State of the Art Science to Support Neonataal Cardiac Compressions ad Medications

Myra H. Wyckoff, MD
Professor of Pediatrics
UT Southwestern Medical Center at Dallas

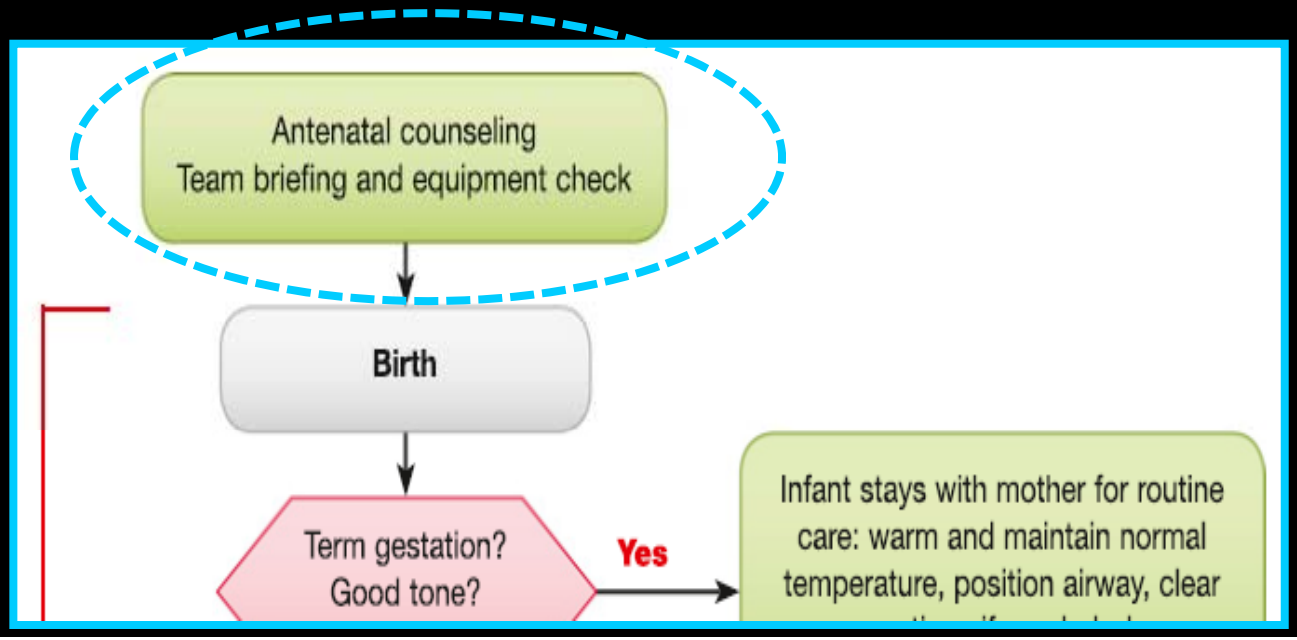
You are on call at your delivery hospital….

- Labor and Delivery is quiet
- The babies in the neonatal intensive care unit are behaving
- You venture out to the cafeteria for a snack…

- The on call phone rings….

Upon Entering OR 9 with Your Team….

- You ask 4 questions in order to brief the team and set up appropriate equipment
  - Gestation?
  - How many babies?
  - Status of fluid?
  - Risk Factors?



Obstetric team informs you….

- 19 yo G1P0 mom
  - no prenatal care
  - abdominal pain
  - vaginal bleeding
  - membranes intact
  - no history of trauma

- Bedside sono suggests 38 wks, singleton
- Agonal fetal bradycardia
- Stat C/S under general anesthesia

How to Prepare?

AAP-NRP photo

- Gather a team
  - Preferably that has trained together using simulation
  - Clearly assign roles
    - Team Leader (usually MD)
    - 2 Medical Provider (MD and/or NNP)
    - Respiratory Therapist
    - Experienced Neonatal Nurse as assessor
    - Nurse to draw up meds
    - Recorder (typically RN)
      - Use a standardized form with data recorded real-time
      - Or video

How to Prepare?

- Gather and Prepare Equipment
  - All the stuff you always prepare for routine delivery
  - Decide on an estimated weight
  - Potentially prepare umbilical catheter
  - Potentially draw up intravenous epinephrine doses and label

Proactive Preparations Can Reduce the Time to Administration of Intravenous Epinephrine

	Passive Guidelines (N=47)	Proactive Guidelines (N=35)	*p* value
1. First dose of Epinephrine given IV	3 (6%)	14 (40%)	<0.001
2. Time to 1st dose of Epinephrine (min)	5 ± 3	5 ± 2	NS
3. Time to 1st IV Epinephrine dose (min)	9 ± 4	5 ± 3	<0.001
M1			

HIE: Hypoxic-Ischemic encephalopathy

Diapositiva 7

M1 May need to add how you defined HIE to the methods. Are these the ones that got cooled. I can't believe only half of them got cooled. How was this defined??

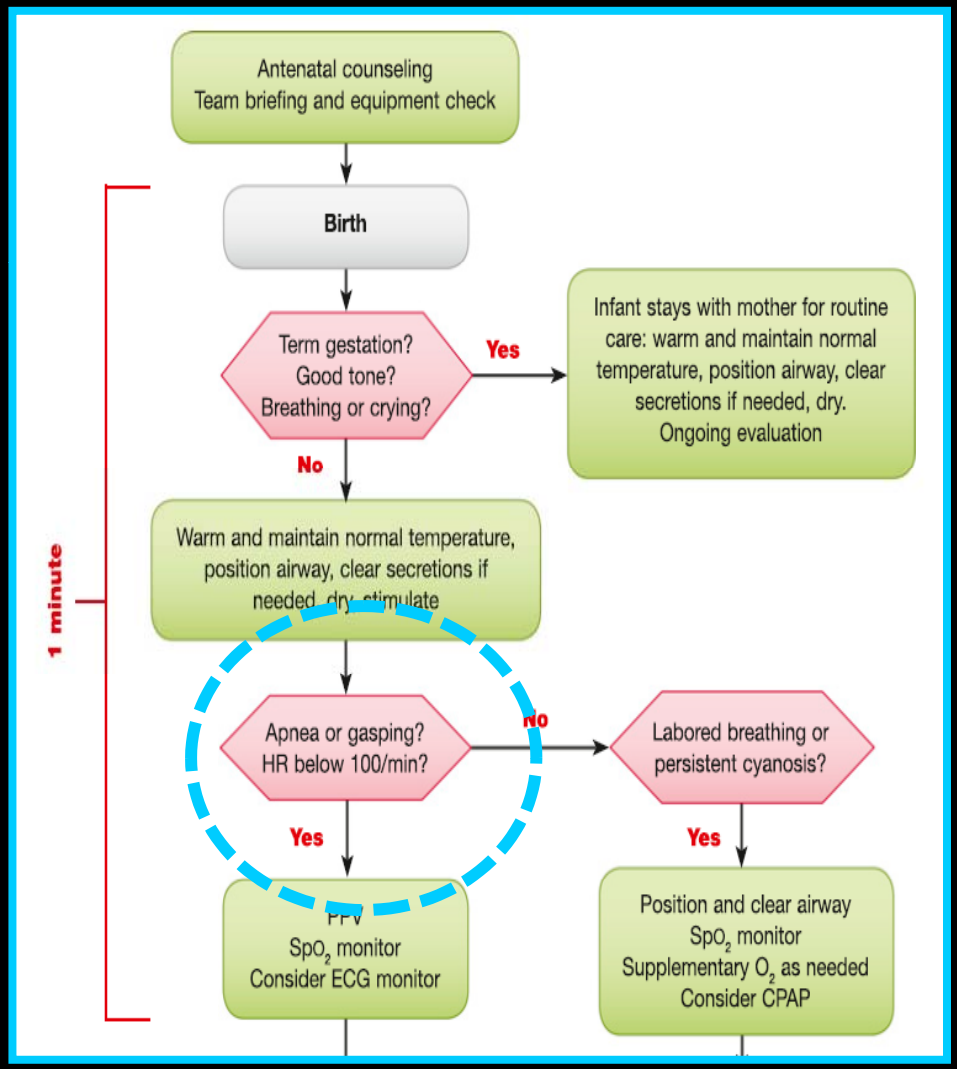
I looked at the charts and looked for the clinical diagnosis of HIE by the attending during the patient's course or on the discharge summary

So could be mild/mod/or severe? I wonder if it would be more meaningful to know how many were cooled for moderate/severe?
Myra Wyckoff; 07/04/2011

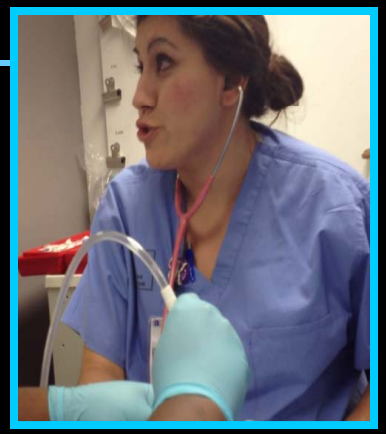
At Uterine Incision…

- Bloody amniotic fluid noted with apparent abruption
- Baby is delivered, cord immediately clamped and passed to the neonatal team
- Limp, gray and apneic
- At the warmer she is dried, positioned, the airway is cleared, stimulation provided

2015 Neonatal Resuscitation Guidelines: Assessment Questions Remain the Same



Nurse reports “No breath sounds, I can’t hear a heart rate”



- You should
  - A. Start cardiac compressions
  - B. Place baby skin to skin with mom to start bonding process
  - C. Initiate positive pressure ventilation
  - D. Try a little more vigorous stimulation

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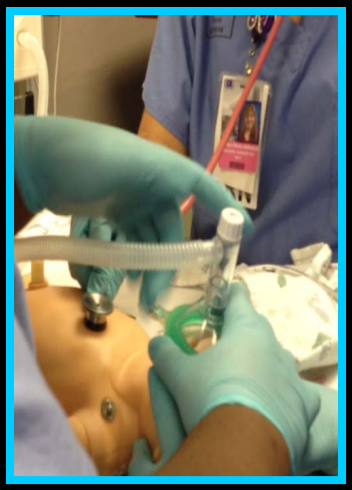


Indications For Cardiac Compressions During Neonatal CPR Have Not Changed in 2016

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

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

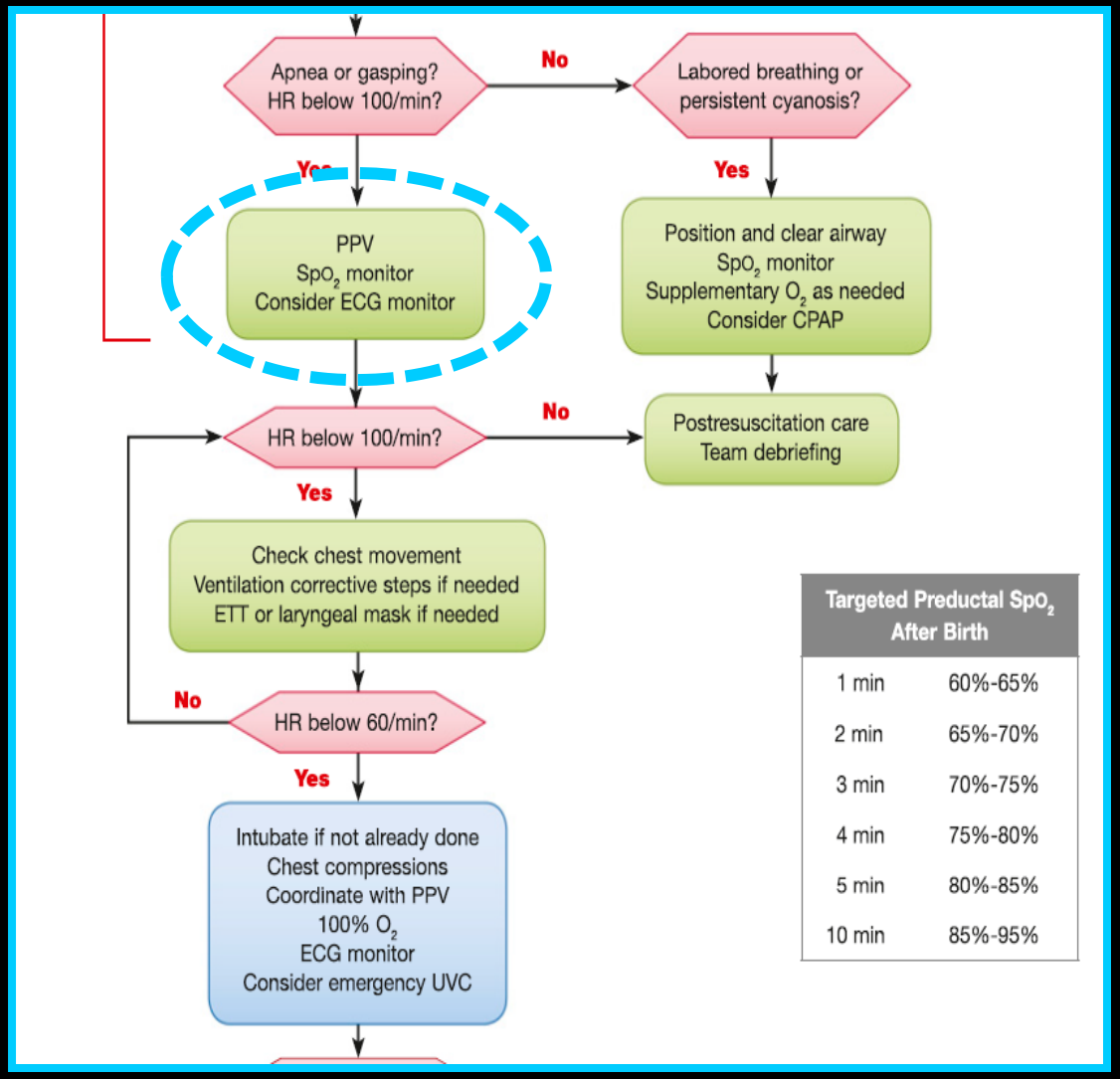
Note: Because chest compressions are likely to compete with effective ventilation, rescuers are encouraged to ensure that assisted ventilation is delivered optimally BEFORE initiation of chest compressions

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

Even When Bradycardic/Asystolic, First Focus on EFFECTIVE VPP

VPP

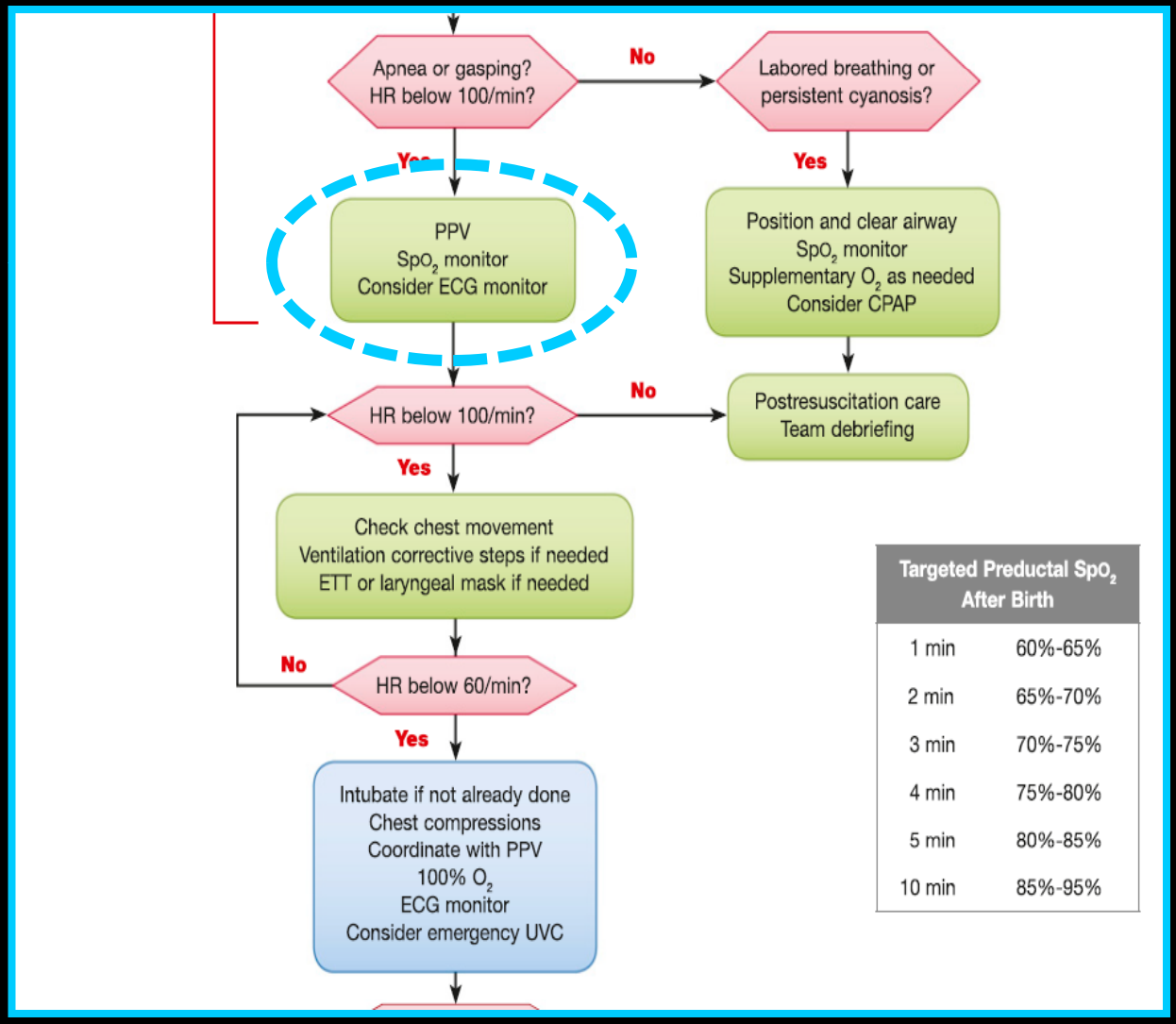
For 999 out of 1000 infants, this will be all that is needed



Targeted Preductal SpO_2 After Birth	
1 min	60%-65%
2 min	65%-70%
3 min	70%-75%
4 min	75%-80%
5 min	80%-85%
10 min	85%-95%

Even When Bradycardic/Asystolic, First Focus on EFFECTIVE VPP

- After a few breaths, infant still has no chest rise and no audible heart rate



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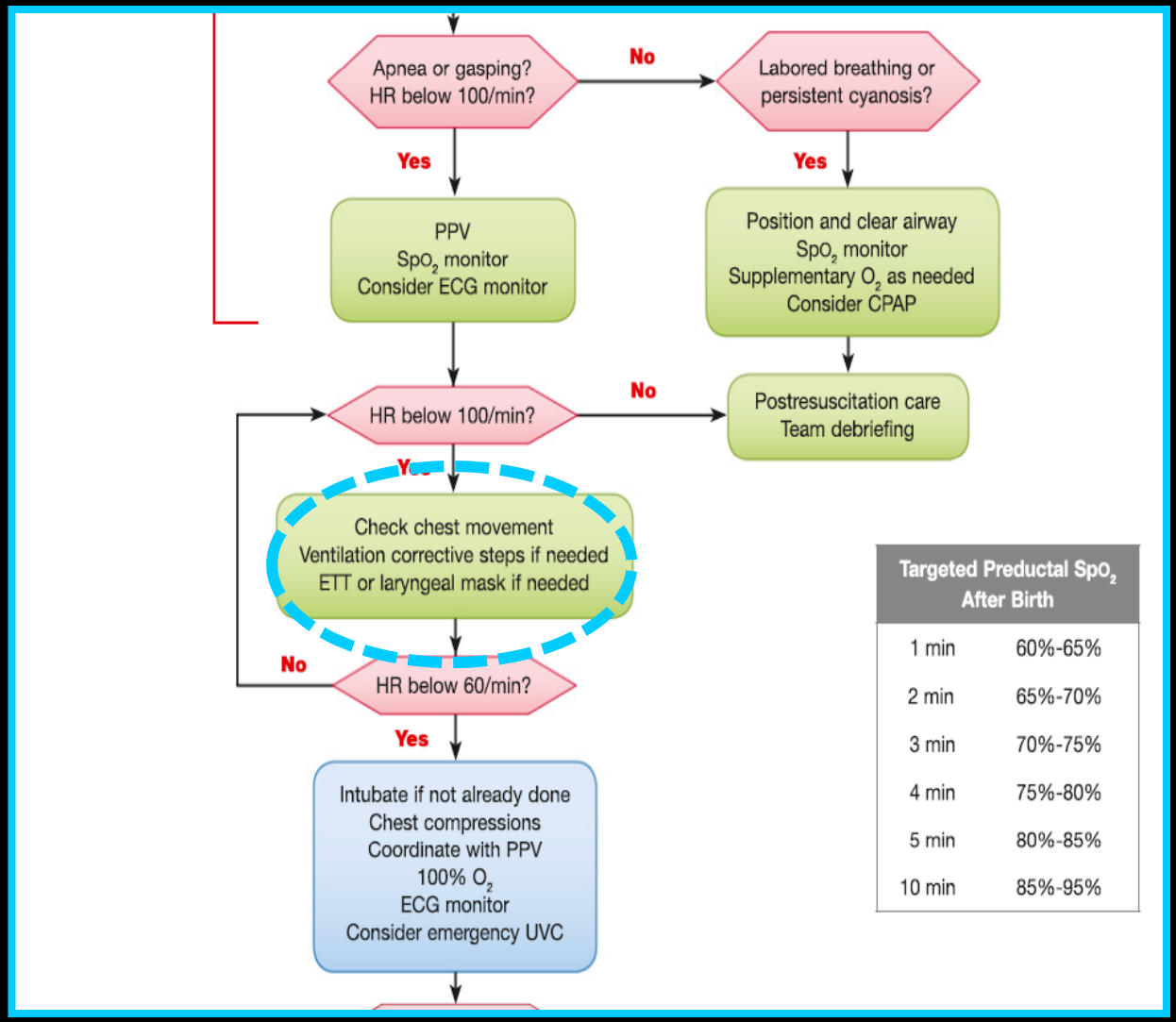
Take Ventilation Corrective Steps to achieve EFFECTIVE Ventilation



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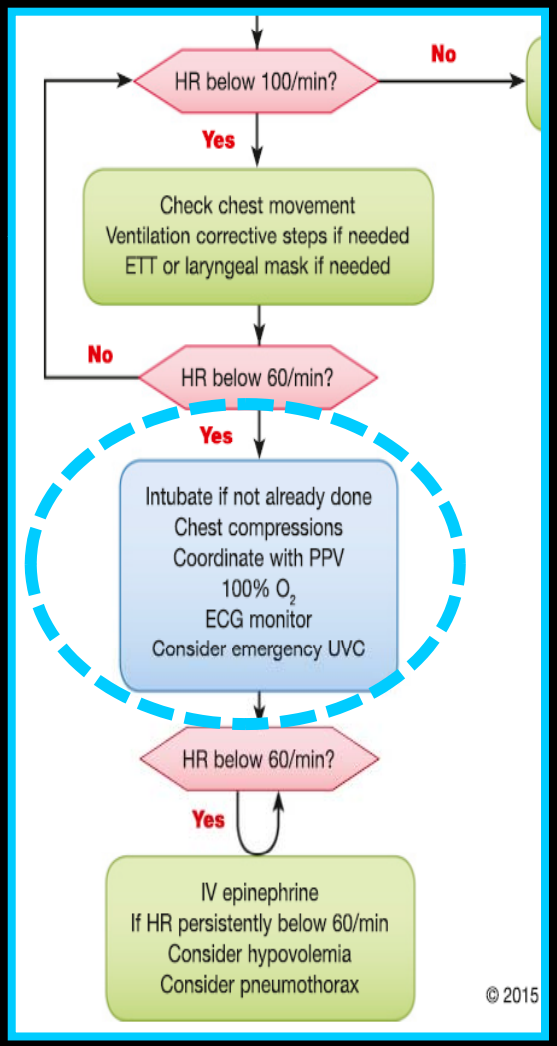
Team Stays Focused on Effective Ventilation

	Actions
M	Adjust **Mask** to assure good seal on the face
R	**Reposition** airway by adjusting head to "sniffing position
S	**Suction** mouth and nose of secretions, if present
O	**Open** mouth slightly and move jaw forward
P	Increase **Pressure** to achieve chest rise
A	Consider **Airway** alternative (endotracheal intubation or laryngeal mask airway)

- Pulse oximeter attached
- 25/5 cm H_2O noted on T-piece resuscitator (therefore no mask leak)
- Sniffing position
- Mouth is open
- Poor chest rise noted
- PIP increased to 30
- Heart Rate faint 30 bpm but not rising
- Attach ECG leads

Intubation STRONGLY Recommended Prior to Compressions

- Tube adjusted to proper depth
- Equal breaths sounds heard
- Chest rise noted
- Heart Rate still 30 bpm



Confirm Advanced Airway Placement

- RT puts the colorimetric CO2 detector on and reports…
- No Color change!

With no color change on the colorimetric CO_2 detector

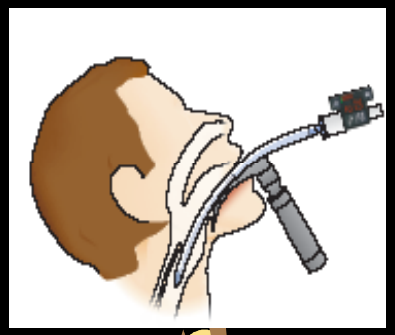
- You should
  - A. Immediately pull the tube and try again
  - B. Determine other confirmatory markers
  - C. Move ahead without a second thought
  - D. Try some more stimulation

With no color change on the colorimetric CO_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
  - C. Move ahead without a second thought
  - D. Try some more stimulation

CO_2 Detection During Asystole/Profound Bradycardia Can Give a False Negative

No CO_2 detected even when intubated



Positive Pressure Ventilation removes CO_2 present in lungs prior to asystole

With cessation of blood flow, the remaining CO_2 cannot reach the lungs

CO_2 production decreases as cellular metabolism slows

Next Steps

- Team provides positive pressure ventilation through the endotracheal tube and determines the heart rate response in 10-20 seconds
- Chest is moving
- Endotracheal tube is secured
- Nurse reports heart rate=30 bpm and is not rising
- Pulse oximeter does not show any signal
- Oxygen increased to 100%

In asystolic/bradycardic neonates receiving cardiac compressions
Does use of 100% O2 as the ventilation gas
Compared to lower concentrations of oxygen
Decrease time to ROSC, decrease oxidative injury, increase survival rates, improve neurologic outcomes

Worksheet identifier: Oxygen delivery during CPR (Neonatal)

Author: Lindsay Mildenhall and Myra Wyckoff

Risk of Bias in Randomized Studies (12 studies)

Dallas 2015

Study	Year	Design	Total Patients	Population	Industry Funding	RCT bias assessment: Allocation: Generation	Allocation: Concealment	Blinding: Participants	Blinding: Assessors	Outcome: Complete	Outcome: Selective	Other Bias
Dannevig	2012	RCT	32	neonatal pigs (12-36 hrs)	No	Unclear	Low	High	High	Low	Low	Low
Dannevig	2013	RCT	32	neonatal pigs (12-36 hrs)	No	Unclear	Low	High	High	Low	Low	Low
Lakshminrusimha	2011	RCT	12	lambs in transition	No	Unclear	Unclear	High	High	Low	Low	Low
Linner	2009	RCT	38	neonatal pigs (12-36 hrs)	No	Unclear	Unclear	High	High	Low	Low	Low
Lipinski	1999	RCT	22	post-transitioned rats	No	Unclear	Unclear	High	High	Low	Low	Low
Markus	2007	RCT	24	preterm lambs in transition	No	Unclear	Unclear	High	High	Low	Low	Low
Mendoza-Paredes	2008	RCT	21	neonatal pigs (2-4 d)	No	Unclear	Unclear	High	High	Low	Low	Low
Perez-de-sa	2009	RCT	18	lambs in transition	No	Unclear	Unclear	High	High	Low	Low	Low
Solevåg	2010	RCT	32	neonatal pigs (12-36 hrs)	No	Unclear	Low	High	High	Low	Low	Low
Temesvari	2001	RCT	26	neonatal pigs (3-6 hr)	No	Unclear	Unclear	High	Low	Low	Low	Low
Walson	2011	RCT	10	post-transitioned rats	No	Unclear	Unclear	High	High	Low	Low	Low
Yeh	2009	RCT	33	post-transitioned rats	No	Low	Unclear	High	High	Low	Low	Low

Treatment Recommendations

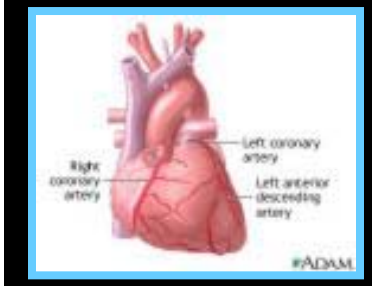
- Given the absence of any human data until further evidence is available, we suggest that the oxygen concentration be increased until the heart rate recovers for neonates receiving cardiac compressions {weak recommendation, very low quality of evidence}.

- Oxygen should be rapidly weaned with the help of pulse oximetry as soon as the heart rate has recovered

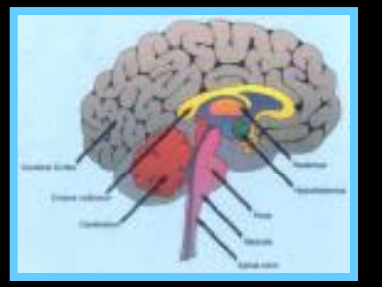
Treatment Recommendations

- Values and Preferences Statement: Although most of the available animal evidence suggests that room air resuscitation during neonatal CPR is feasible and that 100% O_2 as the resuscitation gas during CPR increases oxidative injury
  - Concern that no human data to prove feasibility
  - No studies have evaluated use of room air CPR for more than brief asystole.
  - Value balancing the desire to prevent on-going hypoxic injury in these profoundly asphyxiated neonates with the desire to prevent subsequent hyperoxic injury
  - By the time resuscitation has reached the stage of chest compressions, the steps of achieving effective ventilation with a low concentration of oxygen should have been attempted
  - Thus, it would seem prudent to try increasing the supplemental oxygen concentration.

Team Initiates Compressions



Goal of Compressions

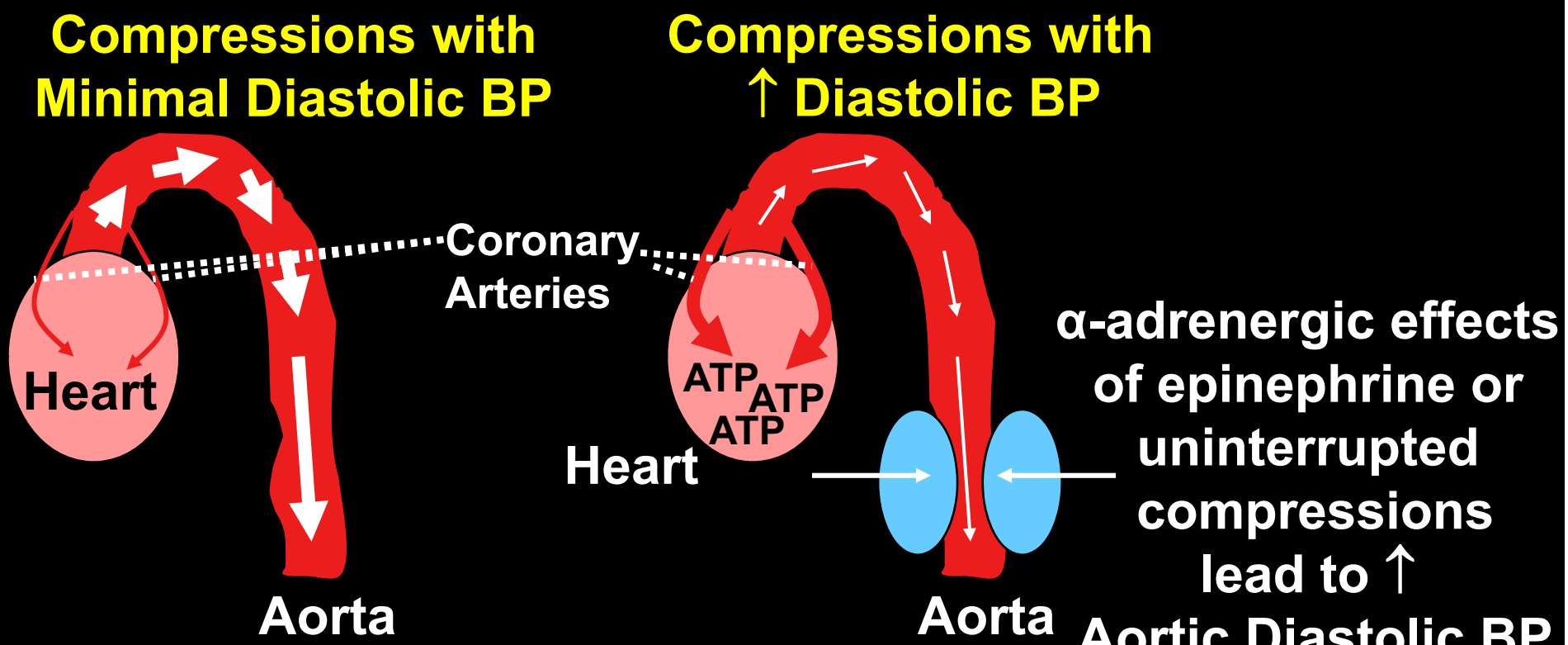


- Generate sufficient O_2 delivery to the coronary and cerebral circulation while waiting for a definitive restoration of a cardiac rhythm by pharmacologic intervention (such as Epi)
- Coronary perfusion is a determinant of return of spontaneous circulation (ROSC) and cerebral perfusion is a determinant of neurologic outcome

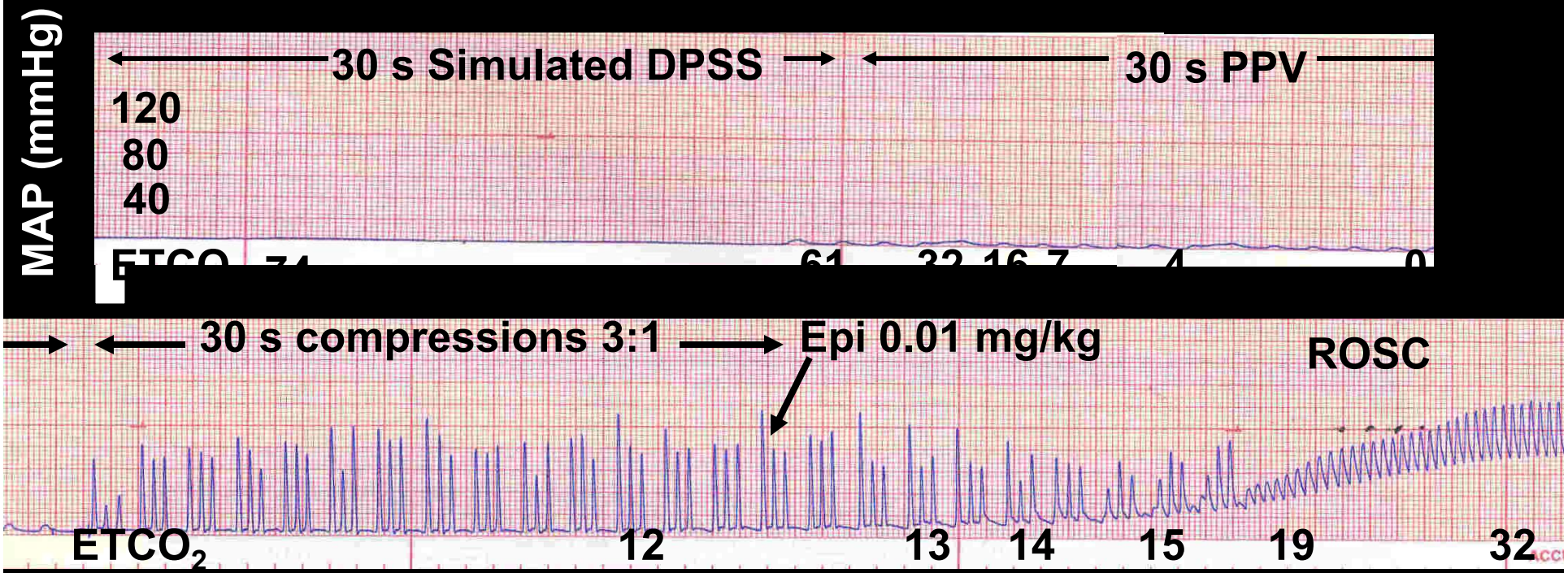
Coronary Perfusion Pressure

Coronary Perfusion Pressure =

Aortic Diastolic BP – Right Atrial Diastolic BP



Adequate Diastolic Blood Pressure is Critical to the Success of CPR



Coronary Perfusion Pressure=Aortic DBP – Right Atrial DBP

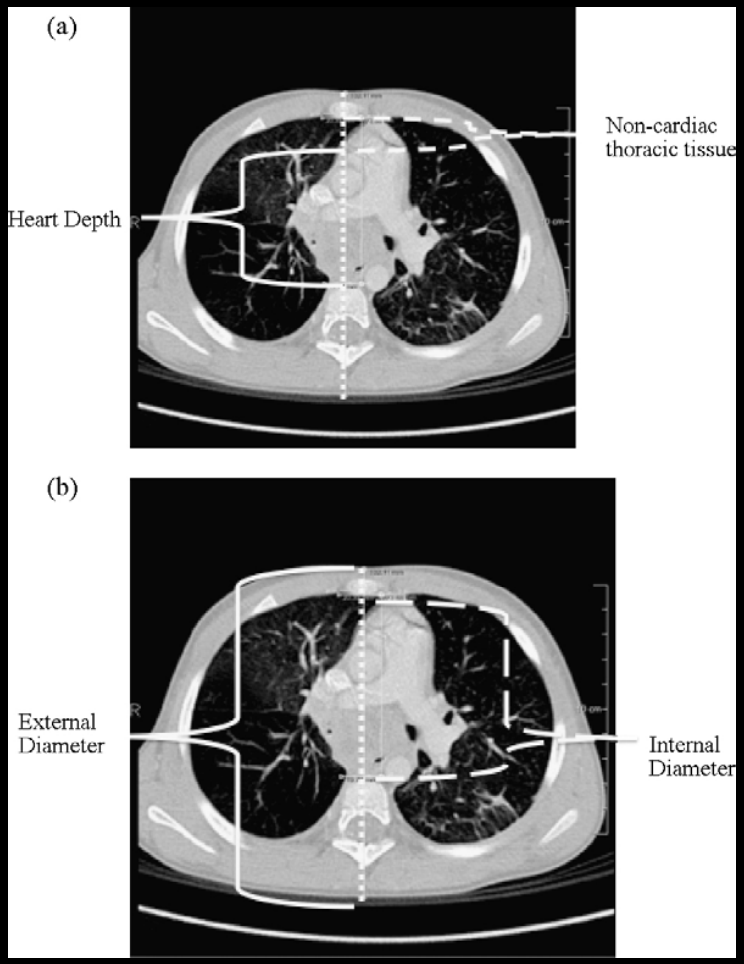
2015: NRP Cardiac Compression Guidelines Remain Unchanged

- Compress to depth of 1/3 AP diameter of chest
- Compress the lower 1/3 of the sternum
- 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



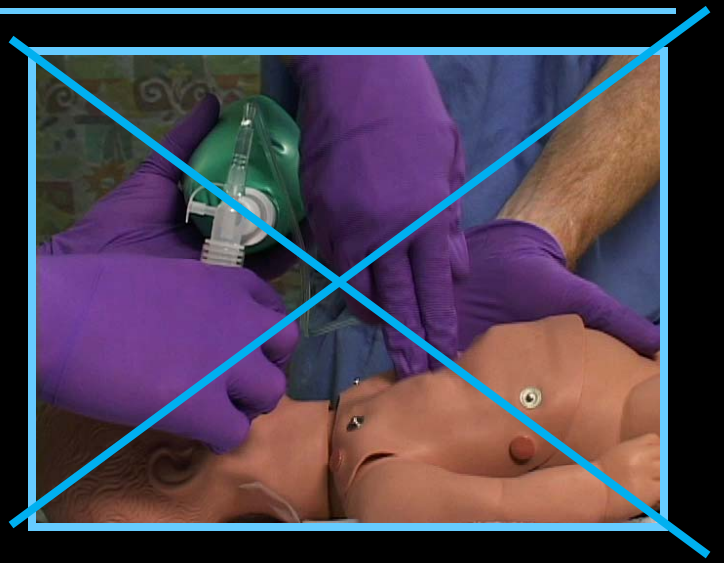
Administer Neonatal Compressions Over Lower 1/3 of Sternum

- 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

?

?



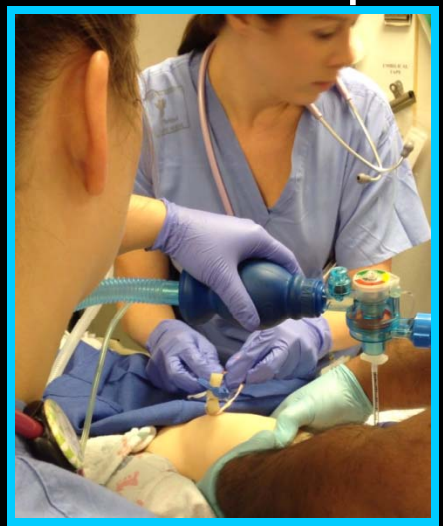
- 2 small human neonate case reports (7 infants)
  - —Two-Thumb Method achieved superior diastolic blood pressures
- 3 randomized animal trials
  - —Two-Thumb Method achieved superior MAP, Coronary Perfusion
- 3 manikin studies-Using newborn manikin and NRP Guidelines
  - — Two-Thumb superior depth of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

Sounds good but…..

- Won't the two-finger technique be needed at least briefly so that the compressors hands are not blocking access to the umbilical cord for emergent umbilical venous line placement?

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 at the patient's side

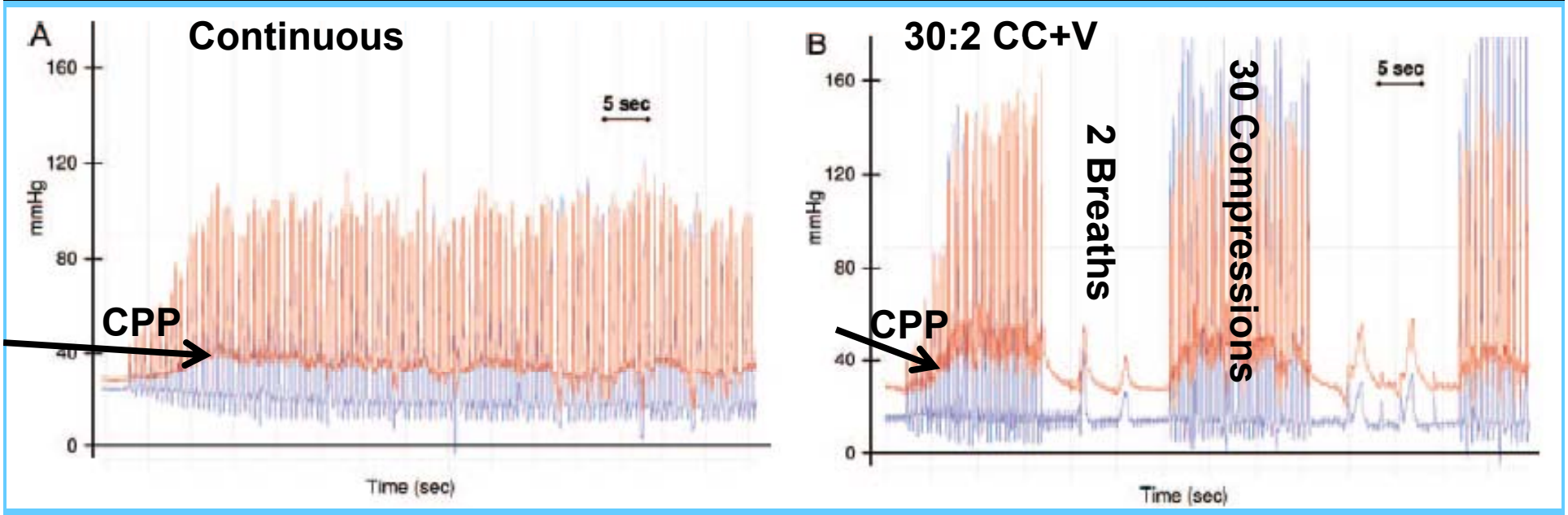


Why should we stick with a 3 compression to 1 ventilation ratio for neonatal CPR?

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

Continuous Compressions vs 15:2 CC+V in Model of Asystole Due to Acute Asphyxia (Clamped ETT)

	CCC (n=10)	CC + V (n=10)
Baseline (before asphyxia)		
Arterial pH	7.42 ± 0.02	7.42 ± 0.01
Arterial pCO_2 (mmHg)	42 ± 1	43 ± 1
After 1 min of CPR		
Arterial pH	7.17 ± 0.04	7.20 ± 0.03
Arterial pCO_2 (mmHg)	77 ± 11	68 ± 5
ROSC obtained in < 2 min, n (%)*	4 (40%)	10 (100%)

*$p \leq 0.01$

Berg RA et al. Circulation 2000

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

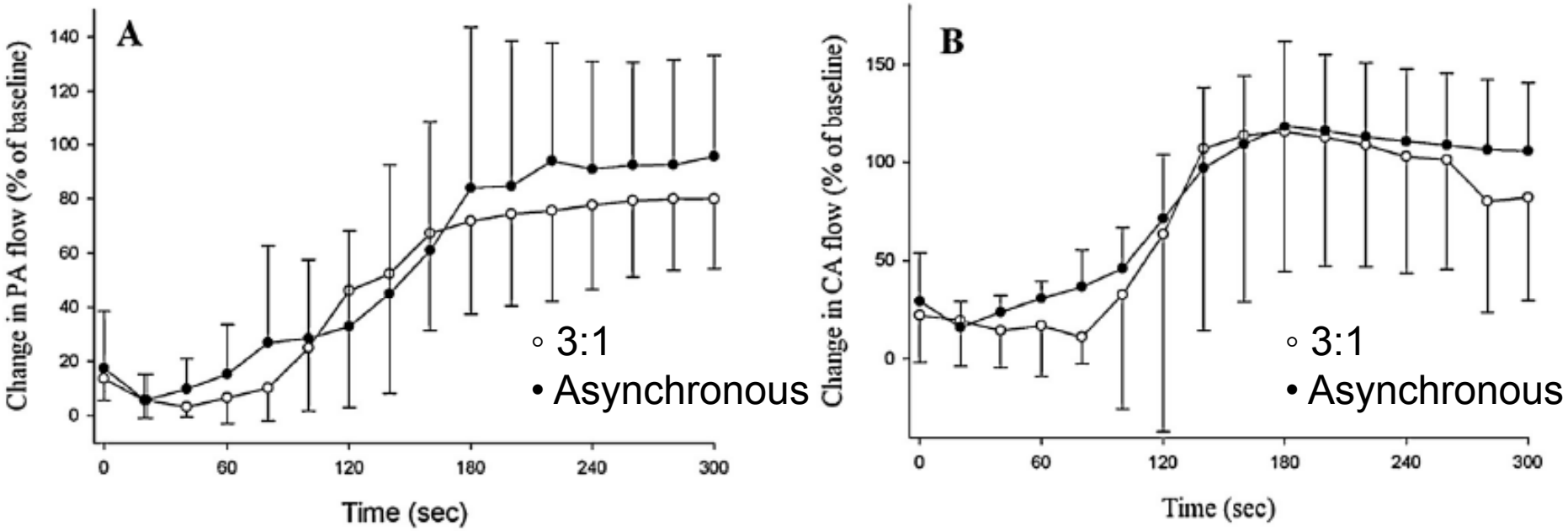
* Median (25^{th}-75^{th} %tile)

Solevåg et al. ADC 2011

Should we continue to coordinate the compressions and ventilations?

Needs ILCOR Evaluation

Asynchronous CPR May be Equivalent to 3:1 CPR in Asphyxiated Neonatal Pigs but no obvious advantage



- ROSC =
- Survival =
- Hemodynamic Recovery =

Schmölzer et al Resuscitation 2014

Reminders….

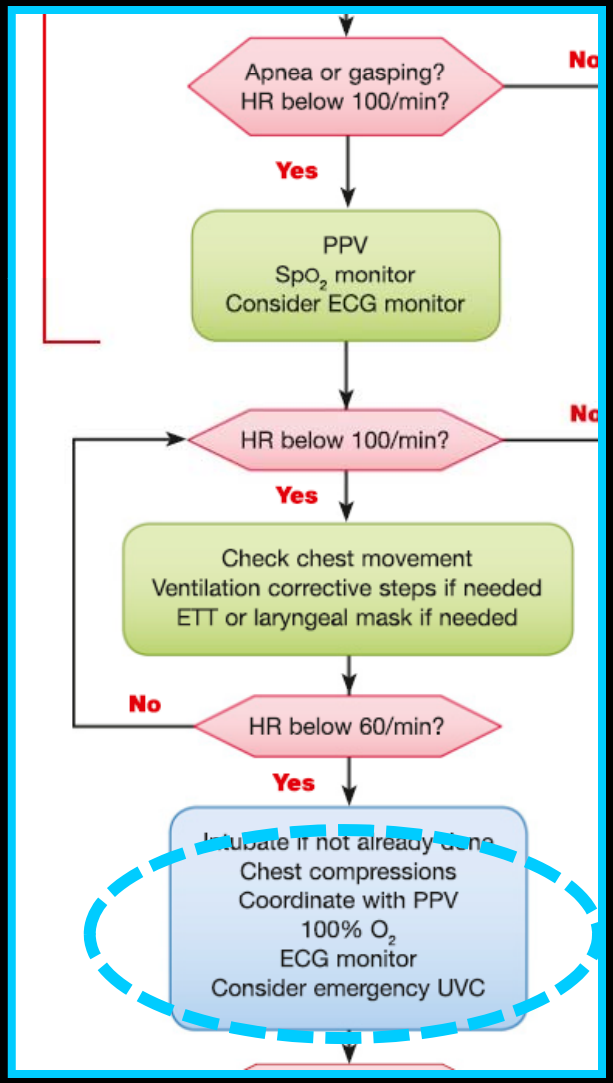
- Be aware of the many pauses in circulation that can inadvertently come up during cardiac compressions and help your team stay focused on optimizing perfusion
- If ECG not on yet, continue compressions for at least 60 seconds before interrupting to listen for heart rate
- Be aware that pulse oximetry will likely not pick up during this time or the heart rate may reflect the compression rate
- ECG tracing will help guide you as to when to pause for auscultation
  - If HR < 60 bpm on monitor continue cardiac compressions
  - If HR > 60 bpm on monitor, confirm by auscultation
- Wouldn't worry too much about pulseless electrical activity- usually occurs at a slow rate where you would do compressions anyway

American Heart Association
Learn and Live

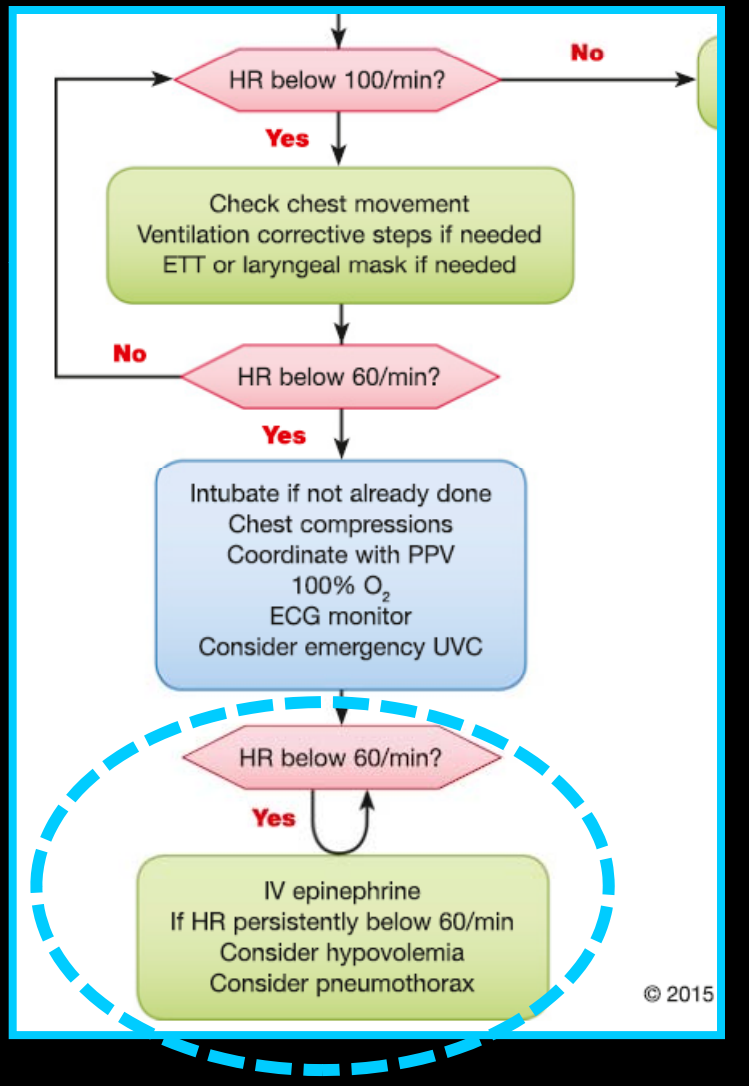
American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

2015 Neonatal Resuscitation Guidelines

- Emergent UVC placed
- Heart rate still 40 bpm



2015: No Major Changes for Medications



- Only 2 meds to remember
  - Epinephrine
    - IV preferred (IO ok) 0.01-0.03mg/kg
    - ETT can be tried while achieving intravascular access (0.05-0.1mg/kg
  - Normal saline or O- blood

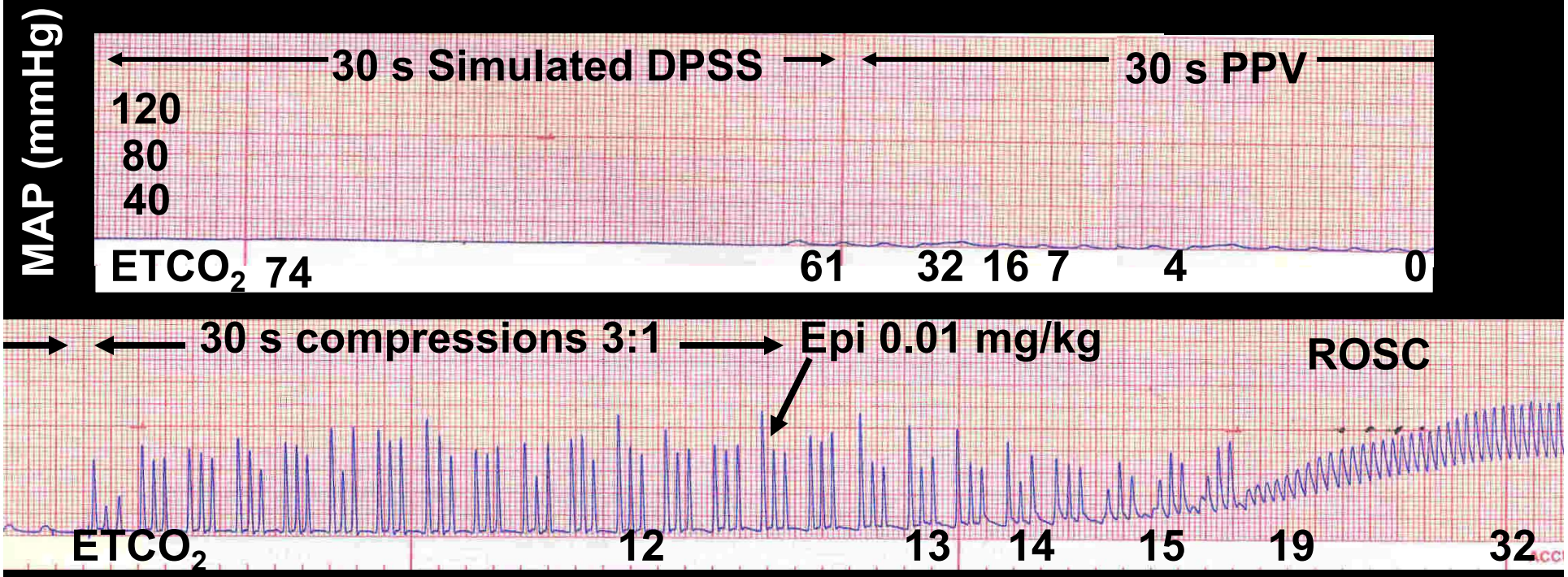
Indication for Epinephrine in the Delivery Room

Epinephrine, a mixed α- and β-adrenergic stimulant, is indicated when the heart rate remains below 60 beats per minute despite…

- **EFFECTIVE** Ventilation (usually with intubation) with 100% Oxygen and
- Coordinated cardiac compressions

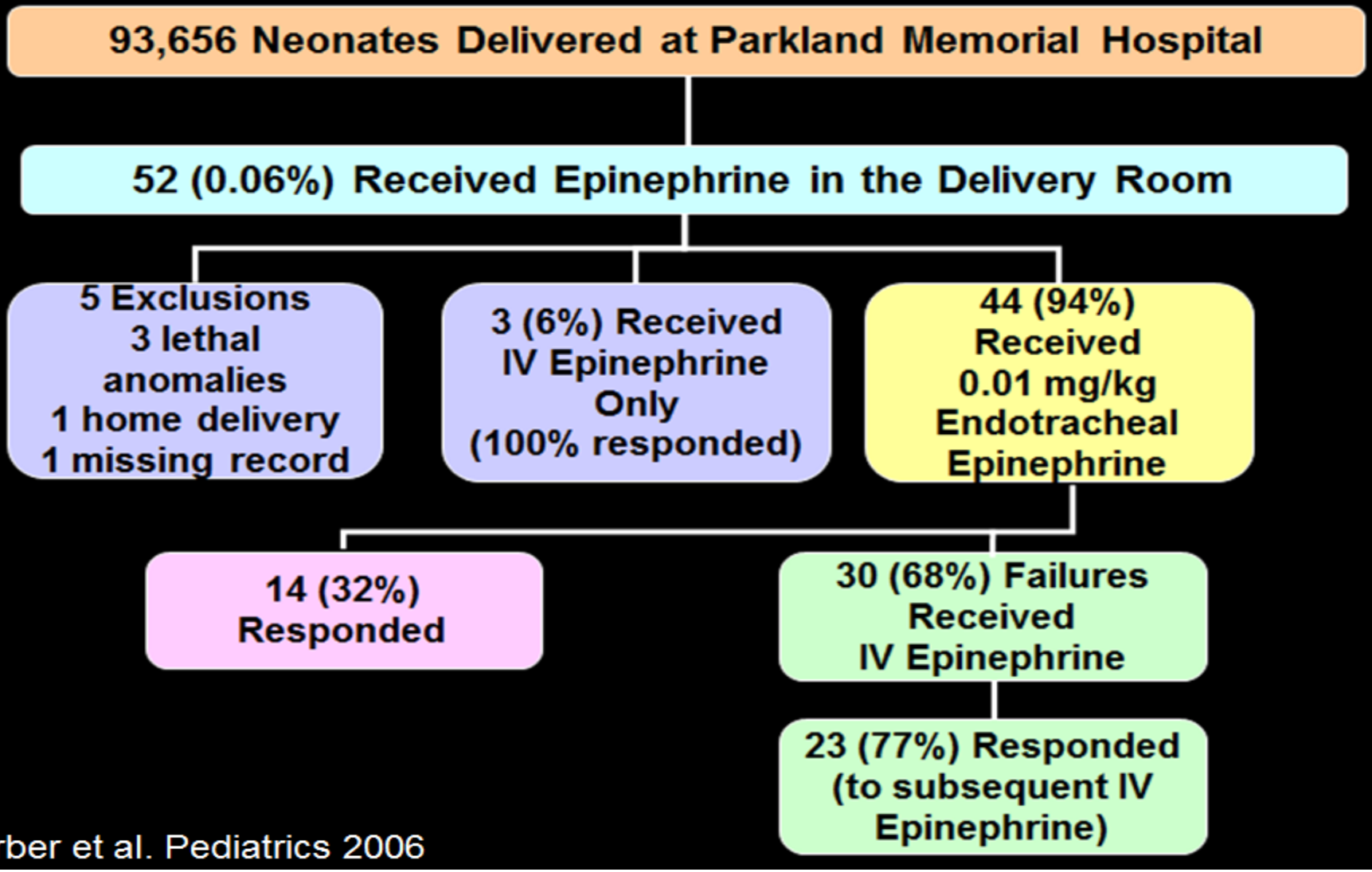
Note: Epinephrine is *not* indicated before adequate ventilation is established

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

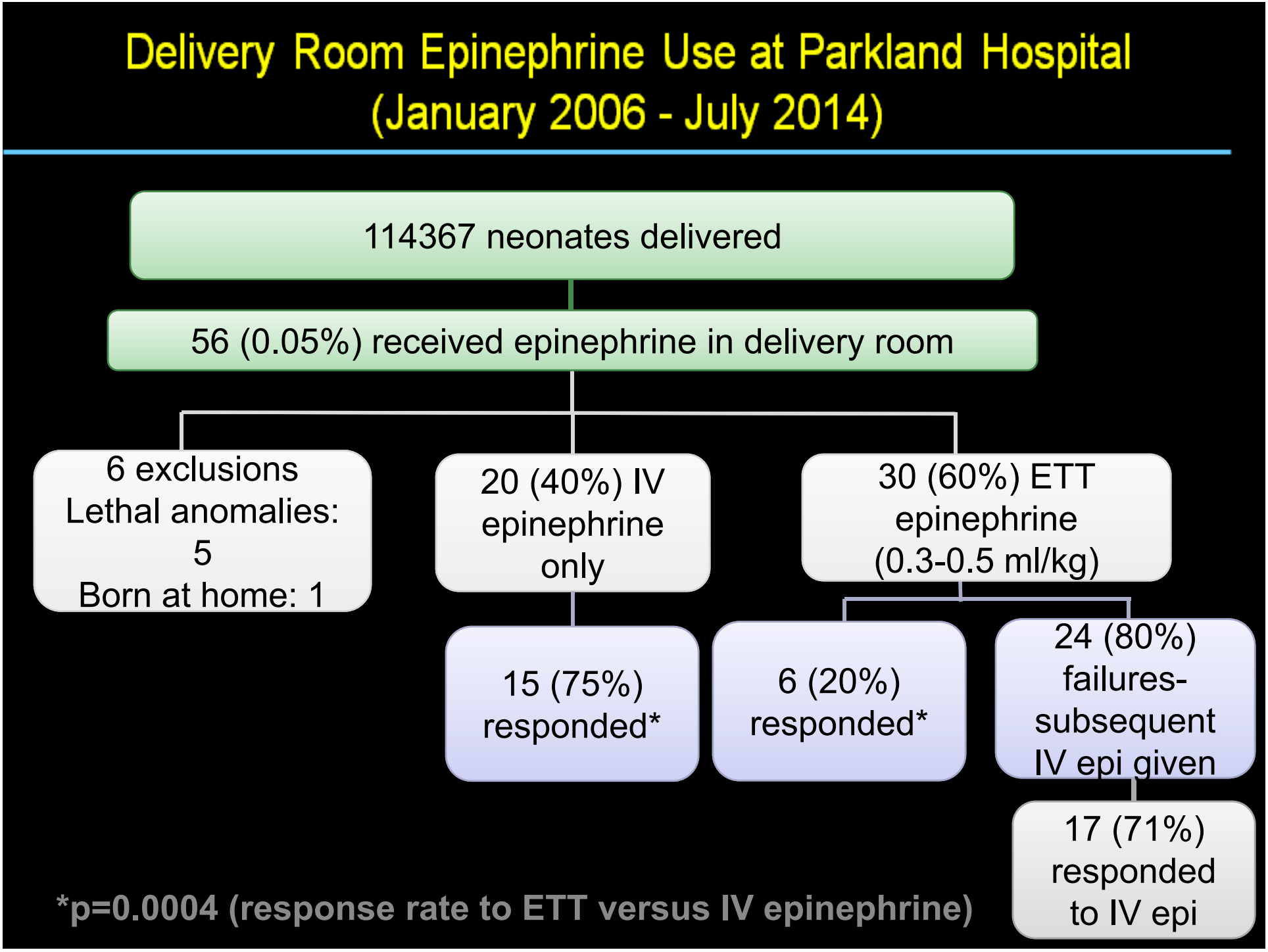


Coronary Perfusion Pressure=Aortic DBP – Right Atrial DBP

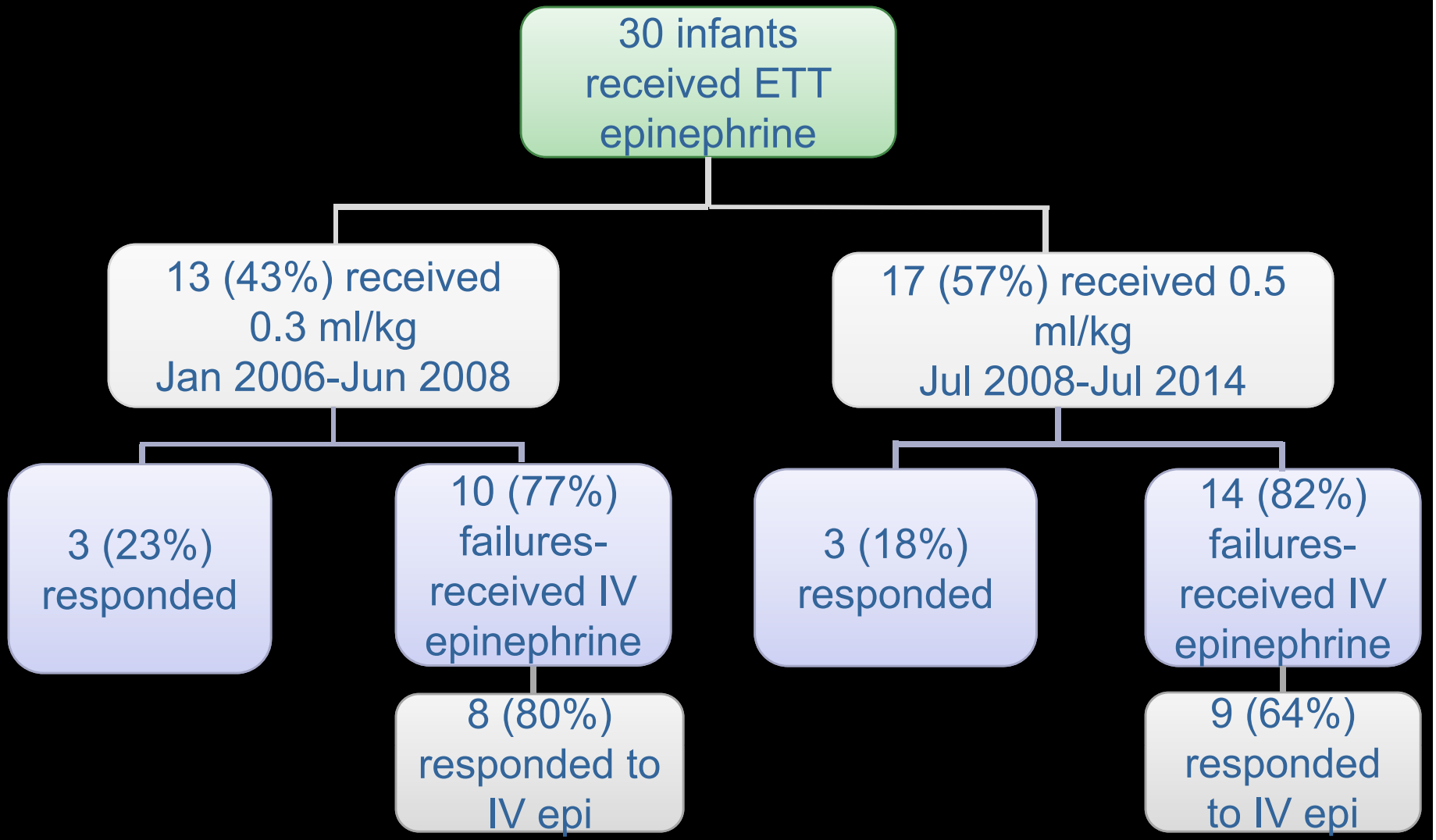
Use of Epinephrine in the Delivery Room Jan 1999- Dec 2004



Barber et al. Pediatrics 2006


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
30 (60%) ETT epinephrine (0.3-0.5 ml/kg)
15 (75%) responded*
6 (20%) responded*
24 (80%) failures- subsequent IV epi given
17 (71%) responded to IV epi
*p=0.0004 (response rate to ETT versus IV epinephrine)

ETT epinephrine: 0.3 ml/kg vs 0.5 ml/kg



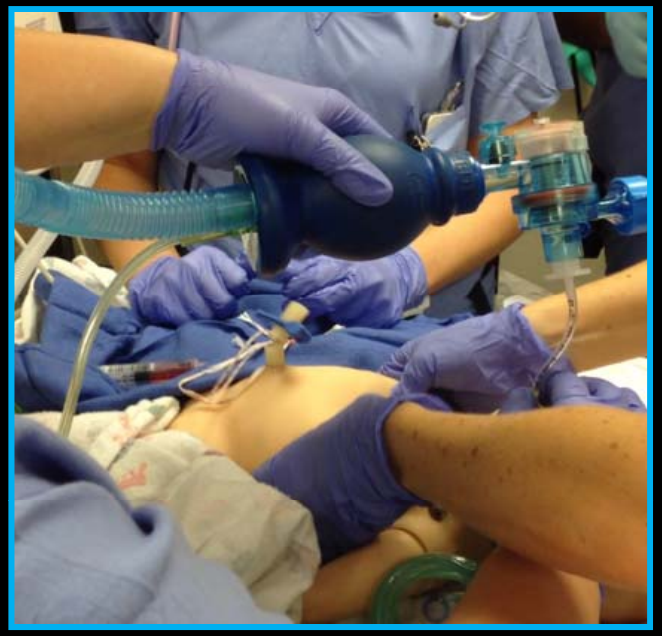
P= 0.71 (response rate to 0.3 vs 0.5 ml/kg ETT epinephrine)

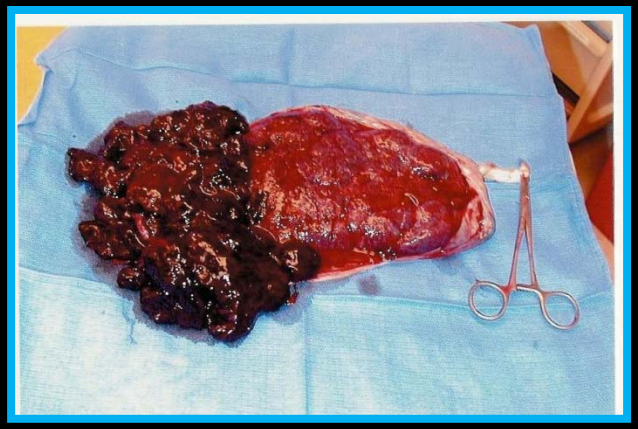
Conclusion

- During neonatal CPR in the delivery room, IV epinephrine should remain a priority
- Team training in rapid placement of UVC is vital
- Randomized trials in appropriate models of neonatal transition are needed to determine if even higher starting doses of ETT epinephrine (1 ml/kg or beyond) will be efficacious

Speculation

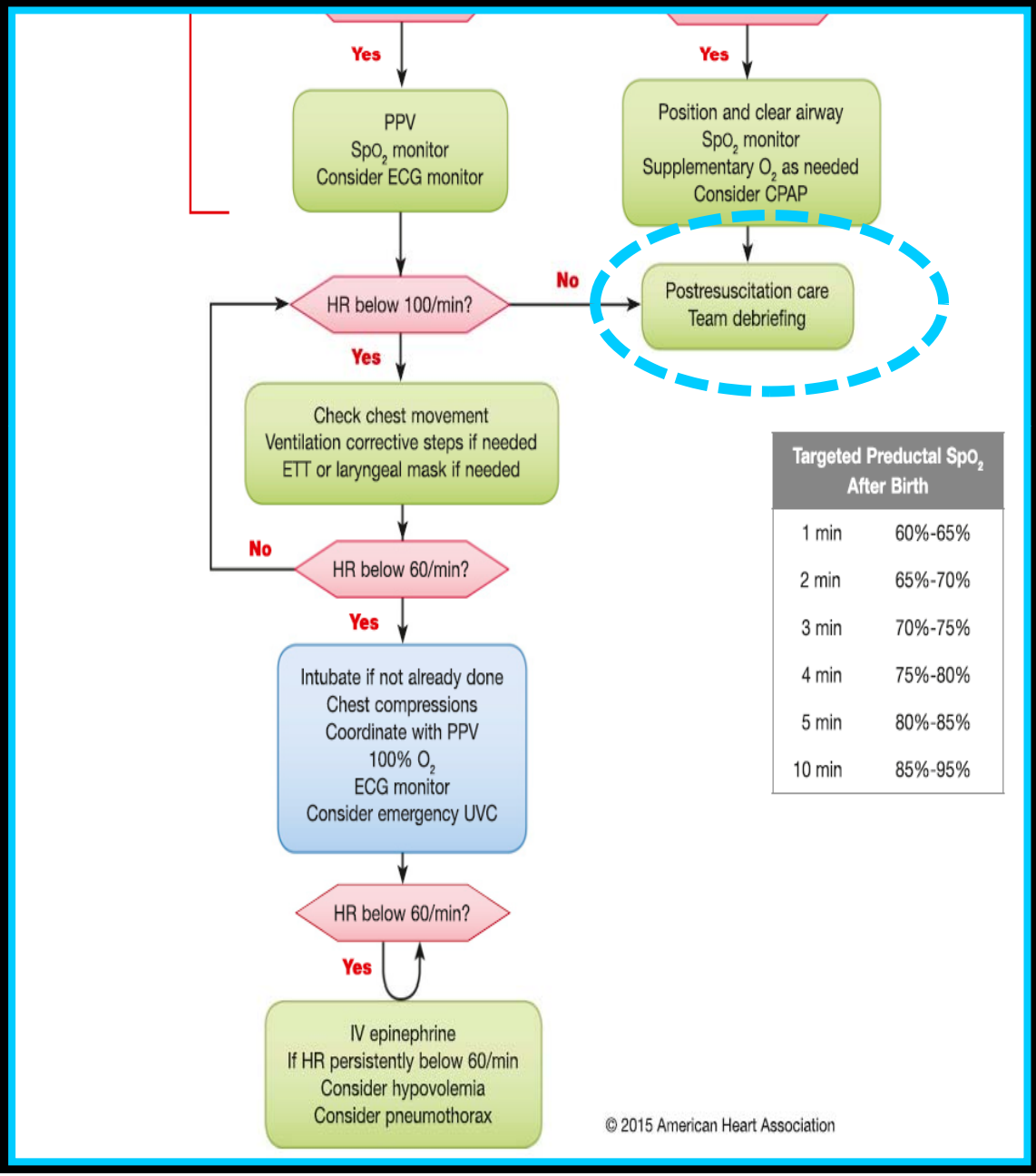
- Newborns in the DR have unique anatomical and pathophysiological differences that may limit absorption of epinephrine from the alveoli
  - Insufficient pulmonary blood flow during CPR
  - Pulmonary vasoconstriction from acidosis
  - Amount of epinephrine (if any) reaching alveoli is unknown
  - Alveolar fluid may dilute the epinephrine
  - Potential right-to-left intracardiac shunts (PDA and PFO) that could bypass pulmonary circulation





- 1 min after Epinephrine given, the ECG monitor shows a HR of 90 bpm
- Team stops to listen and detects HR>60 and rising.
- Compressions stopped
- PPV continued
- OB reports 50% abruption
- Ask for cord gas
- Get to the NICU
- Consider cooling exam
- Get gas, EBG

Debrief!


Yes
PPV
SpO2 monitor
Consider ECG monitor
Yes
Position and clear airway
SpO2 monitor
Supplementary O2 as needed
Consider CPAP
HR below 100/min?
No
Postresuscitation care
Team debriefing
Yes
Check chest movement
Ventilation corrective steps if needed
ETT or laryngeal mask if needed
No
HR below 60/min?
Yes
Intubate if not already done
Chest compressions
Coordinate with PPV
100% O2
ECG monitor
Consider emergency UVC
HR below 60/min?
Yes
IV epinephrine
If HR persistently below 60/min
Consider hypovolemia
Consider pneumothorax
Targeted Preductal SpO2 After Birth
1 min 60%-65%
2 min 65%-70%
3 min 70%-75%
4 min 75%-80%
5 min 80%-85%
10 min 85%-95%
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Ackowledgments

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(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