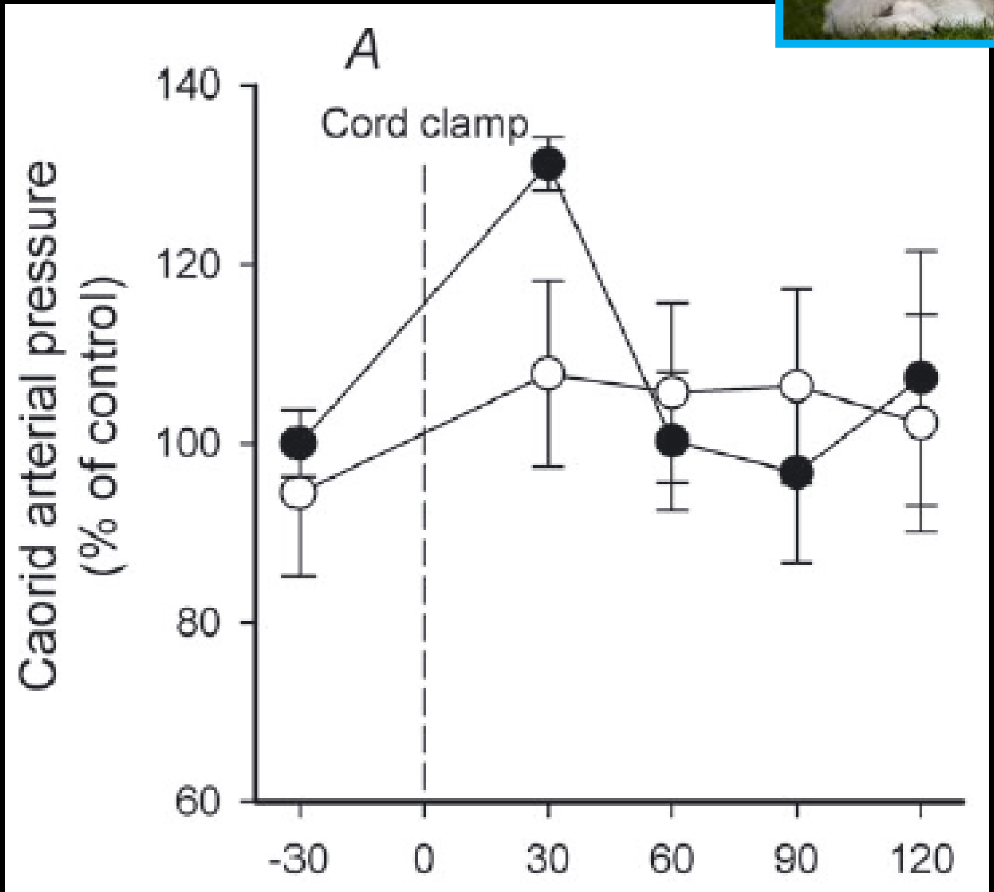




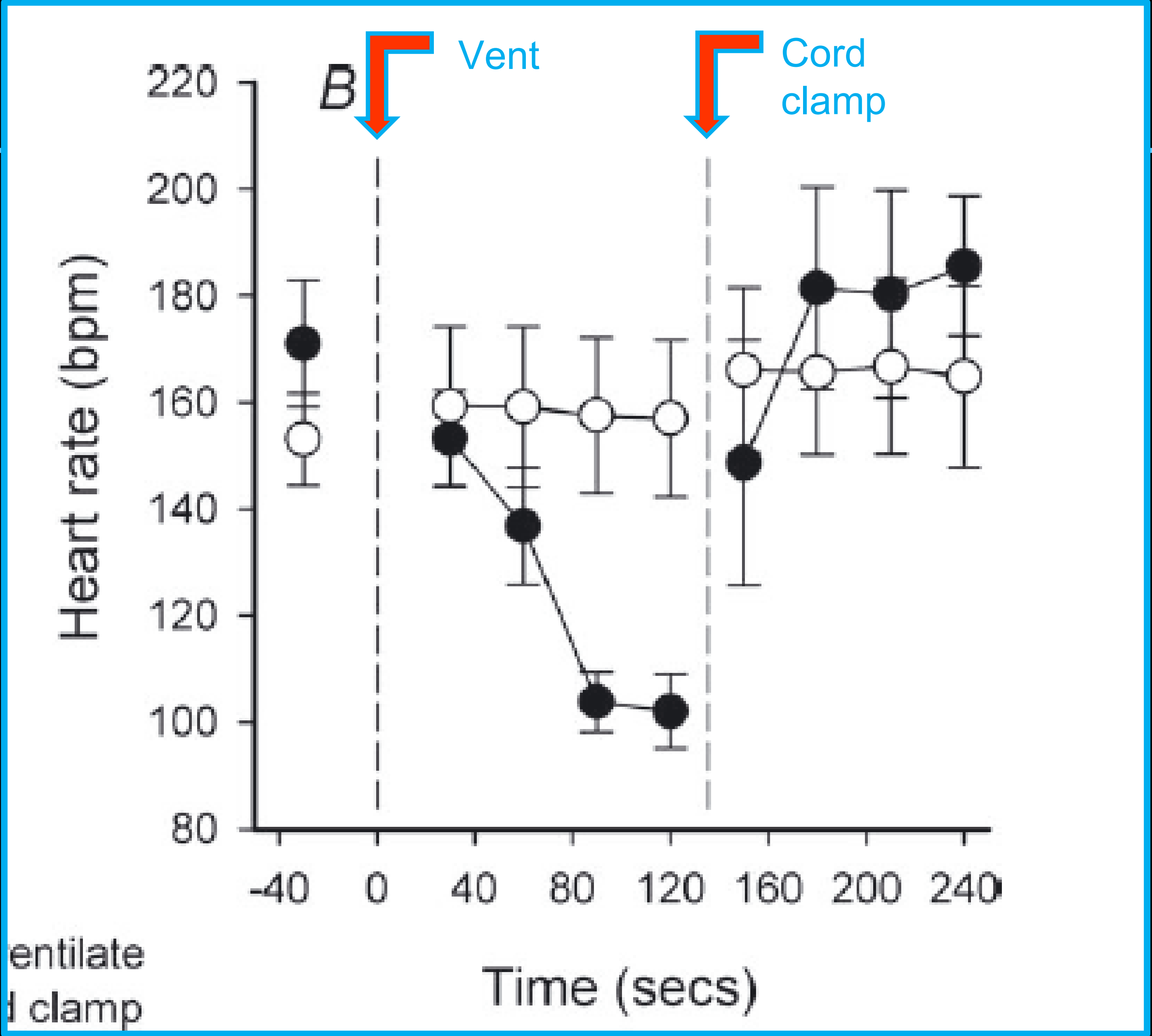
Bhatt, *J Physiol* 591.8 (2013) pp 2113–2126

Carotid blood flow

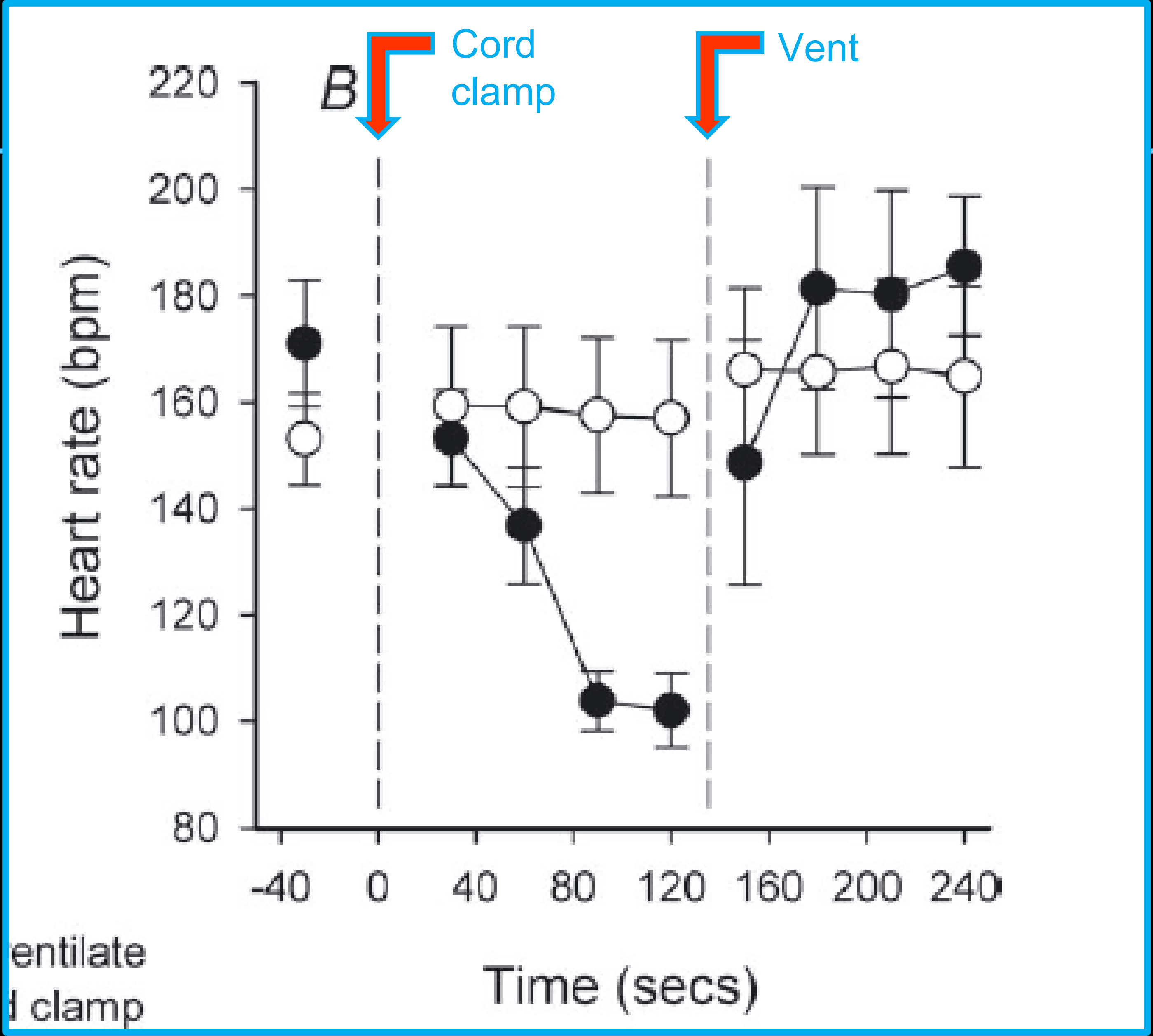




Bhatt, *J Physiol* 591.8 (2013) pp 2113–2126



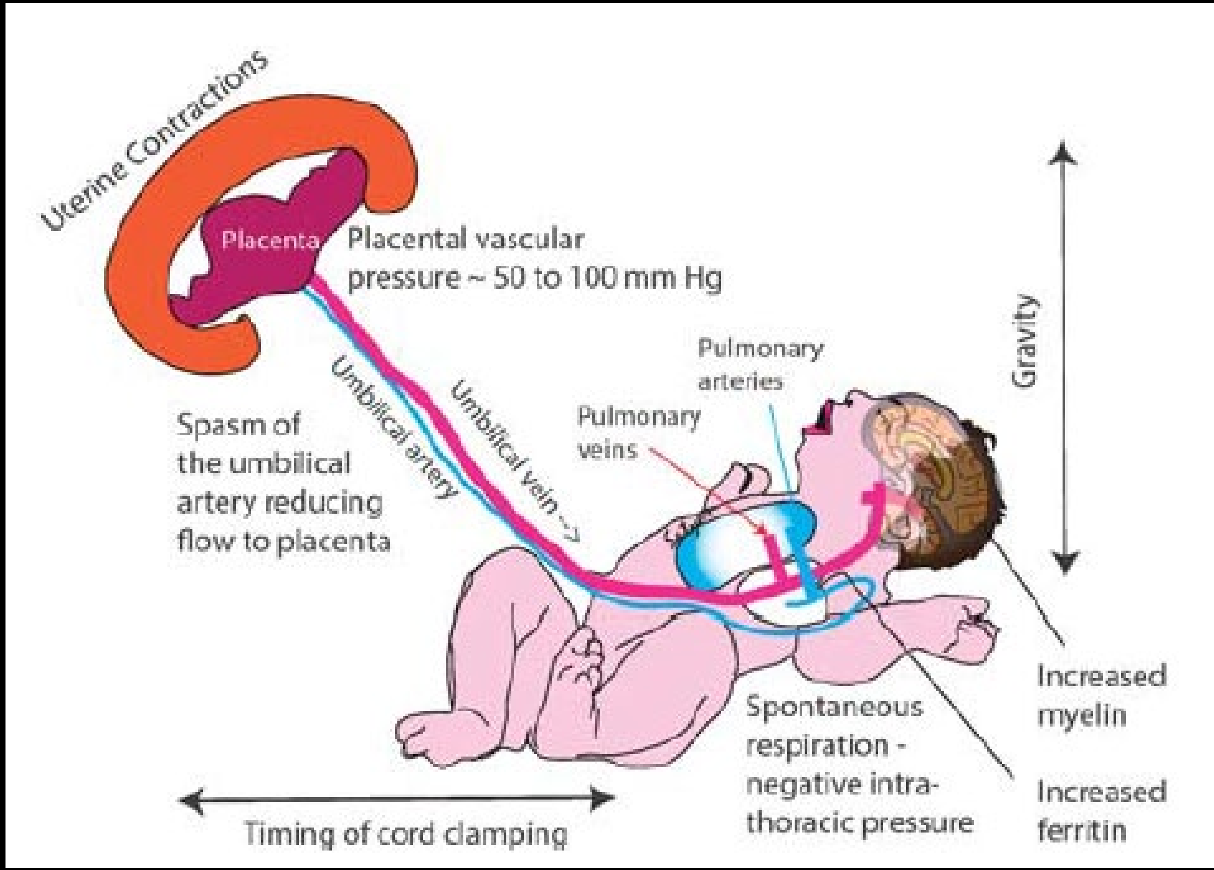
Bhatt, *J Physiol* 591.8 (2013) pp 2113–2126



Bhatt, *J Physiol* 591.8 (2013) pp 2113–2126

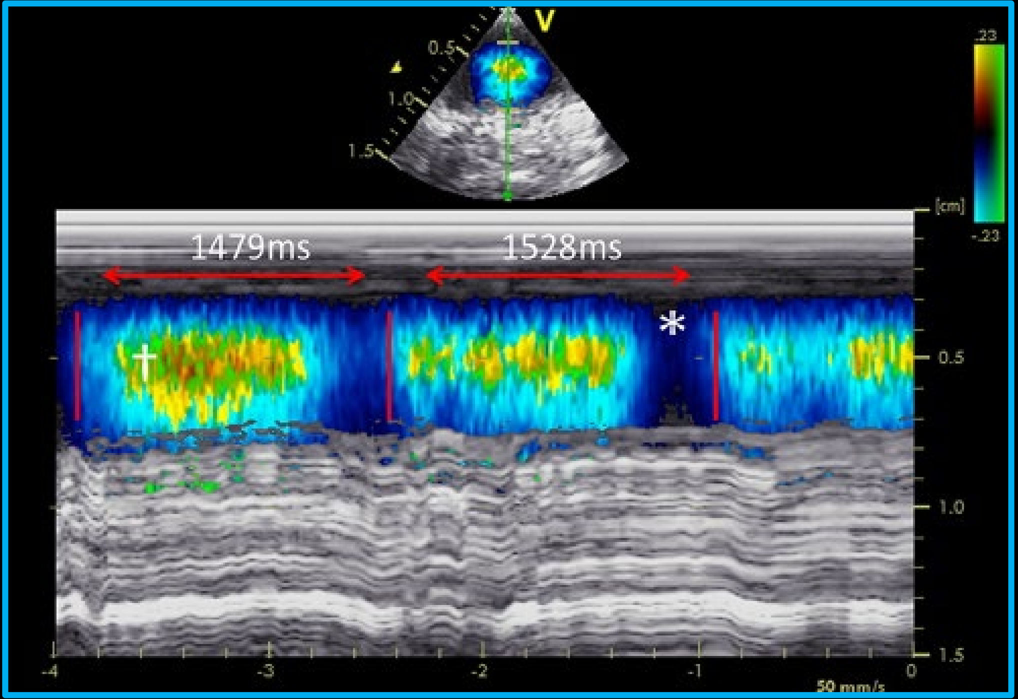
Logistics of Blood Volume Transfer

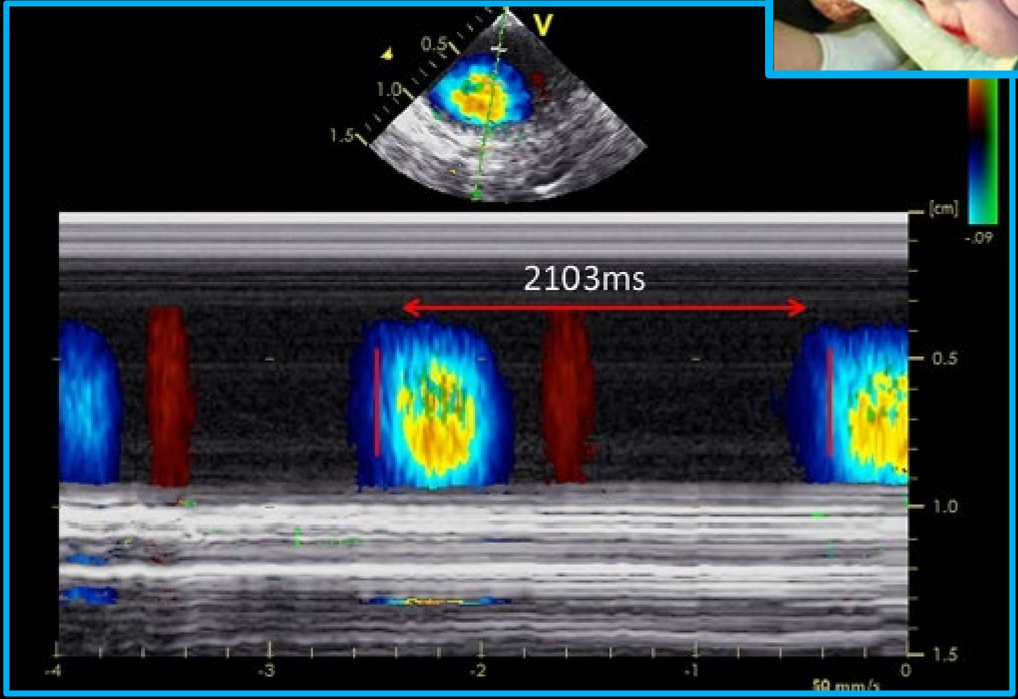
- Time
- Vascular spasm
- Uterine contractions
- Respiratory effort
- Gravity



Katheria, Journal of Perinatology (2017) 37, 105–111

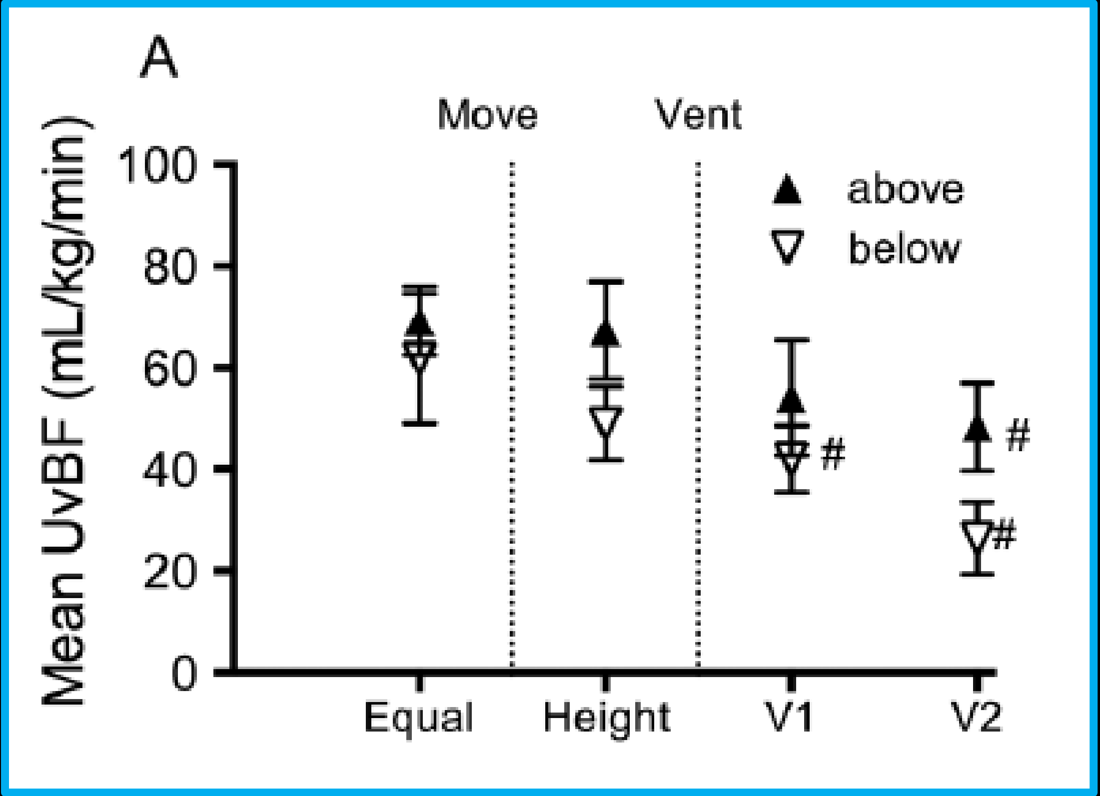
Respiratory Effort and Blood Volume

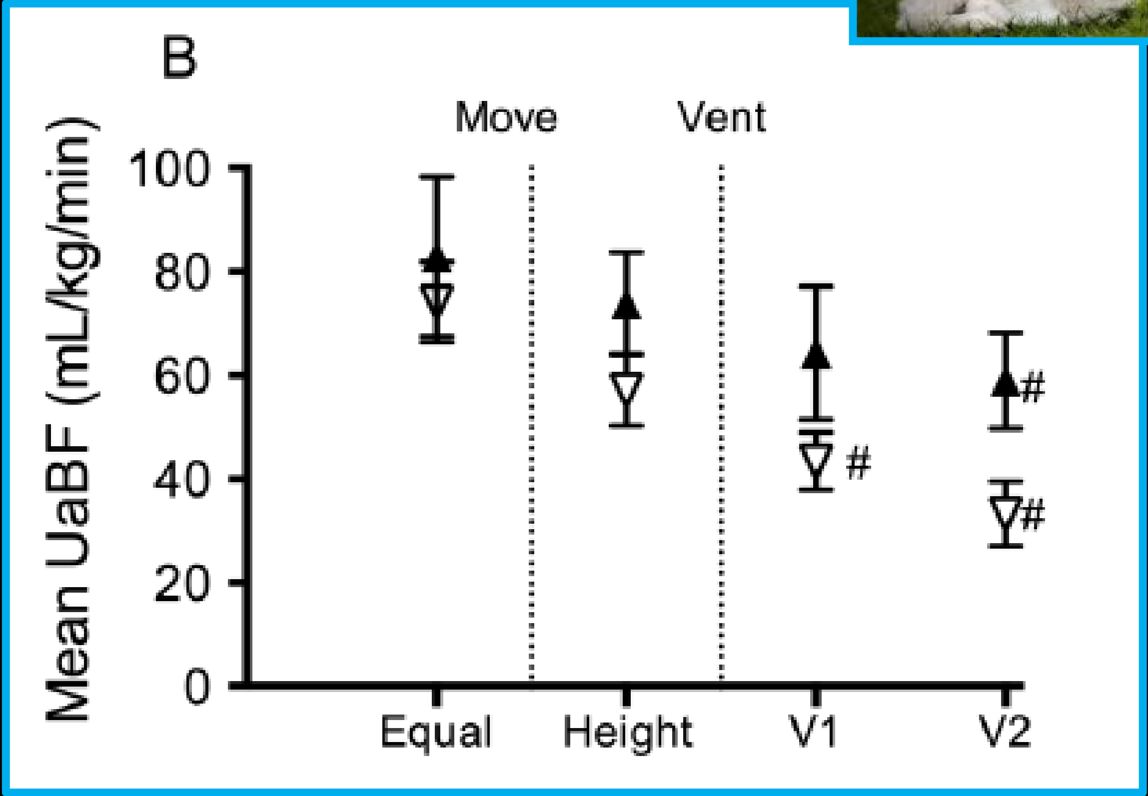




Boere I, et al. Arch Dis Child Fetal Neonatal Ed 2015;100:F121–F125.

Gravity





Hooper SB, et al. Arch Dis Child Fetal Neonatal Ed 2017;

Gravity

	Introitus group		Abdomen group		Difference, g (mean, 95% CI)	p value
	n	Mean weight change, g (SD, 95% CI)	n	Mean weight change, g (SD, 95% CI)		
All women	197	56 (47, 50–63)	194	53 (45, 46–59	3 (–5·8 to 12·8)	0·45
Semi-sitting or sitting position	81	52 (48, 42–62)	74	54 (47, 43–65)	1·6 (–16·0 to 13·0)	0·82
Lying down position	114	59 (48, 50–68)	120	52 (45, 44–60)	6·7 (–5·0 to 18·0)	0·27

Data are mean (SD), 95% CI.

Table 2: **Weight increase in the first 2 min after birth and mother's position during delivery**

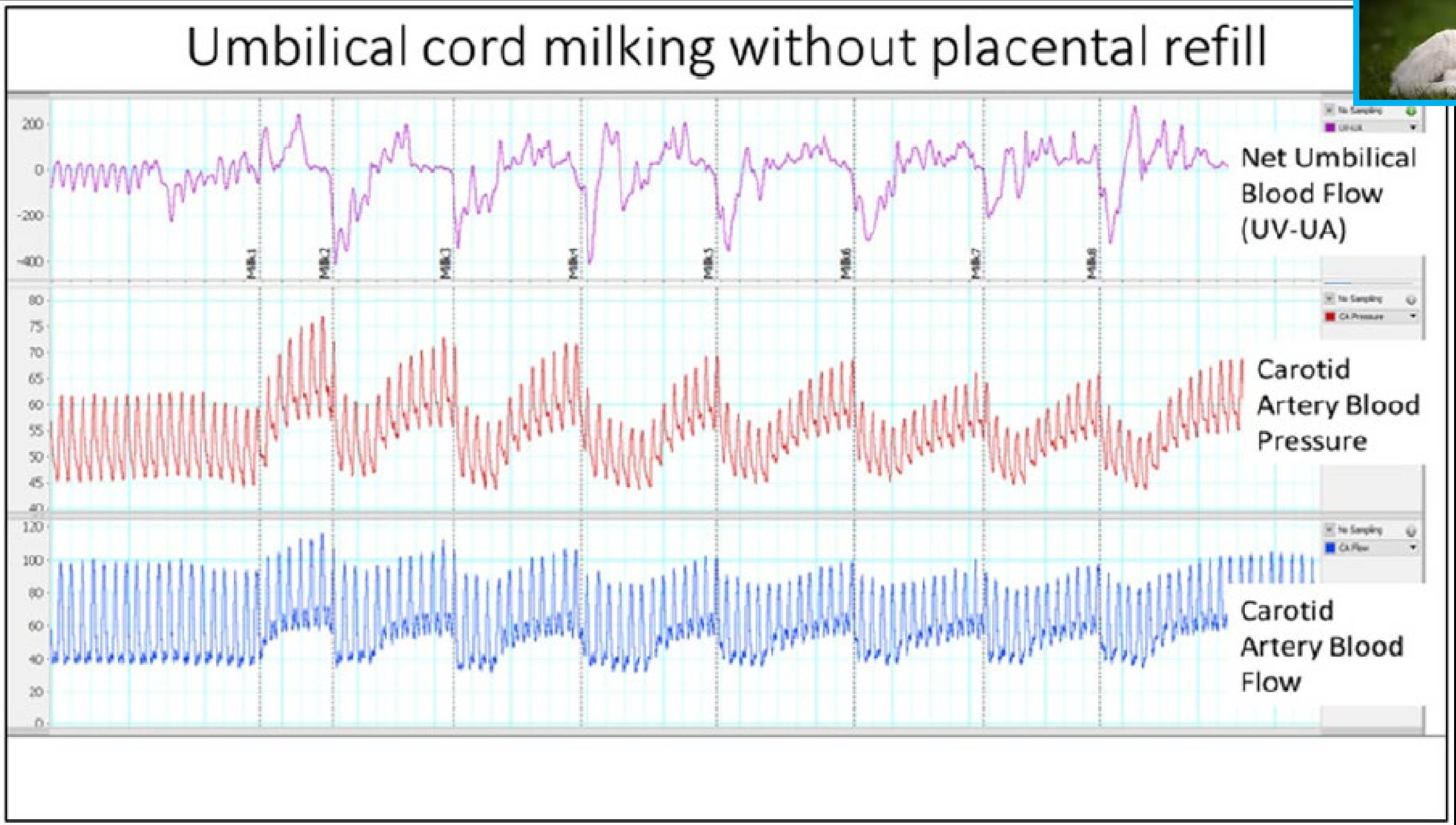
Vain, ***Lancet*** **2014; 384: 235–40**

Logistics of DCC

Cord milking

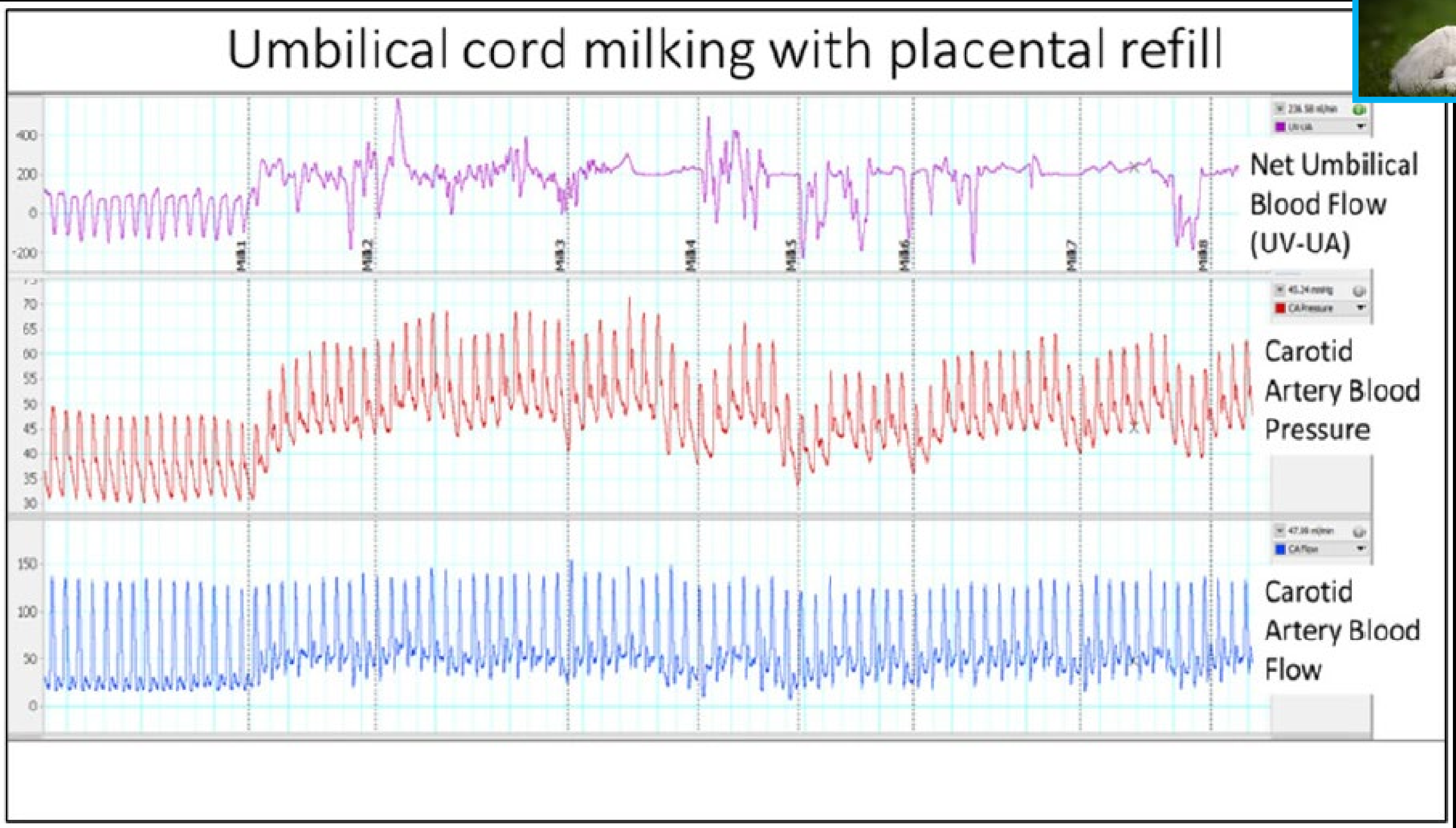
- May increase cardiovascular stability, decrease need for transfusion in newborns
- Not currently recommended due to lack of evidence and long-term follow up

Cord Milking



Blank DA, et al. Arch Dis Child Fetal Neonatal Ed 2018;**103**:F539–F546

Cord Milking



Blank DA, et al. Arch Dis Child Fetal Neonatal Ed 2018;**103**:F539–F546

Clamping the Umbilical Cord

- Has significant effect on transitional physiology
  - Eliminates blood return from placenta and potentially decreases cardiac output
  - Increases peripheral vascular resistance
- Is better tolerated from cardiovascular standpoint when lungs are inflated and pulmonary perfusion is established
- Can be performed physiologically for both vaginal and cesarean deliveries
- Milking the cord is not yet proven safe for newborns

When ventilation that inflates the lung fails: physiology of cardiac compressions

Indications For Cardiac Compressions During Neonatal CPR Have Not Changed in 2015

Chest Compressions are indicated when the heart rate remains below 60 bpm despite

- Providing warmth, position, suction (if needed), dry and stimulate
- 30 s of EFFECTIVE assisted ventilation (focus on MRSOPA steps to achieve inflation of the lung first including an advanced airway)

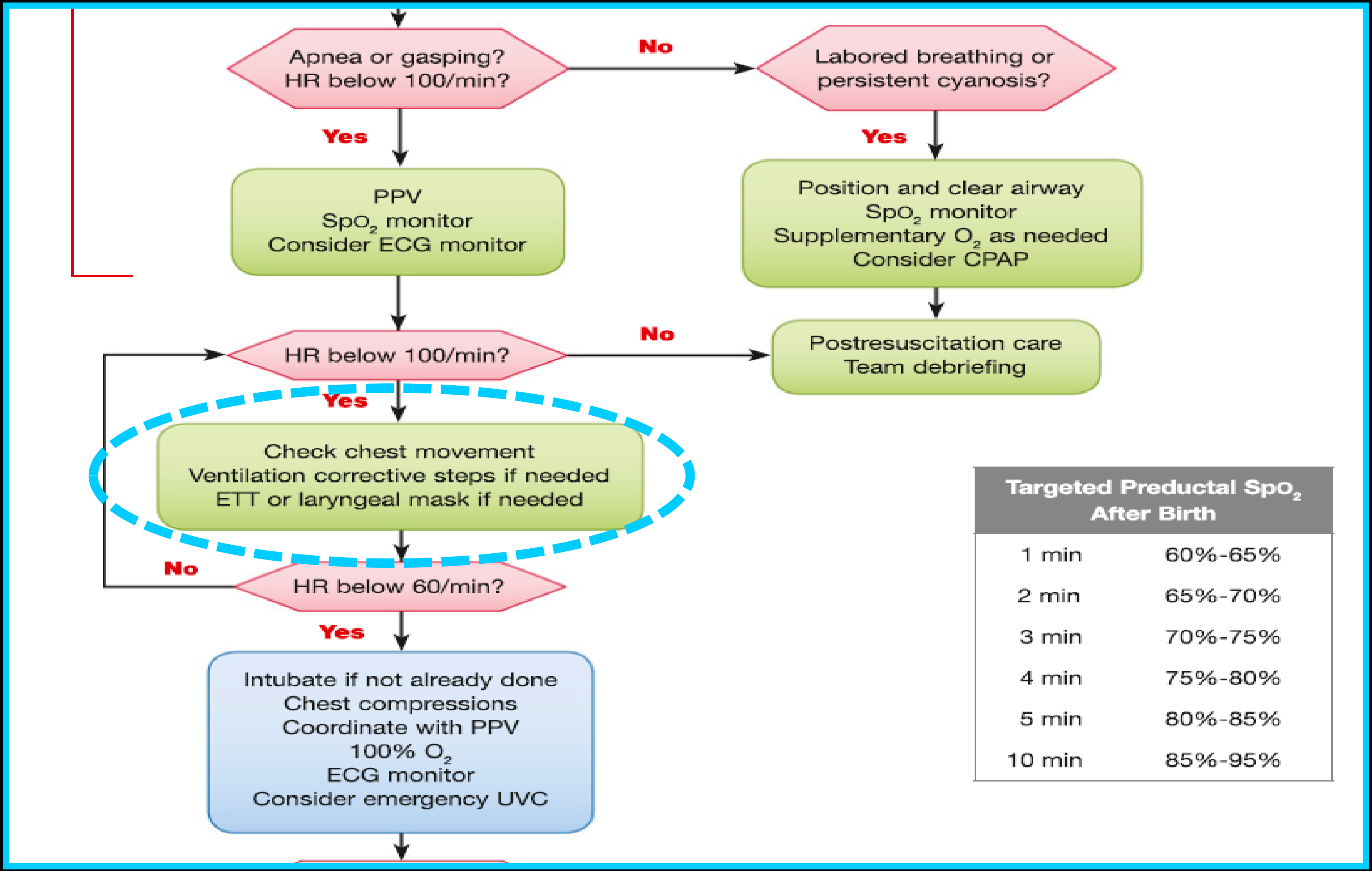
Note: Because chest compressions are likely to compete with effective ventilation, rescuers are encouraged to ensure that assisted ventilation is delivered optimally BEFORE initiation of chest compressions

Huynh, T., et al. (2015). Arch Dis Child Fetal Neonatal Ed **100**(1): F39-42.

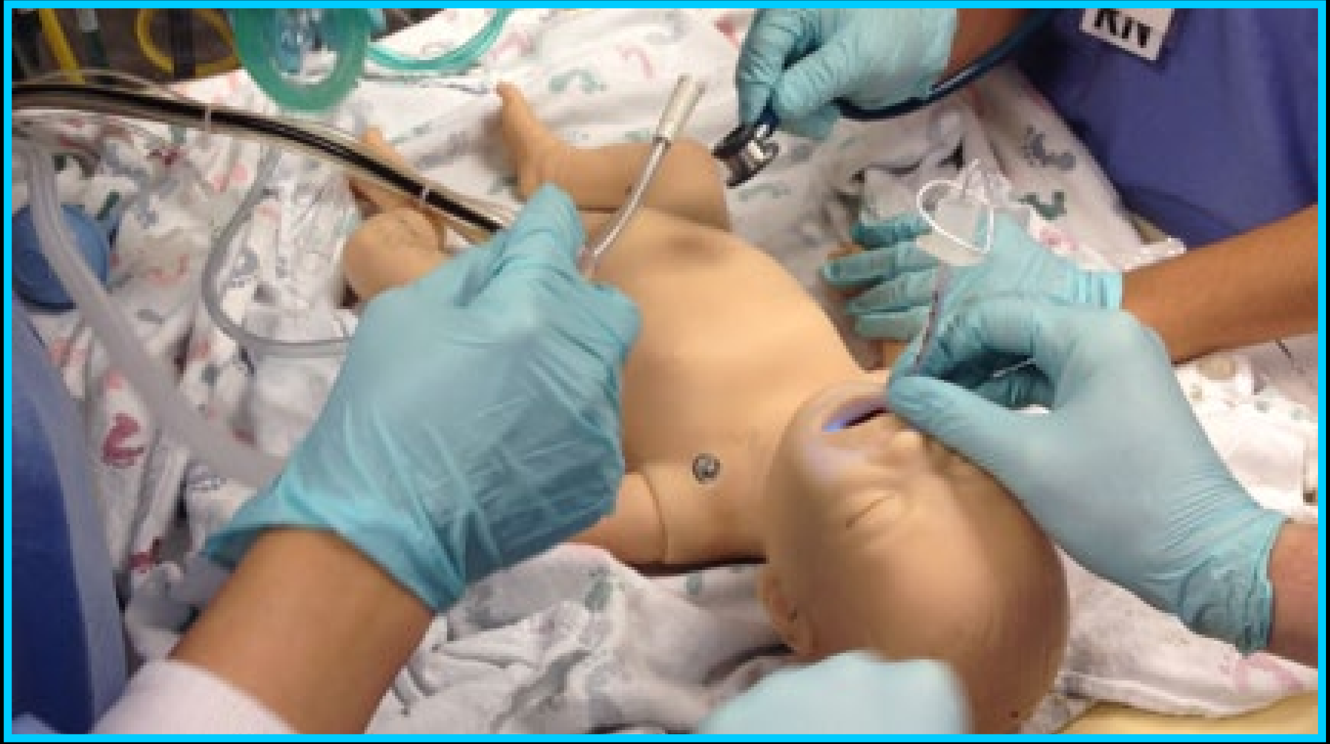
Focus Intently on Achieving **Effective** Ventilation

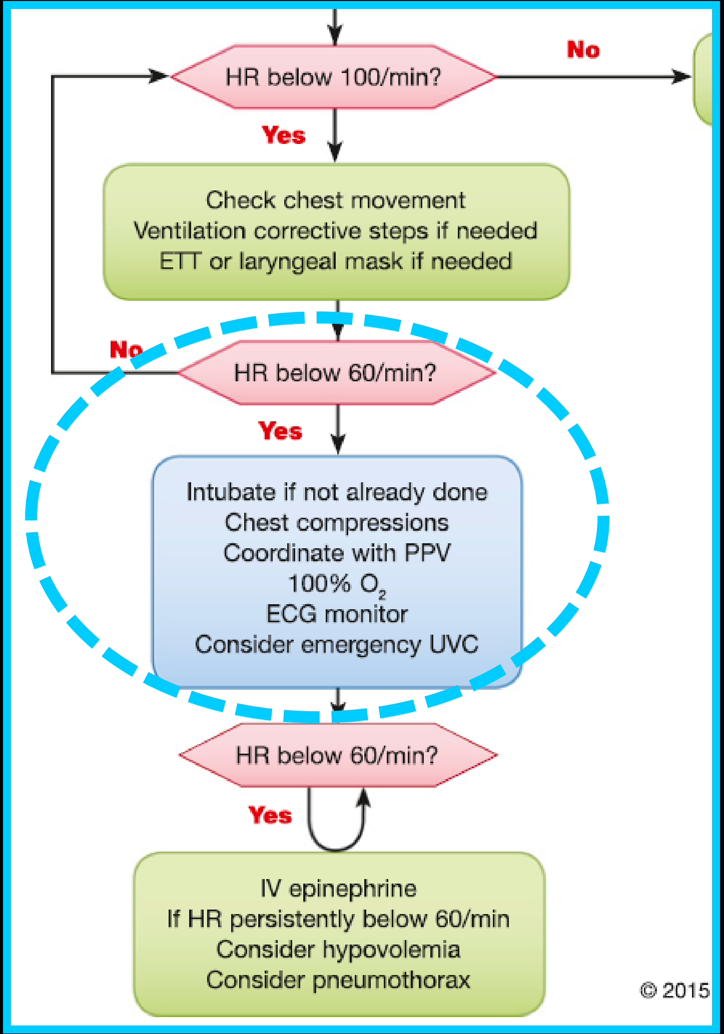
MR.SOPA

- Mask
- Reposition
- Suction
- Open the Mouth
- Increase Pressure
- Advanced Airway



Intubation STRONGLY Recommended Prior to Compressions





Confirm Advanced Airway Placement

- RT puts the colorimetric $ETCO_2$ detector on to confirm tube placement and reports…
- No Color change!
  - Stays purple

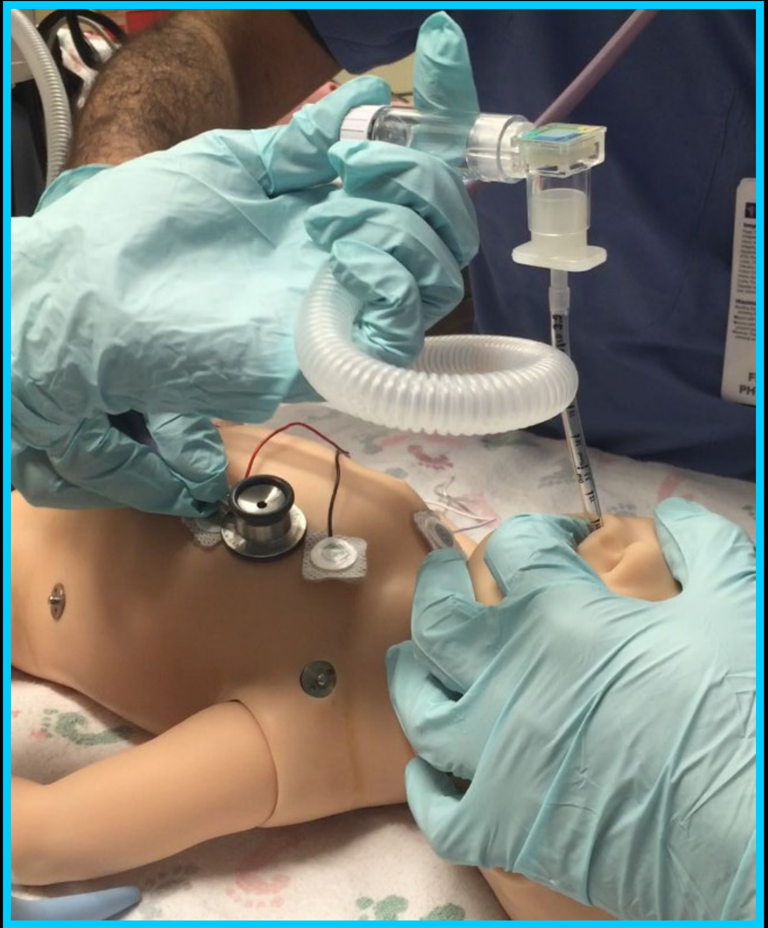
With no color change on the colorimetric $ETCO_2$ detector

- You should
  A. Immediately pull the tube and try again
  B. Determine other confirmatory markers
  C. Move ahead without a second thought
  D. Try some more stimulation

With no color change on the colorimetric $ETCO_2$ detector

- You should
  A. Immediately pull the tube and try again
  B. Determine other confirmatory markers
     - Chest rise with bilateral breath sounds
     - Mist in tube
     - Appropriate tip to lip measurement
     - Did the provider confidently say they saw it pass between the cords
     - Visually confirm with laryngoscope if there is any question
  C. Move ahead without a second thought
  D. Try some more stimulation

ETCO$_2$ Detection During Asystole



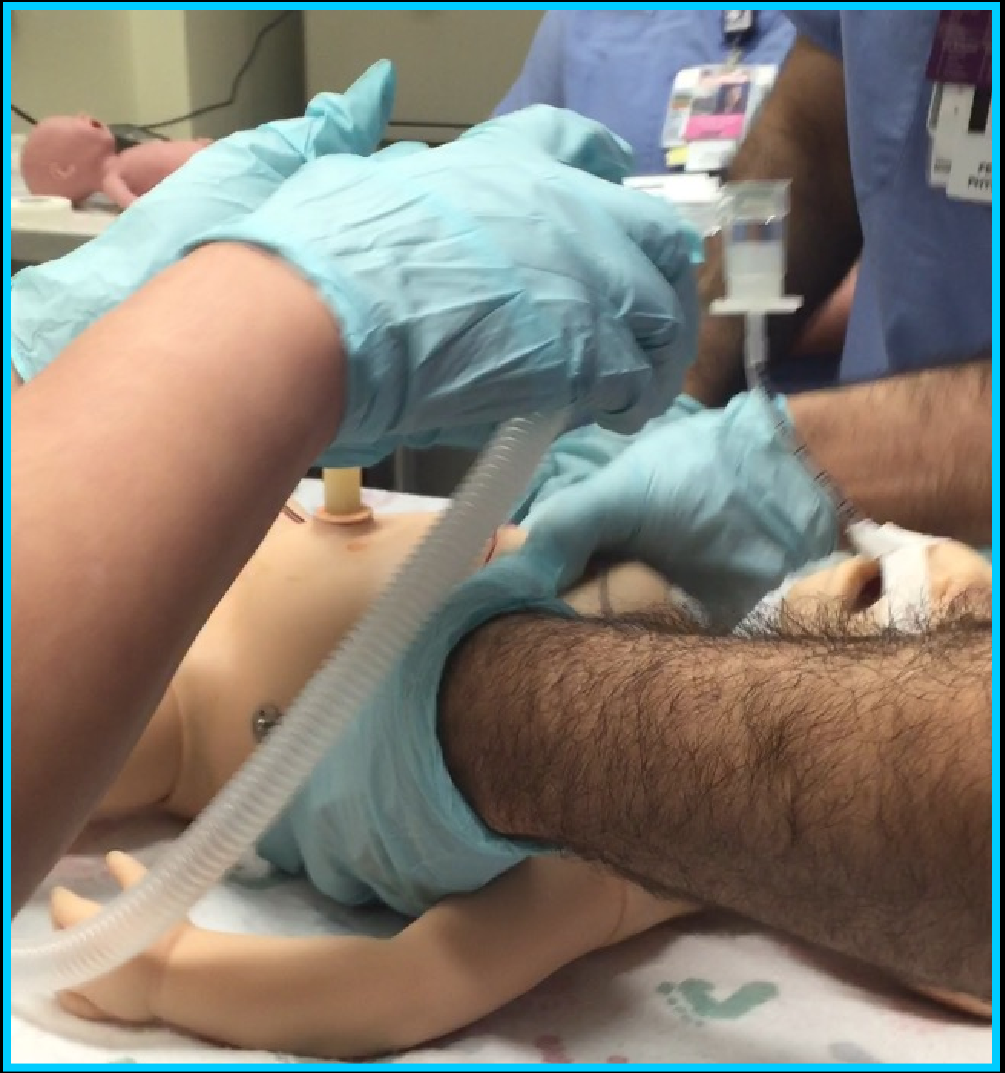
No CO$_2$ detected even when intubated

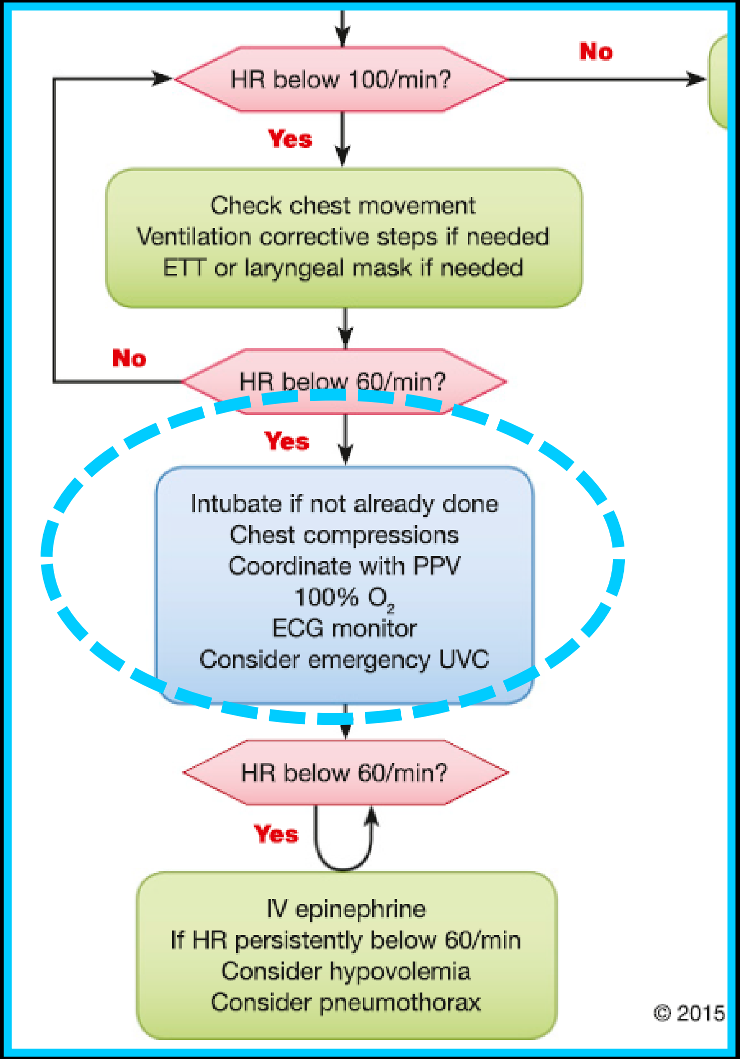
PPV removes CO$_2$ present in lungs prior to asystole

CO$_2$ production decreases as cellular metabolism slows

With cessation of blood flow remaining CO$_2$ cannot reach the lungs

Turn O2 to 100% and Initiate Cardiac Compressions

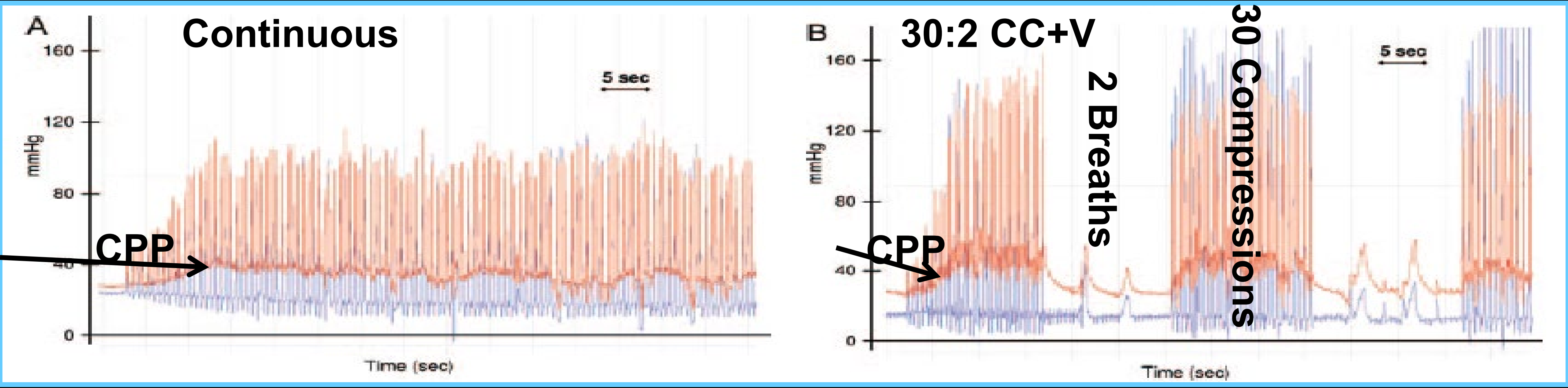




In Adult V-fib Cardiac Arrest…

- Immediately after the cardiac arrest:
  - Aortic oxygen and carbon dioxide concentrations are close to pre-arrest state
  - When compressions are initiated, this is the blood that will be flowing to the coronaries
  - The problem is the lack of flow and not so much the content of the blood
- Ventilation from chest compressions and gasping seems to provide adequate ventilation and oxygenation for resuscitation in the short term

Coronary Perfusion Pressure is Enhanced by Continuous Cardiac Compressions Compared to Pausing for Breaths in 30:2 CC+V ratio in an Adult V-fib Arrest



Coronary Perfusion Pressure=Aortic DBP – Right Atrial DBP

Ewy GA et al. Circulation 2007

Asphyxia-induced Cardiac Arrest is Different…..

- At arrest, there is significant hypoxemia, hypercarbia, and acidemia
- This promotes maximal systemic vasodilation and very low diastolic blood pressure
- Piglet studies of CPR for asphyxial arrests show that in addition to compressions rescue breathing is critical to achieve return of spontaneous circulation

Goal of Compressions

- Generate sufficient O_2 delivery to the coronary and cerebral circulation while waiting for a definitive restoration of a cardiac rhythm by pharmacologic intervention (such as Epi)

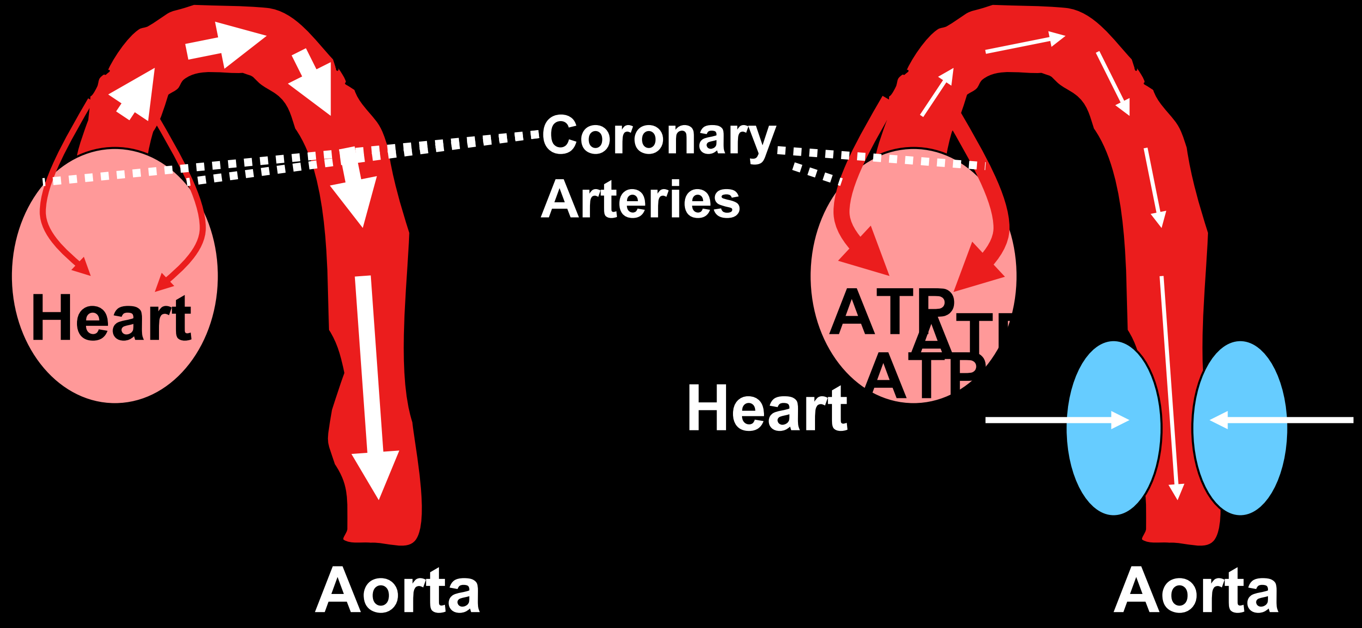
- Coronary perfusion is a determinant of return of spontaneous circulation (ROSC) and cerebral perfusion is a determinant of neurologic outcome

Coronary Perfusion Pressure

Coronary Perfusion Pressure=Aortic DBP – Right Atrial DBP

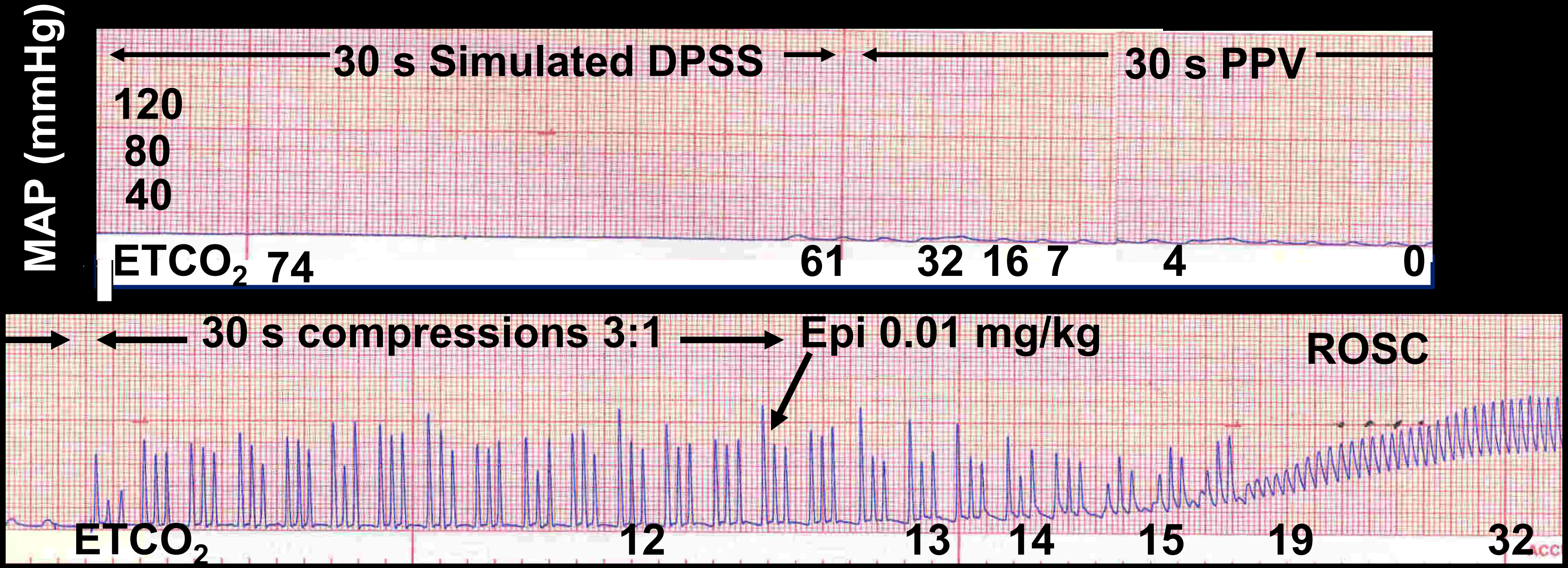
Compressions with Minimal Diastolic BP

Compressions with ↑ Diastolic BP



α-adrenergic effects of epinephrine or uninterrupted compressions lead to ↑ Aortic DBP

Adequate Diastolic Blood Pressure is Critical to the Success of CPR



Coronary Perfusion Pressure=Aortic DBP – Right Atrial DBP

NRP Cardiac Compression Guidelines Remain Unchanged

- Compress to depth of 1/3 AP diameter of chest
- Compress the lower 1/3 of the sternum
- What technique?
  - Use 2-thumb technique
- 3:1 compressions to ventilation ratio for asphyxial arrest
- Coordinate compressions and ventilations to avoid simultaneous delivery
- Avoid frequent interruptions in compressions

Administer Compressions at a Depth of 1/3 the AP Diameter of the Chest

- Meyer et al. *Resuscitation* 2010
  - Neonates (n=54, age<28 d)
  - Mathematical modeling based upon neonatal chest CT scan dimensions
  - 1/3 AP chest depth should be more effective than ¼ compression depth, and safer than 1/2 AP compression depth

Administer Neonatal Compressions Over Lower 1/3 of Sternum

- Orlowski et al. *Ann Emerg Med* 1986
  - Heart lies under lower 1/3 of sternum in > 67% of children (n=187, age < 17yrs) as noted on CXR
  - Significantly better MAP achieved with compressions administered over lower 1/3 compared to mid sternum (n=10, age 1 mo – 3 yrs).
- Philips et al. *Lancet* 1986
  - Heart under lower 1/3 of sternum in 87% of infants (n=55, age 27 wks EGA - 13 mo post-term)

Use Two-Thumb Method Rather than Two-Finger Method for Neonatal Cardiac Compressions

- 2 small human neonate case reports (7 infants)
  —Two-Thumb Method achieved superior diastolic blood pressures
- 3 randomized animal trials
  —Two-Thumb Method achieved superior MAP, Coronary Perfusion
- 3 manikin studies-Using newborn manikin and NRP Guidelines
  — Two-Thumb superior depth of compression with less fatigue
  —Less malposition of finger placement with Two-Thumb method

Head of Bed Compressions Allows Continuous Two-thumb Technique

- Once an airway is established and secured, move the provider giving compressions to head of bed

- Potential Advantages:
  - Arms are in a more natural position (less fatigue)
  - Umbilical access is more readily available while continuing Two-thumb technique
  - More space for person giving meds or volume at the patient's side

Extended Series of Compressions to Ventilations: 3:1 vs 15:2

	3:1 (n=9)	**15:2 (n=9)**	**P value**
Cardiac Compression/min	58 ± 7	75 ± 5	<0.001
Increase in DBP during compression cycles (mmHg)	4.8 ± 2.6	7.1 ± 2.8	0.004
Number of animals with no ROSC	2	2	NS
Time to ROSC (sec)*	150 (140-180)	195 (145-358)	NS

DBP=Diastolic Blood Pressure, ROSC=return of spontaneous circulation

* Median (25^{th}-75^{th} %tile)

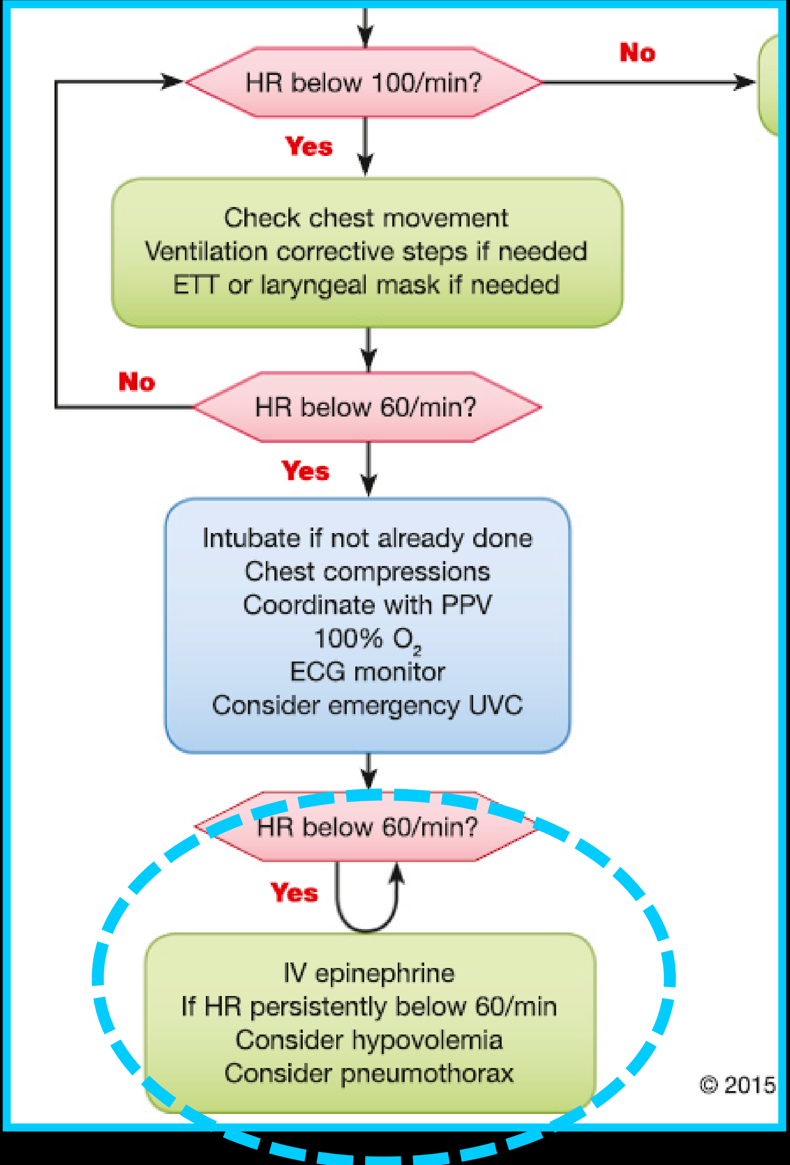
Adapted from Solevåg et al. ADC 2011;96(6):F417-421

Reminders….

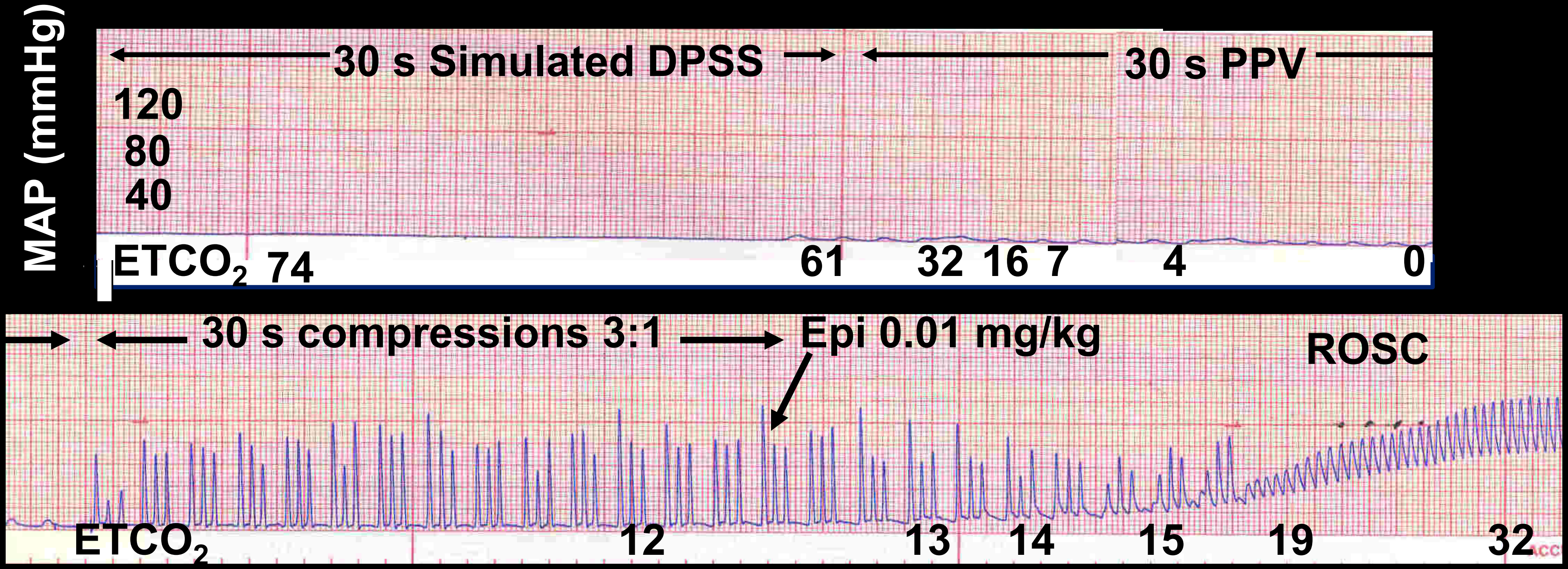
- Be aware of the many pauses in circulation that can inadvertently occur and help your team stay focused on optimizing perfusion
- If ECG not on yet, continue compressions for at least 60s before interrupting to auscultate for heart rate
- Pulse oximetry will likely not pick up during this time or the heart rate may reflect the compression rate
- ECG will guide you as to when to pause for auscultation
  - If HR < 60 bpm on monitor continue CPR
  - If HR > 60 bpm on monitor, confirm by auscultation
  - Pulseless electrical activity usually occurs at a slow rate where you would do compressions anyway. $ETCO_2$ can help as well

Medications For Neonatal Delivery Room CPR

- Epinephrine
  - IV preferred (IO ok)
  - ETT while achieving intravascular access
- Normal saline or O- blood



Epinephrine Helps Achieve Adequate Diastolic Blood Pressure via its Alpha Adrenergic effects During CPR



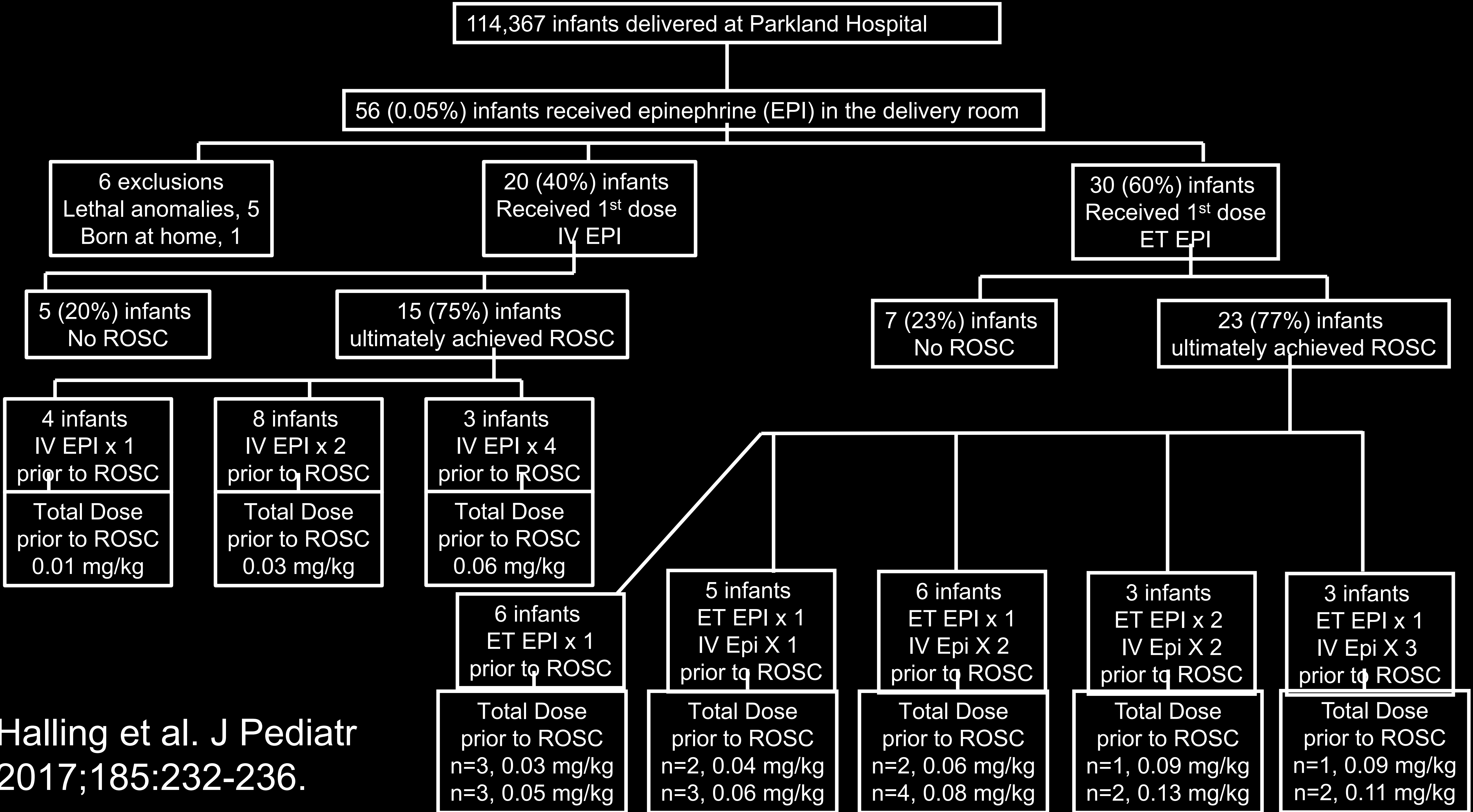
Coronary Perfusion Pressure=Aortic DBP – Right Atrial DBP

Delivery Room Epinephrine Use at Parkland Hospital (January 2006 - July 2014)

- 114367 neonates delivered
  - 56 (0.05%) received epinephrine in delivery room
    - 6 exclusions: lethal anomalies 5, Born at home 1
    - 20 (40%) IV epinephrine only
      - 15 (75%) responded*
    - 30 (60%) ETT epinephrine
      - 6 (20%) responded*
      - 24 (80%) failures- subsequently given IV epi
        - 17 (71%) responded to IV epi

*p=0.0004 (response rate to ETT versus IV epinephrine)

Halling et al. J Pediatr 2017;185:232-236



Halling et al. J Pediatr 2017;185:232-236.

Summary of Findings

- Both IV and ET routes at currently recommended dosing, frequently require multiple doses to achieve ROSC
- Total dose needed for ROSC is less for IV versus ET followed by IV dosing although we found no evidence of increased harm from the exposure to the higher dose
- Response rates to ET epinephrine are low even with the higher initial epinephrine dose of 0.5 ml/kg

Timing and Incidence of ROSC with ETT vs IV Epinephrine

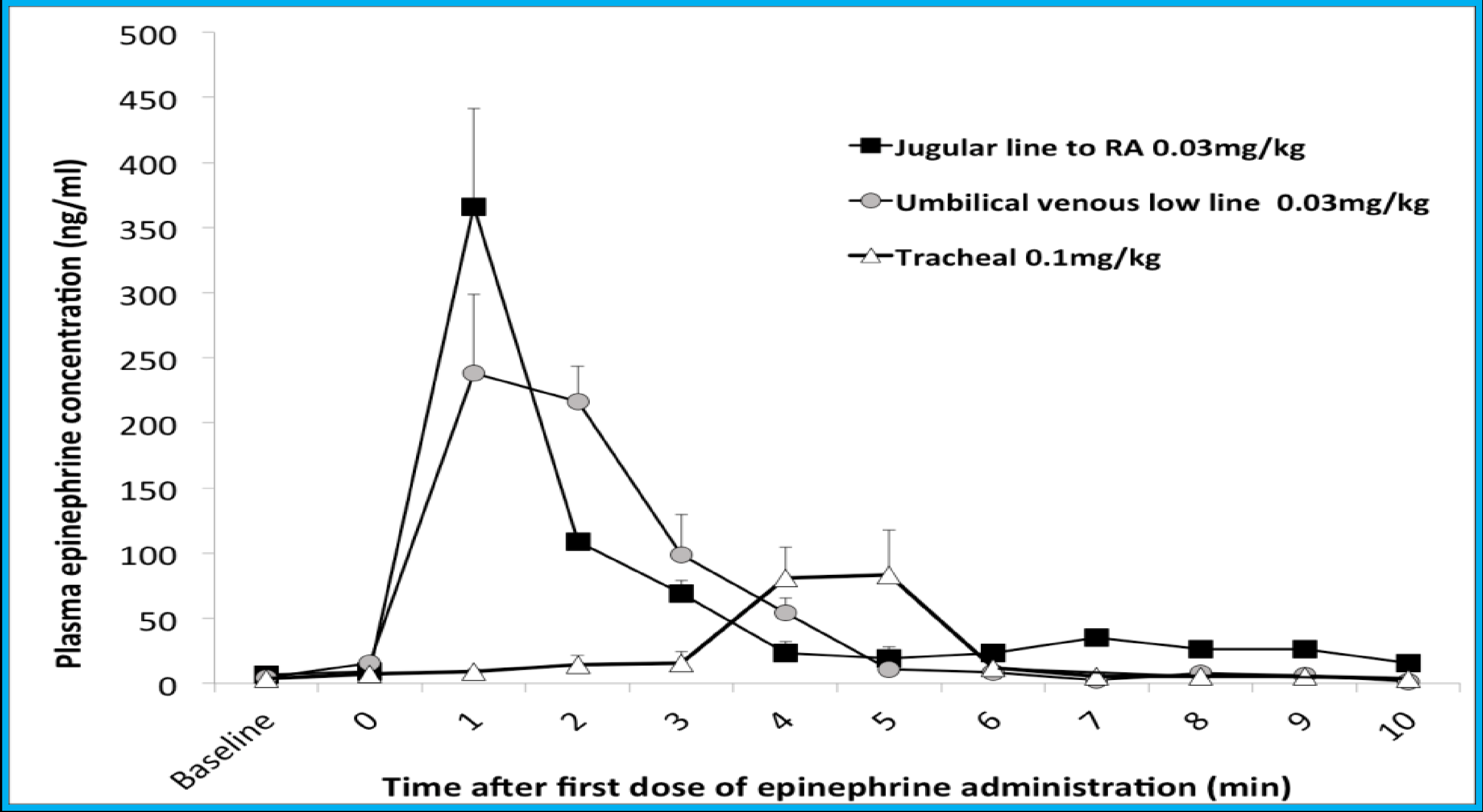
	Right Atrial N=11	Low UV N=11	Standard ETT N=11	Early ETT N=11
Weight (kg)	3.6±0.6	3.6±0.8	3.7±0.9	3.9±0.9
Sex (M:F)	7:4	5:6	6:5	5:6
Time to Asystole, min (median, IQR)	18 (16-21)	14 (12-20)	15 (14-16)	14 (12-14)
Time to ROSC, min (median, IQR)	2 (1.6-2.9)	2.5 (2.0-3.0)	4.0 (2.9-4.8)*	7.0 (3.0-8.0)**
ROSC, n (%)	10 (91%)	9 (82%)	4 (36%)	4 (36%)
At Arrest				
pH	6.85 ± 0.07	6.80 ± 0.09	6.85 ± 0.06	6.85 ± 0.04
$PaCO_2$ (mmHg)	130 ± 27	146 ± 25	139 ± 17	132 ± 17
PaO_2 (mmHg)	5.5 ± 3.5	6.0 ± 4.5	6.0 ± 4.5	5.8 ± 3.5
Lactate (mmol/L)	12.1 ± 5.4	14.6 ± 6.7	13.9 ± 4.9	14.8 ± 5.1

*-indicates $p<0.05$ compared to group 1

**-indicates $p<0.05$ compared to group 1 and group 2

Vali et al. J Am Heart Assoc. 2017;6(2):

Systemic Absorption of ETT Epinephrine Through Liquid-filled Lungs is Low and Delayed



Vali et al. J Am Heart Assoc. 2017;6(2)

Conclusions

- Right atrial and low UV epinephrine administration achieve significantly higher and quicker peak plasma epinephrine concentrations with a high ROSC success rate (81 – 91%)
- Systemic absorption of ETT epinephrine through liquid-filled lungs is low and delayed and has low ROSC success rate (36%).
- The high frequency of initial use of ETT epinephrine clinically (while attempting to establish UVC access) makes it critical that the recommended ETT dose be as effective as possible.
- Future studies evaluating a single higher dose of epinephrine (0.2 mg/kg) are warranted.

Speculation

- It is possible that there is no optimal dose of ET Epinephrine
- Newborns in transition have unique anatomical and pathophysiological differences that are the likely cause of limited absorption of epinephrine from the alveoli
  - Insufficient pulmonary blood flow during CPR
  - Pulmonary vasoconstriction from acidosis
  - Amount of epinephrine reaching the alveoli from ET delivery is unknown
  - Alveolar fluid may dilute the epinephrine
  - Potential right-to-left intracardiac shunts (PDA and PFO) that could bypass pulmonary circulation

Acknowledgments

- Thanks to the AAP for use of the algorithm used for illustration and several pictures
- Thanks to Stuart Hooper for videos and pictures

(ILCOR CoSTR)

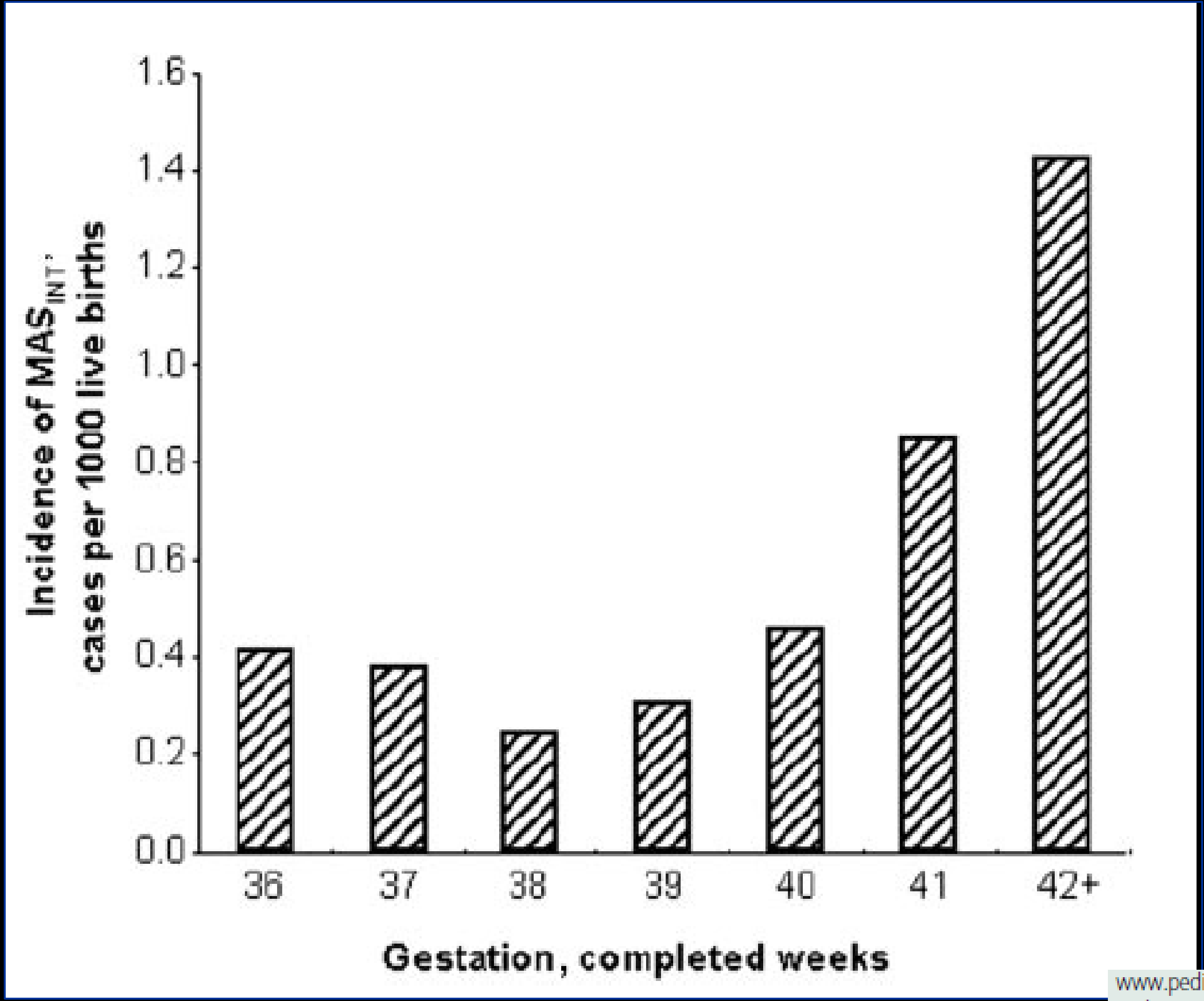
http://circ.ahajournals.org/content/132/16_suppl_1/S204.full.pdf+html

(USA Guidelines)

http://pediatrics.aappublications.org/content/136/Supplement_2/S196

Meconium and the Current Guidelines

MAS—Epidemiology

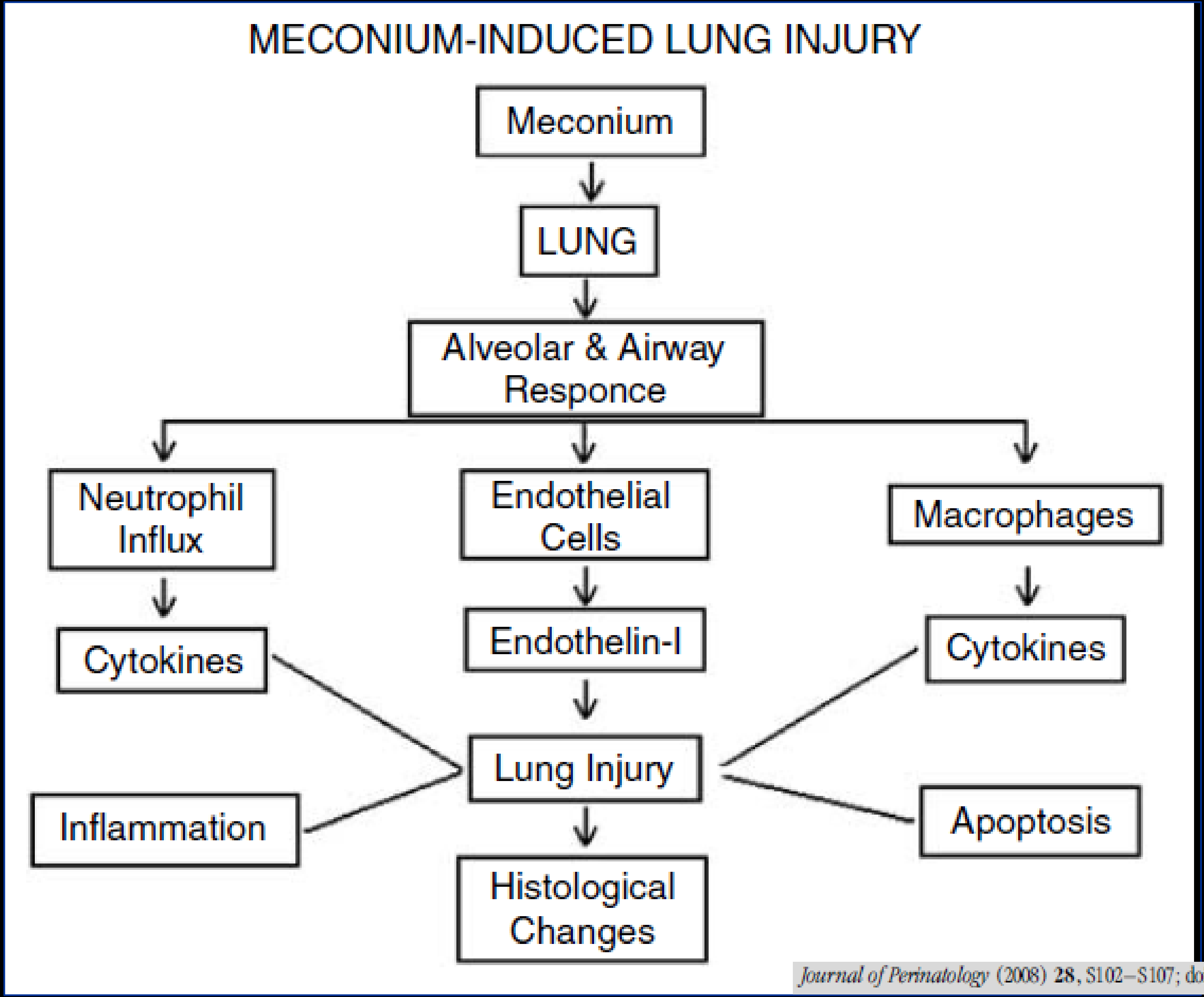


www.pediatrics.org/cgi/doi/10.1542/peds.2005-2215

MAS pathophysiology

- Often associated with intrapartum events, asphyxia, acidosis

Inflammatory process



Journal of Perinatology (2008) 28, S102–S107; doi:10.1038/jp.2008.153

Meconium-stained infants 💩

- If an infant born through meconium stained amniotic fluid presents with poor muscle tone and inadequate breathing efforts, the initial steps of resuscitation should be completed under the radiant warmer. PPV should be initiated if the infant is not breathing or the heart rate is less than 100/min after the initial steps are completed. Routine intubation for tracheal suction in this setting is not suggested, because there is insufficient evidence to continue recommending this practice. However, a team that includes someone skilled in intubation of the newborn should still be present in the delivery room.

American Heart Association. Web-based Integrated Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care – Part 13: Neonatal Resuscitation. ECCguidelines.heart.org.

Randomized Data Available

- Chettri, 2015
  - 122 babies
  - India
  - No difference in MAS (31 v 33%)
  - No difference in mortality (13 v 11%)
- Nangia, 2016
  - 175 babies
  - India
  - No difference in MAS (26 v 32%)
  - No difference in mortality (5 v 10%)
- Singh, 2018
  - 152 babies
  - India
  - Borderline difference in MAS (57 v 41%)
  - No difference in mortality (9 v 5%)

Values & Preferences

- Experts placed greater value on *harm avoidance* (ie, delays in providing bag-mask ventilation, potential harm of the procedure) over the *unknown benefit of the intervention* of routine tracheal intubation and suctioning. Appropriate intervention to support ventilation and oxygenation should be initiated as indicated for each individual infant. This may include intubation and suction if the airway is obstructed.

American Heart Association. Web-based Integrated Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care – Part 13: Neonatal Resuscitation. ECCguidelines.heart.org.