Evidence Based Newborn Resuscitation

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Professor of Pediatrics

Resuscitation History

But one day the woman's son became sick and died..."Give him to me," Elijah replied...and he stretched himself upon the child three times ...and the spirit of the child returned, and he became alive again.

1 Kings 17:17-24

Resuscitation History

When Elisha arrived, the child was indeed dead, lying there upon the prophet's bed...then he lay upon the child's body, placing his mouth upon the child's mouth, and his eyes upon the child's eyes, and his hands upon the child's hands. And the child's body began to grow warm again!

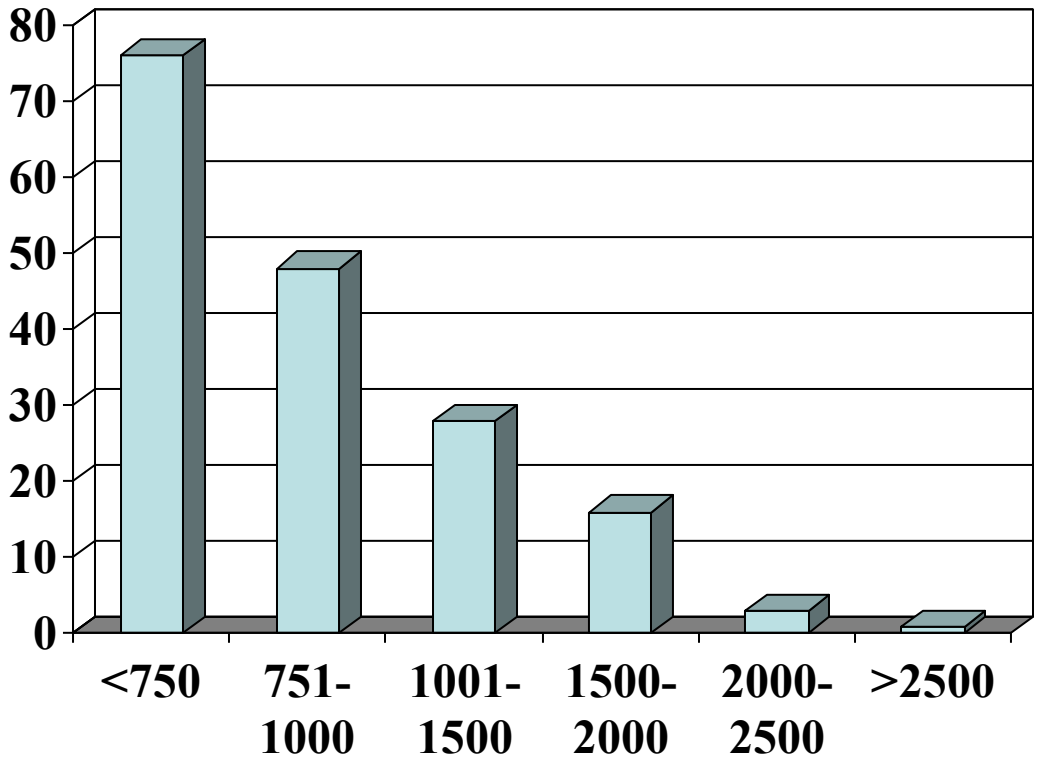
2 Kings 4:32-35

Resuscitation History

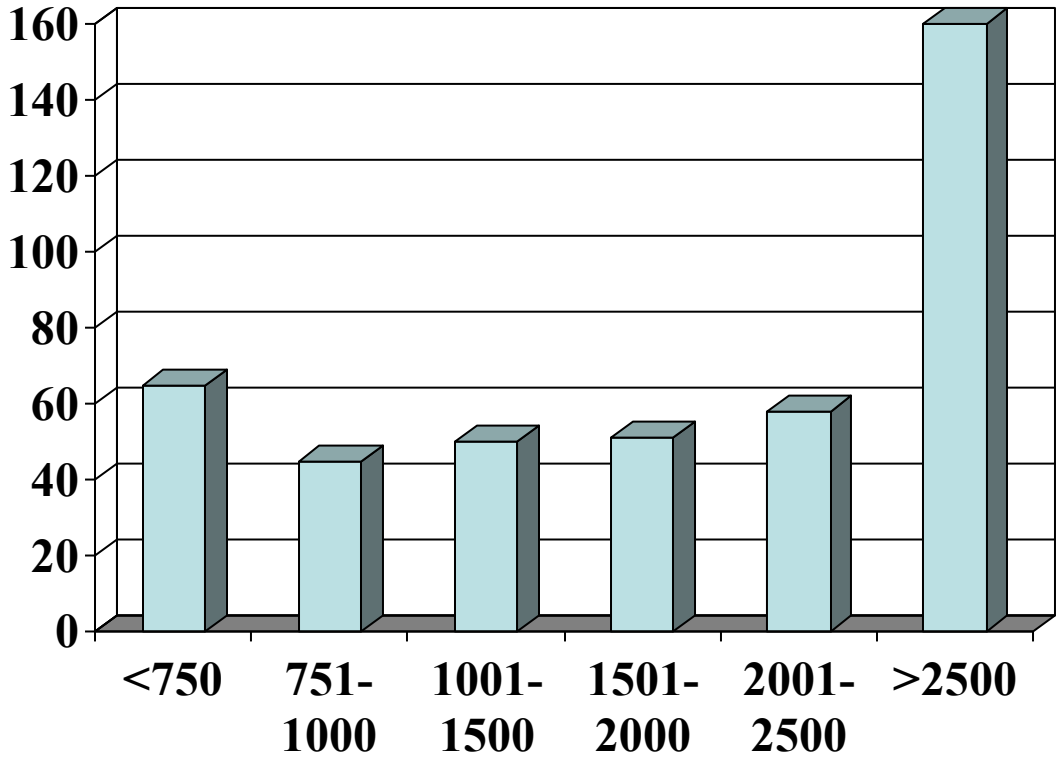
"If the child does not breathe immediately upon Delivery, which sometimes it will not, especially when it has taken Air in the womb; wipe its Mouth, and press your Mouth to the Child's, at the same time pinching the Nose with your Thumb and Finger, to prevent the Air escaping; inflate the lungs; rubbing it before the Fire; by which Method I have saved many."

Benjamin Pugh, 1754

Incidence for Neonatal Resuscitation



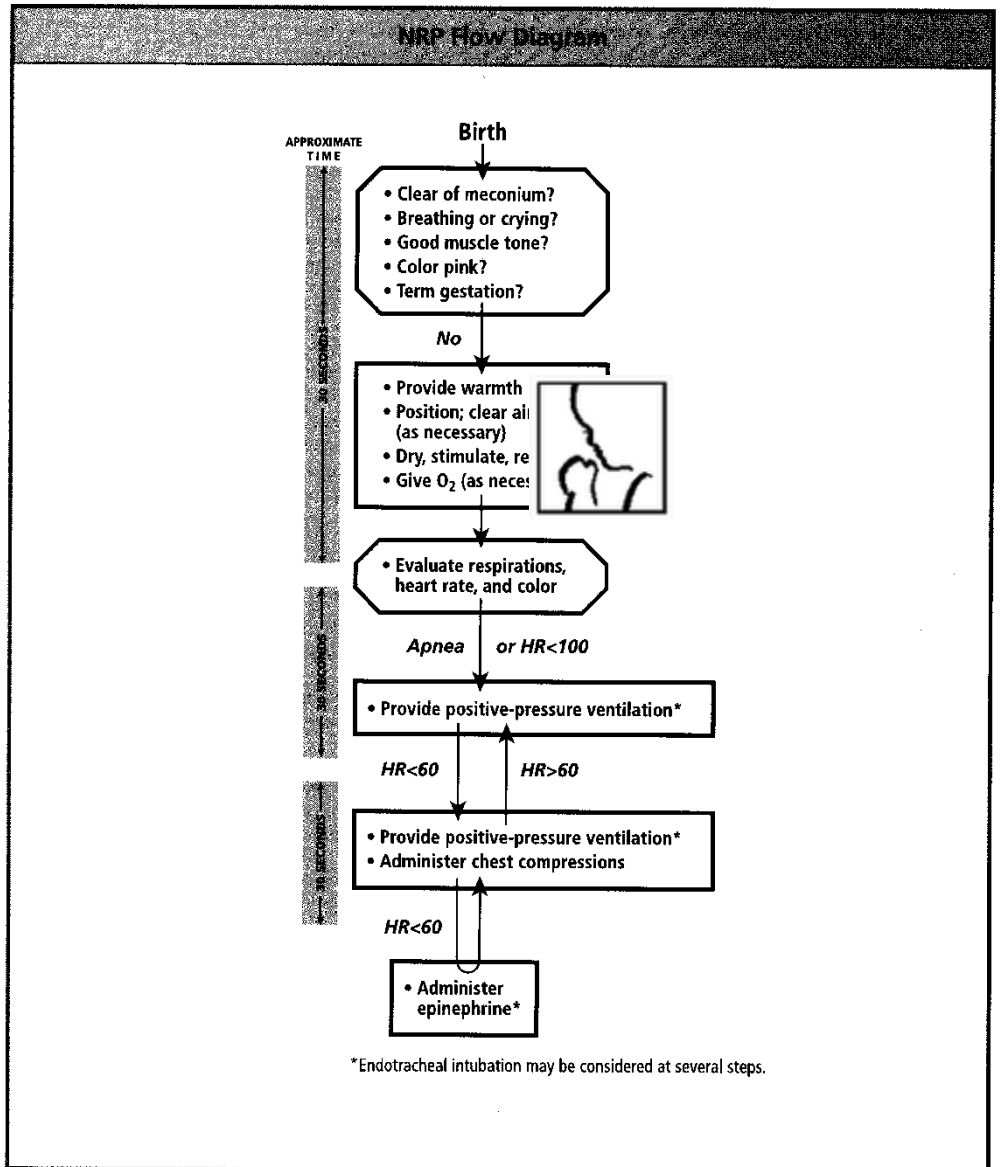
Prevalence of Neonatal Resuscitation



Need for CPR in the Delivery Room

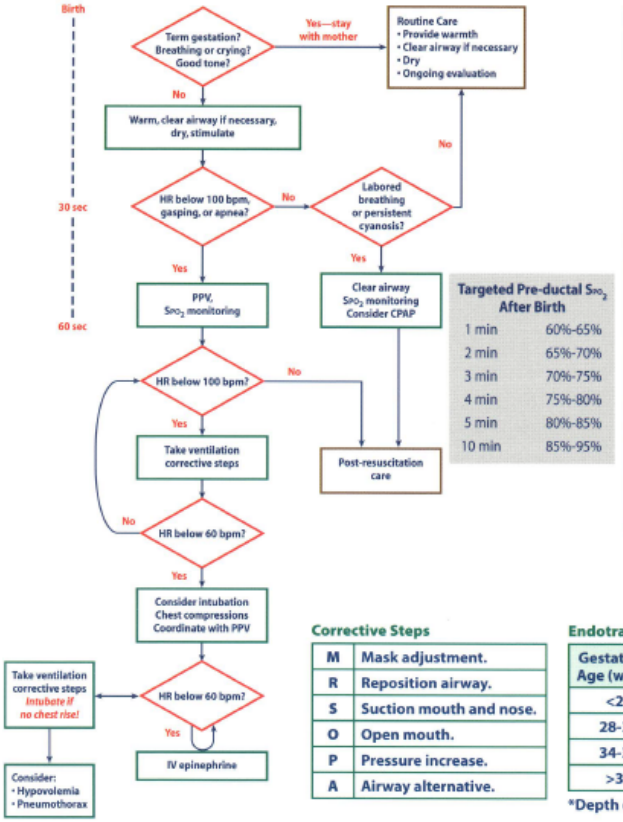
- 30,839 consecutive deliveries
  - 39 with CPR ± epinephrine (0.12%)
  - 1/3 with severe fetal acidemia
  - If no fetal acidemia, correction of ventilation improved heart rate

Neonatal Resuscitation Program (NRP)



Neonatal Resuscitation Program™ - Reference Chart

The most important and effective action in neonatal resuscitation is ventilation of the baby's lungs.



Targeted Pre-ductal 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%

A Airway
- Put baby's head in "sniffing" position
- Suction mouth, then nose
- Suction trachea if meconium-stained and NOT vigorous

B Breathing
- PPV for apnea, gasping, or pulse <100 bpm
- Ventilate at rate of 40 to 60 breaths/minute
- Listen for rising heart rate, audible breath sounds
- Look for slight chest movement with each breath
- Use CO_2 detector after intubation
- Attach a pulse oximeter

C Circulation
- Start compressions if HR is <60 after 30 seconds of effective PPV
- Give (3 compressions: 1 breath) every 2 seconds
- Compress one-third of the anterior-posterior diameter of the chest

D Drugs
- Give epinephrine if HR is <60 after 30 seconds of compressions and ventilation
- Caution: epinephrine dosage is different for ET and IV routes

Corrective Steps

M	Mask adjustment.
R	Reposition airway.
S	Suction mouth and nose.
O	Open mouth.
P	Pressure increase.
A	Airway alternative.

Endotracheal Intubation

Gestational Age (weeks)	Weight (kg)	ET Tube Size (ID, mm)	Depth of Insertion* (cm from upper lip)
<28	<1.0	2.5	6-7
28-34	1.0-2.0	3.0	7-8
34-38	2.0-3.0	3.5	8-9
>38	>3.0	3.5-4.0	9-10

*Depth of Insertion (cm) = 6 + weight (in kg)

Medications Used During or Following Resuscitation of the Newborn (Canadian recommendation)

Medication	Dosage/Route	Concentration	Wt (kg)	Total IV Volume (mL)	Precautions
Epinephrine*	IV (UVC preferred route) 0.1 mL/kg Endotracheal 1 mL/kg ETT (MAXIMUM 3 mL/dose)	1:10,000	1 2 3 4	0.1 0.2 0.3 0.4	Give rapidly. Repeat every 3-5 minutes if HR<60 with chest compressions.
Volume expanders Isotonic crystalloid (normal saline) or blood	10 mL/kg IV		1 2 3 4	10 20 30 40	Indicated for shock. Give over 5 to 10 minutes. Reassess after each bolus.

*Note: Endotracheal dose may not result in effective plasma concentration of drug, so vascular access should be established as soon as possible. Drugs given endotracheally require higher dosing than when given IV.

American Heart Association®

American Academy of Pediatrics
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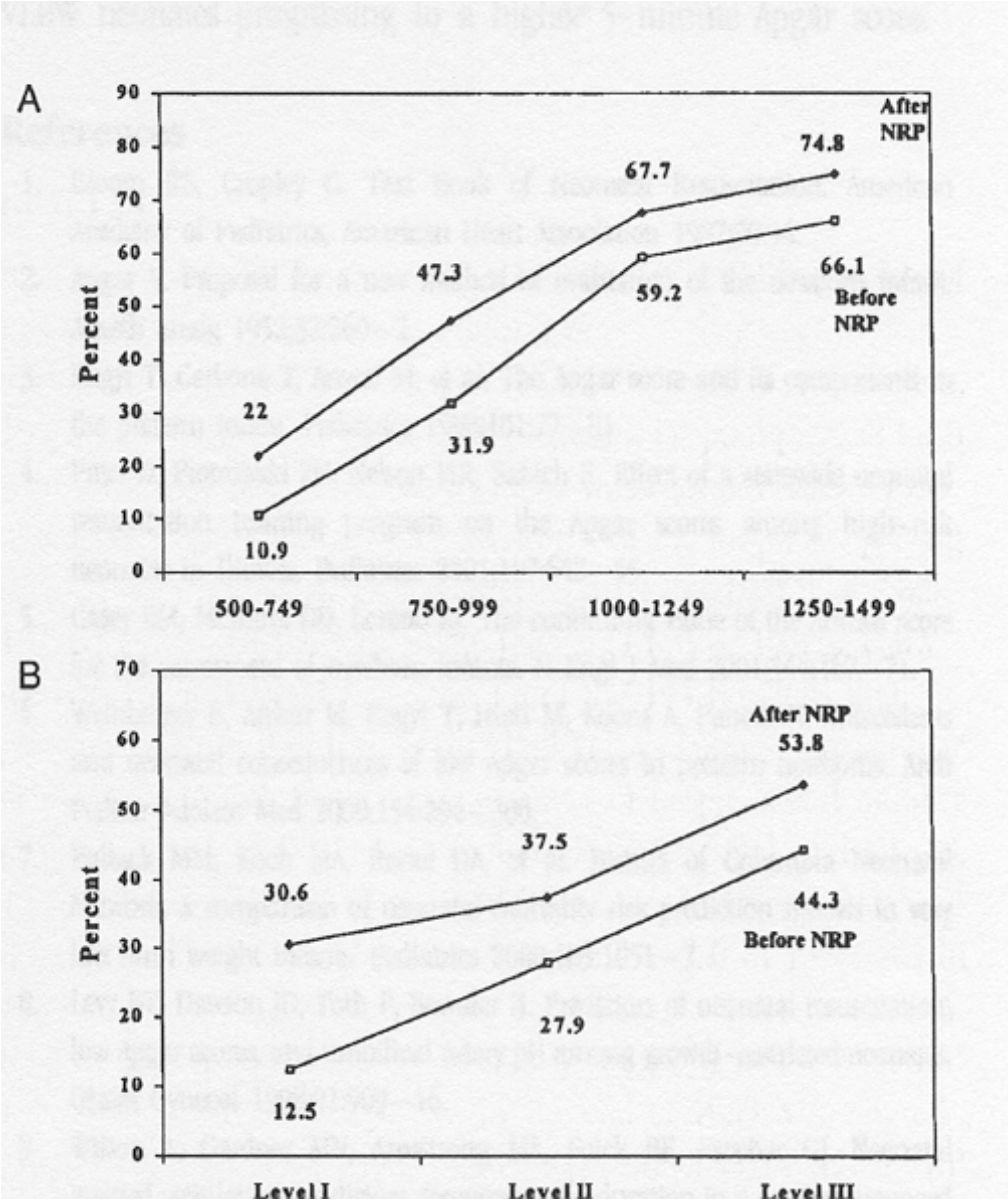
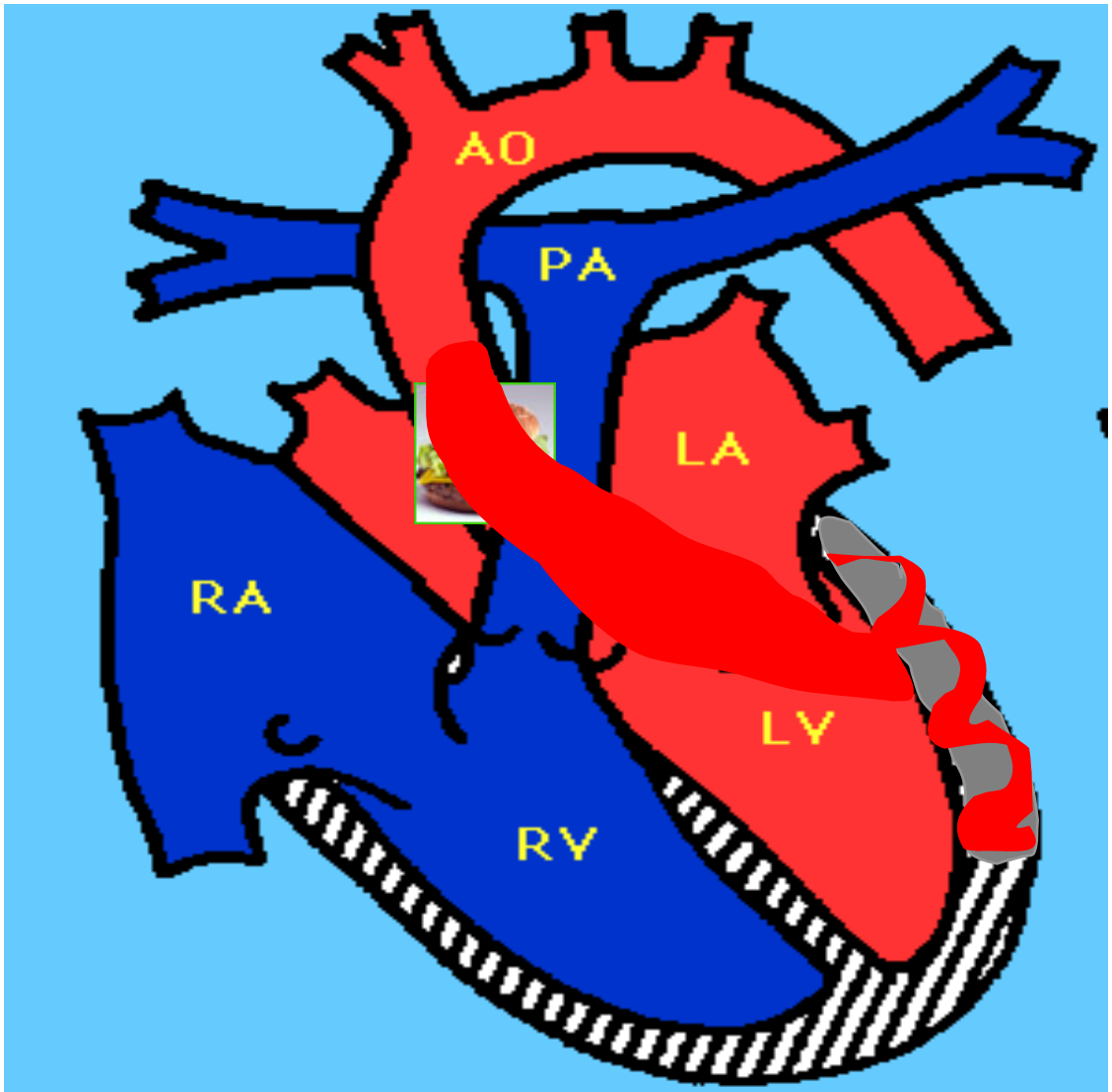
NRP305

The recommendations in this publication do not indicate an exclusive course of treatment or serve as a standard of medical care. Variations, taking into account individual circumstances, may be appropriate.

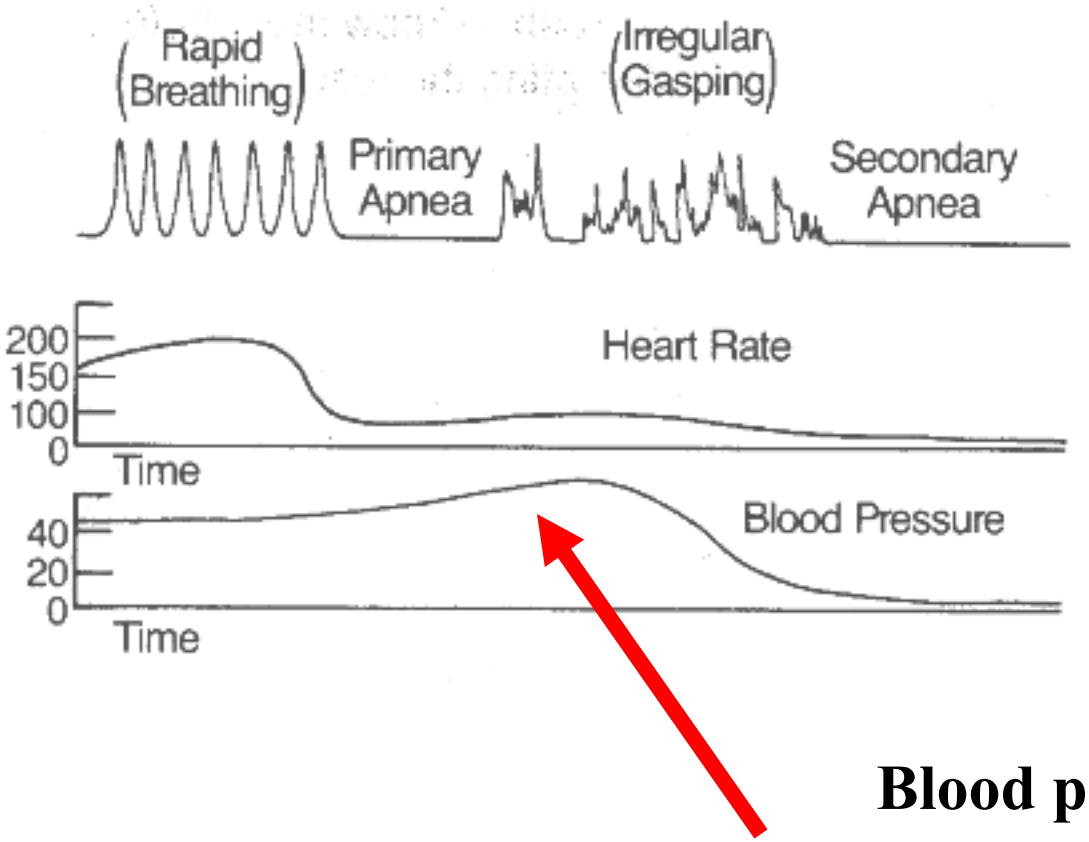
NRP--Has it done any good?



Pathophysiology of Adult Cardiac Arrest

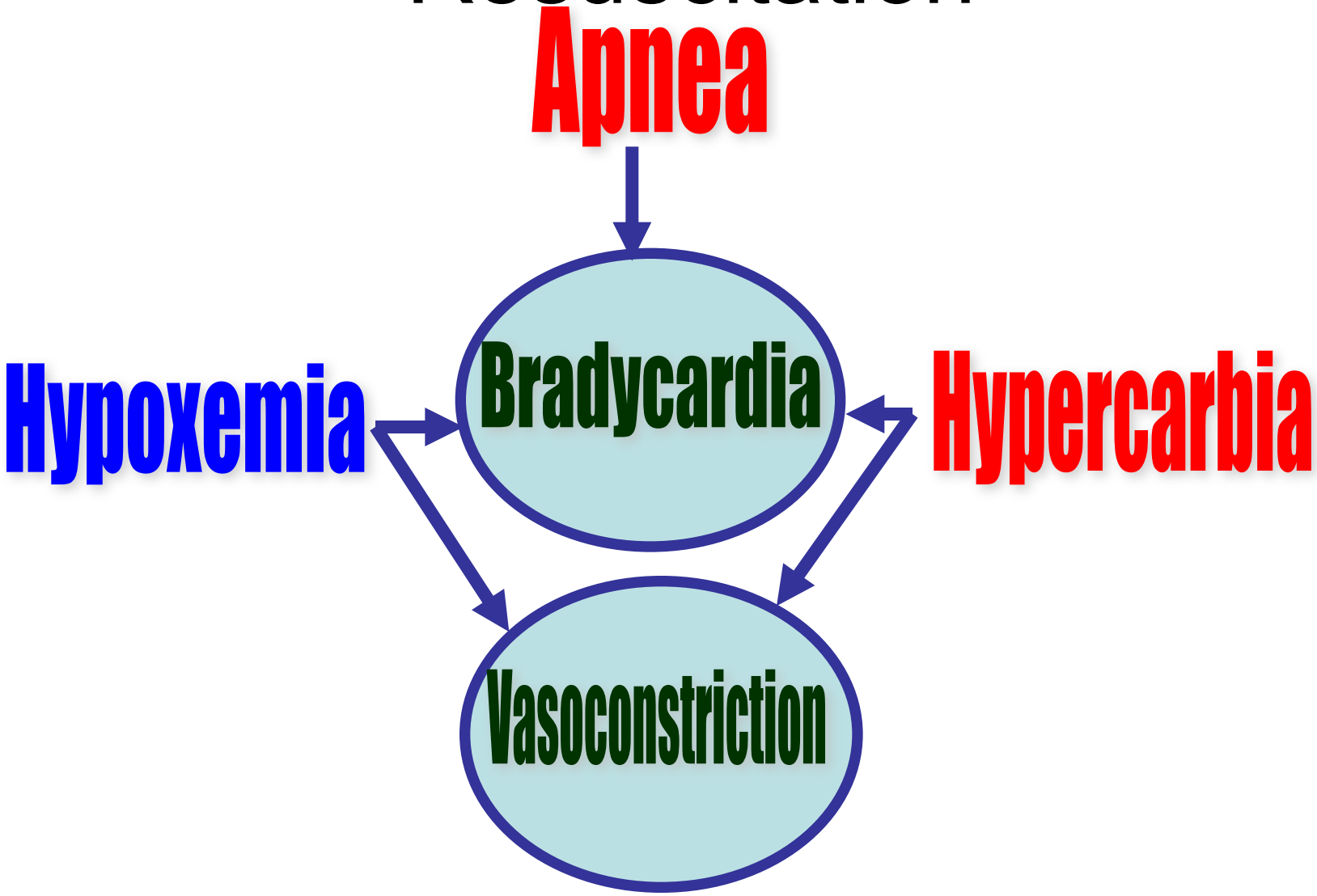


Mechanisms of Cardiac Arrest in Neonates



Blood pressure trends upward during the asphyxial process

Neurophysiology of Resuscitation

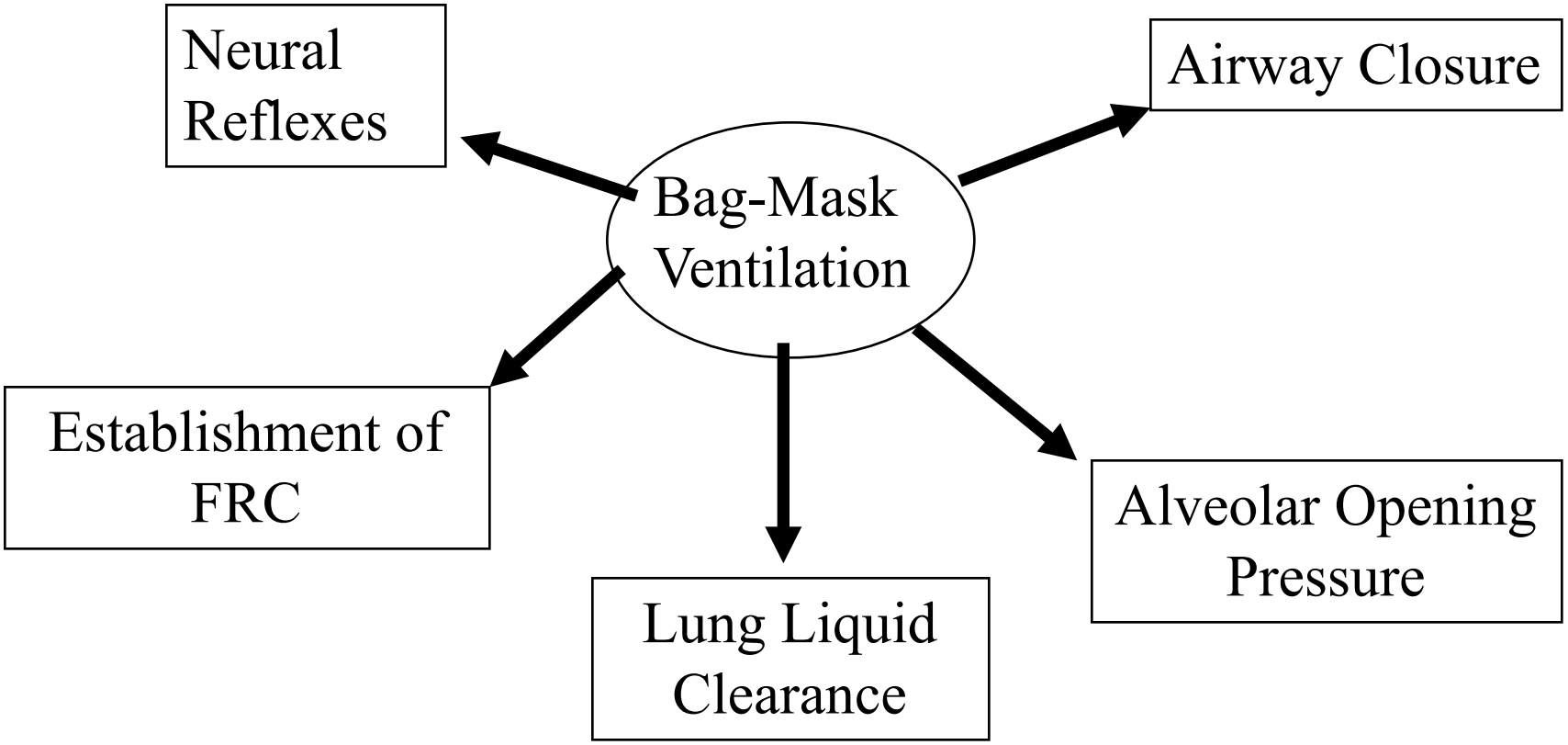


Artificial Respiration Class 1930's

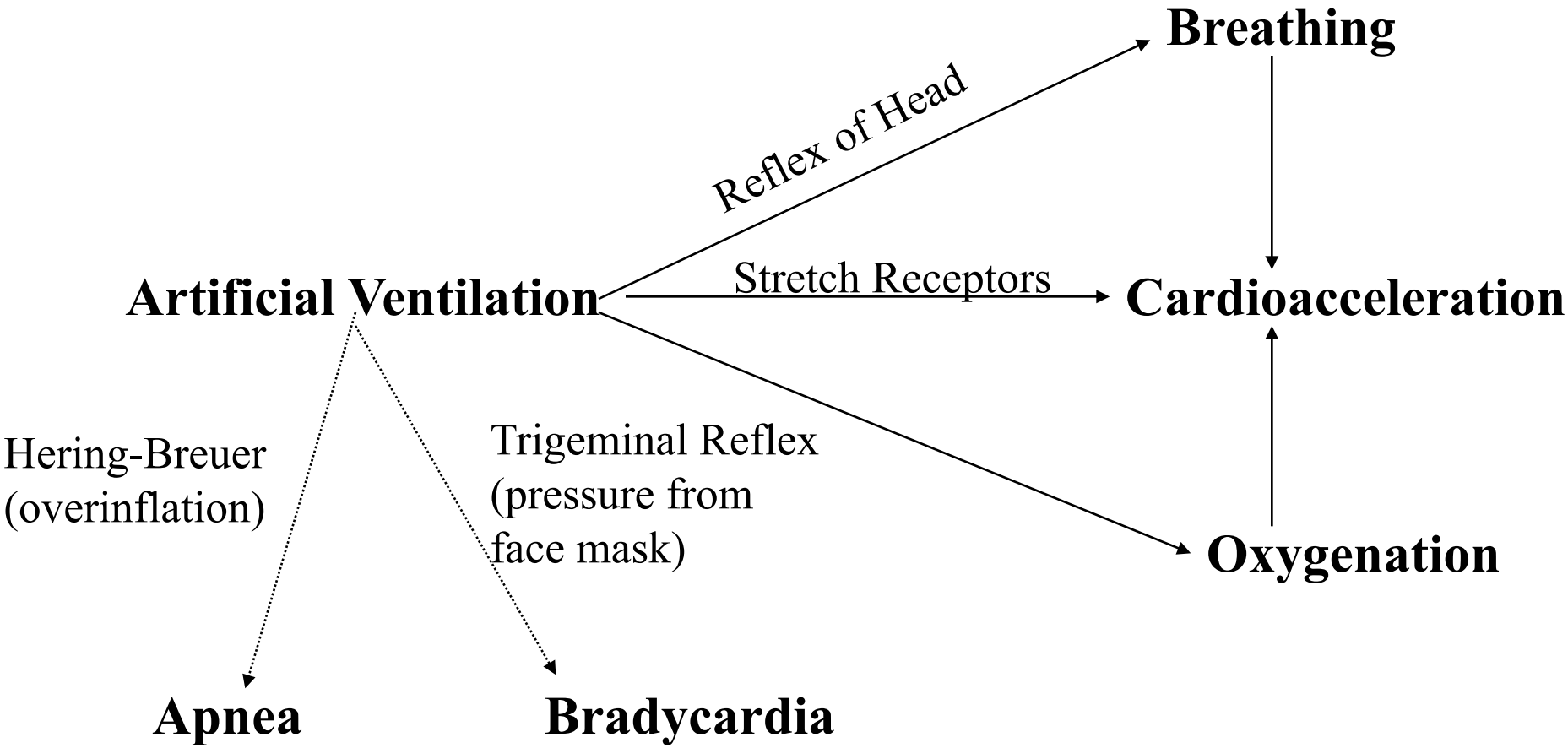
Ventilation in Neonatal Resuscitation

- 1950's, investigators showed hypopharyngeal structures occluded airway, making chest compressions ineffective for ventilation--this was not the case with mouth to mouth
- 1958, the self-inflating bag introduced

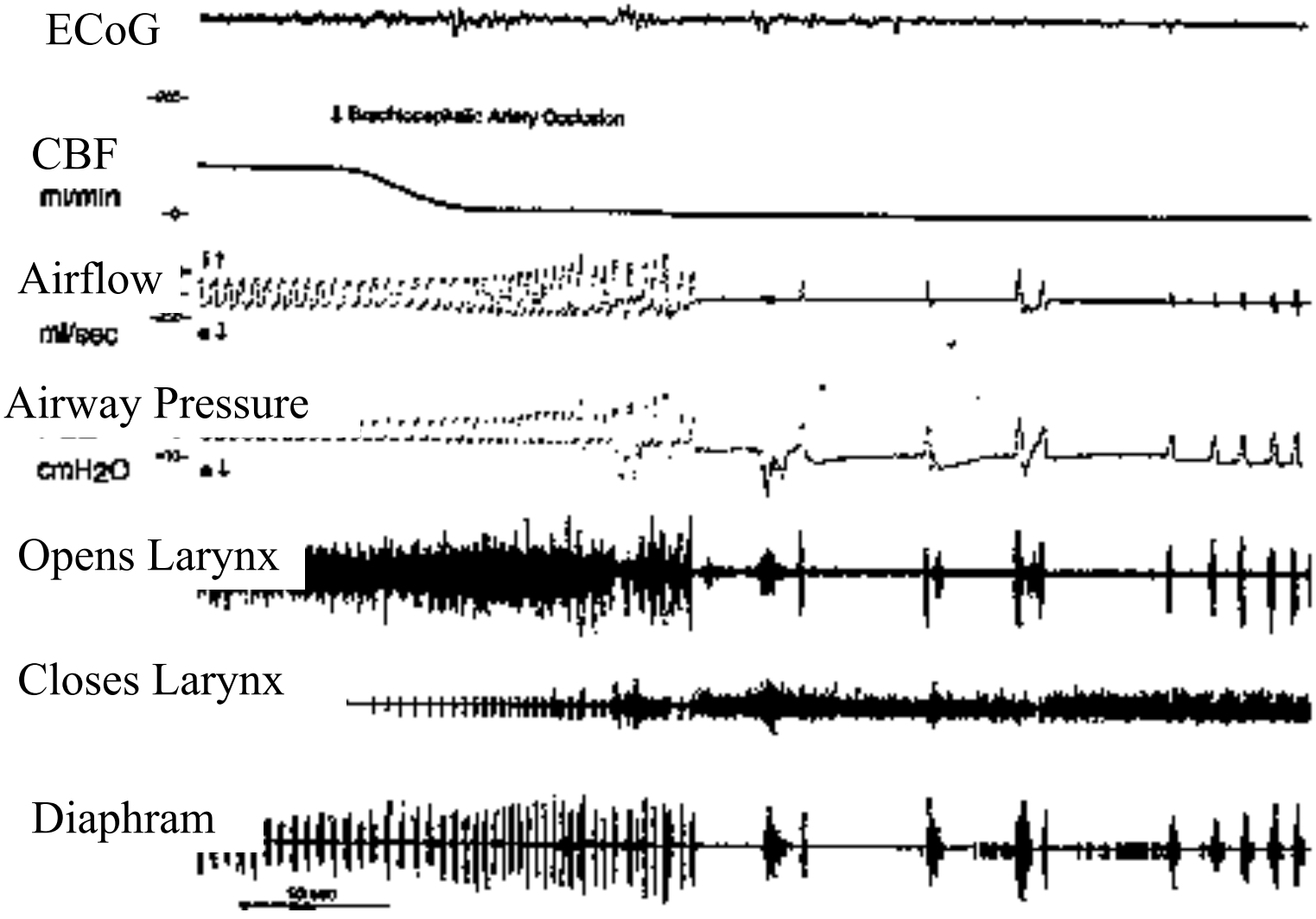
Physiological Impediments to Artificial Ventilation in the Newborn



Effects of Artificial Ventilation on Resuscitation



Airway Closure



Alveolar Opening Pressure

Inspiratory pressure that must be overcome to begin delivering a tidal volume

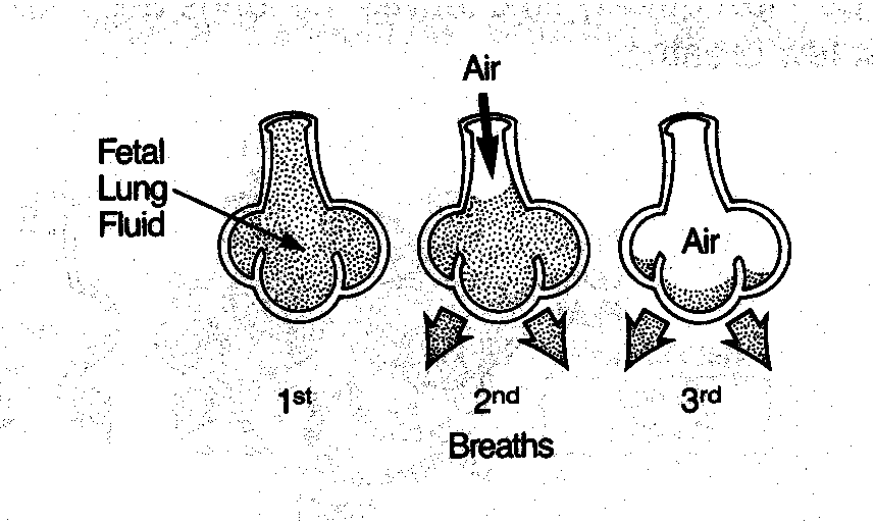
- Spontaneously Breathing
  - Not present... that is, some flow for any change in pressure
- Asphyxiated, BVM ventilated
  - 13-32 cm H_2O in asphyxiated neonates receiving PPV

Establishment of FRC

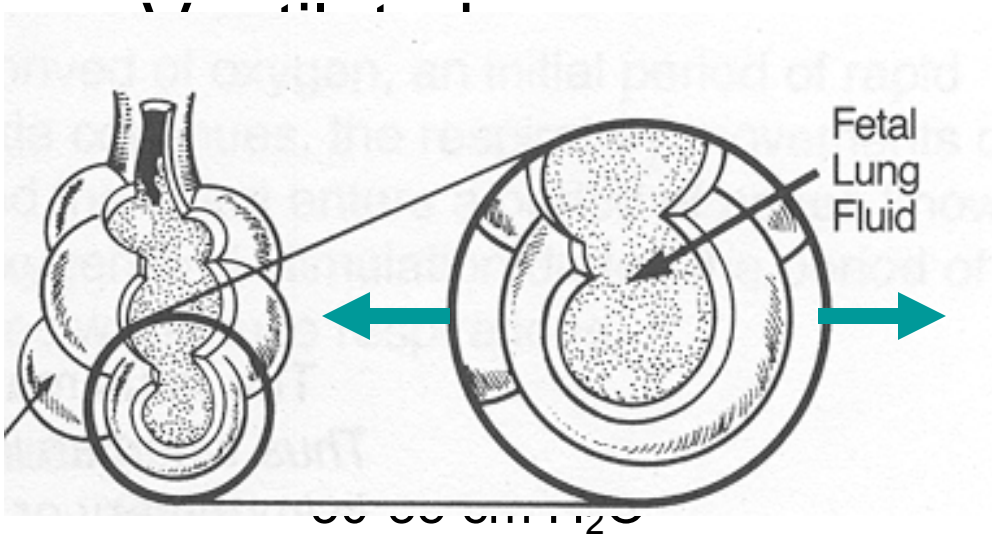
- Spontaneously breathing
  - 1st few breaths are exhaled against closed glottis, generating 71 cm H_2O pressure
- Asphyxiated, BVM Ventilated
  - Difficult to mimic this with BVM ventilation

Lung Liquid Clearance

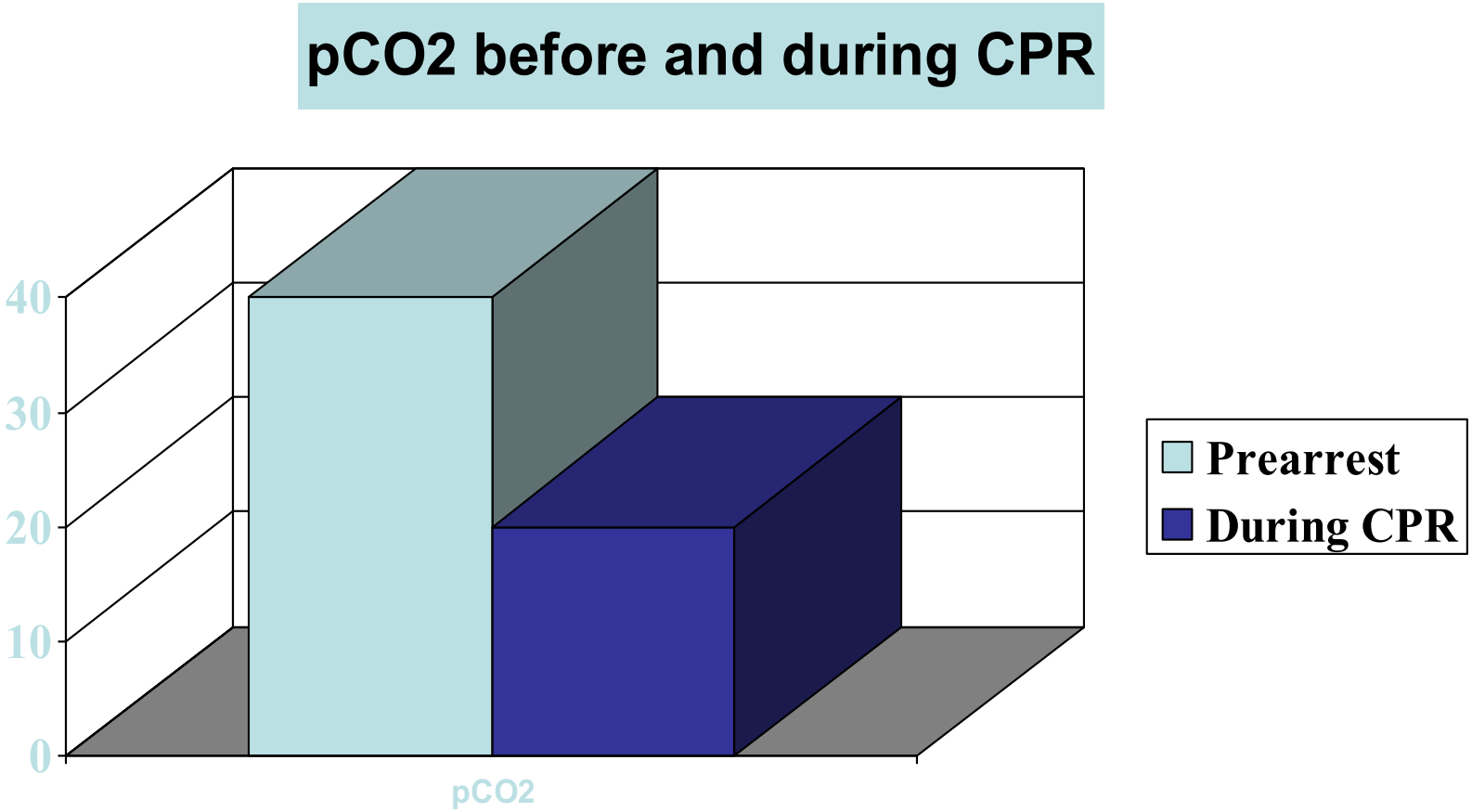
- Spontaneously



- Asphyxiated, BVM

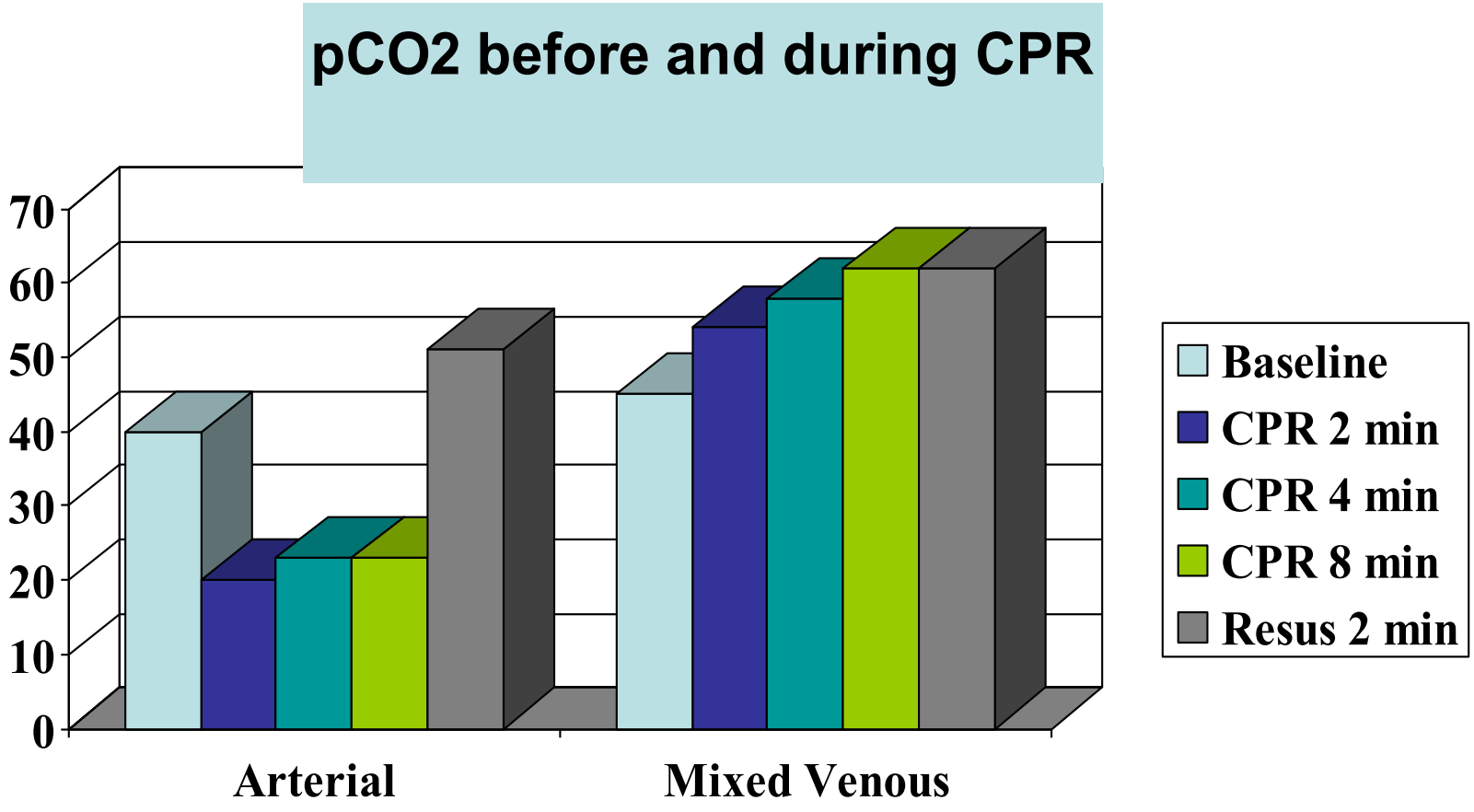


Ventilation During Cardiac Arrest



Angelos 1992

Ventilation During Cardiac Arrest



Grundler 1986

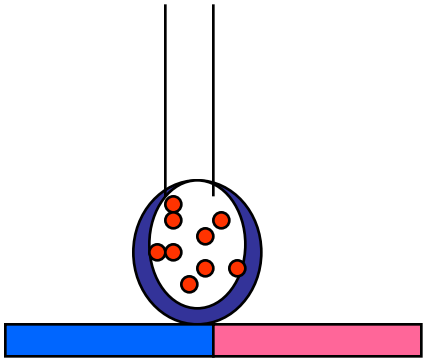
Oxygen in Newborn Resuscitation

- 1891, Bonnaire first gave oxygen to a “blue baby” and concluded:

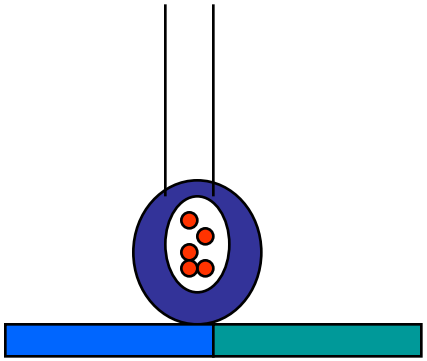
  “Whenever there is insufficient pulmonary haematosis, either from obstruction of the respiratory passages or from weak action of the mechanical apparatus of respiration, or from want of excitation of the respiratory nerve-centre, <u>oxygen administration is indicated</u>. Apparent death in the newborn is, therefore, the first indication…”

Advantages of 100% Oxygen

- Overcome diffusion barriers
  - lung liquid
  - lung disease



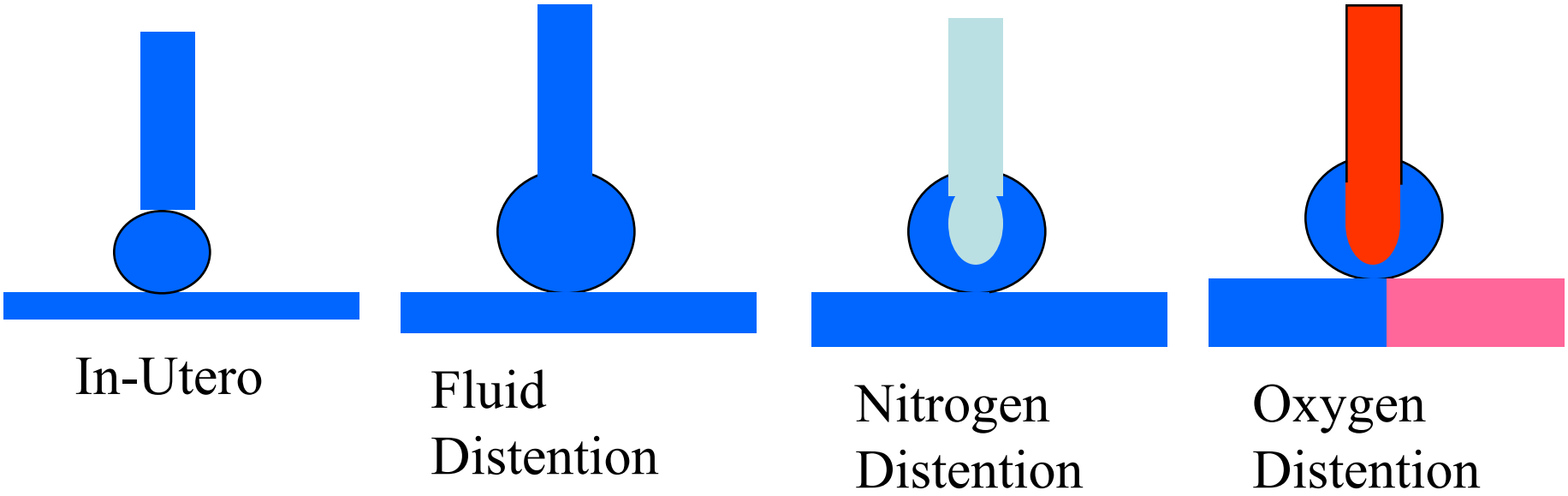
Normal



Diffusion Barrier

Advantages of 100% Oxygen

- Pulmonary Vasodilation



Physiology of 100% Oxygen

Alveolar Gas Equation with **FiO_2 = 0.21** and $pCO_2 = 40$

$P_AO_2 = (713 \times 0.21) - 40 = 110$ torr

Assume 0.45 aA gradient, **pO2 = 50 torr**

Alveolar Gas Equation with **FiO_2 = 1.0** and $pCO_2 = 40$

$P_AO_2 = (713 \times 1.0) - 40 = 673$ torr

Assume 0.45 aA gradient, **pO2 = 300 torr**

Physiology of 100% Oxygen

Oxygen Content = (1.34 x Hb x O_2 saturation) + 0.003 x pO_2

For **pO_2 of 25 torr** and Hb 17:

Oxygen Content = (1.34 x 17 x 0.63) + 0.003 x 25

14.3 + 0.1 = **14.4**

For **pO_2 of 50 torr** and Hb 17:

Oxygen Content = 21.7 + 0.15 = **20.9**

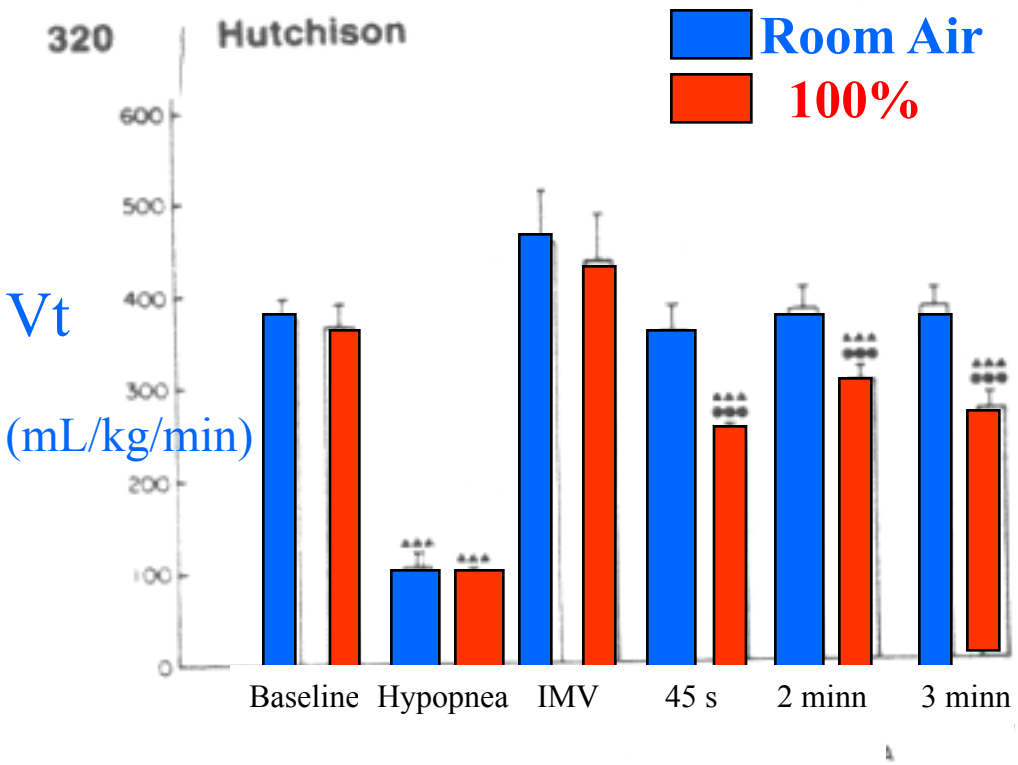
45%

For **pO_2 of 300 torr** and Hb 17:

Oxygen Content = 22.8 + 0.9 = **23.7**

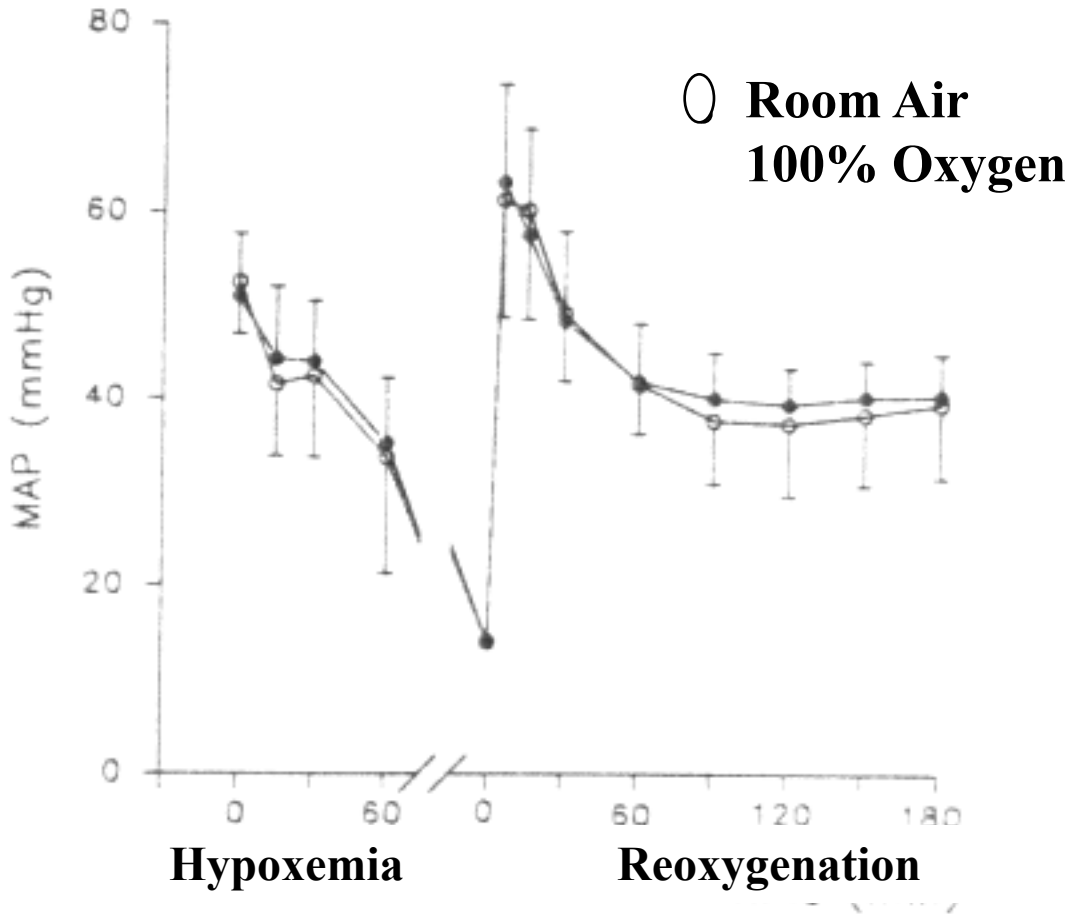
13%

Room Air vs 100% in Resuscitation of Lambs



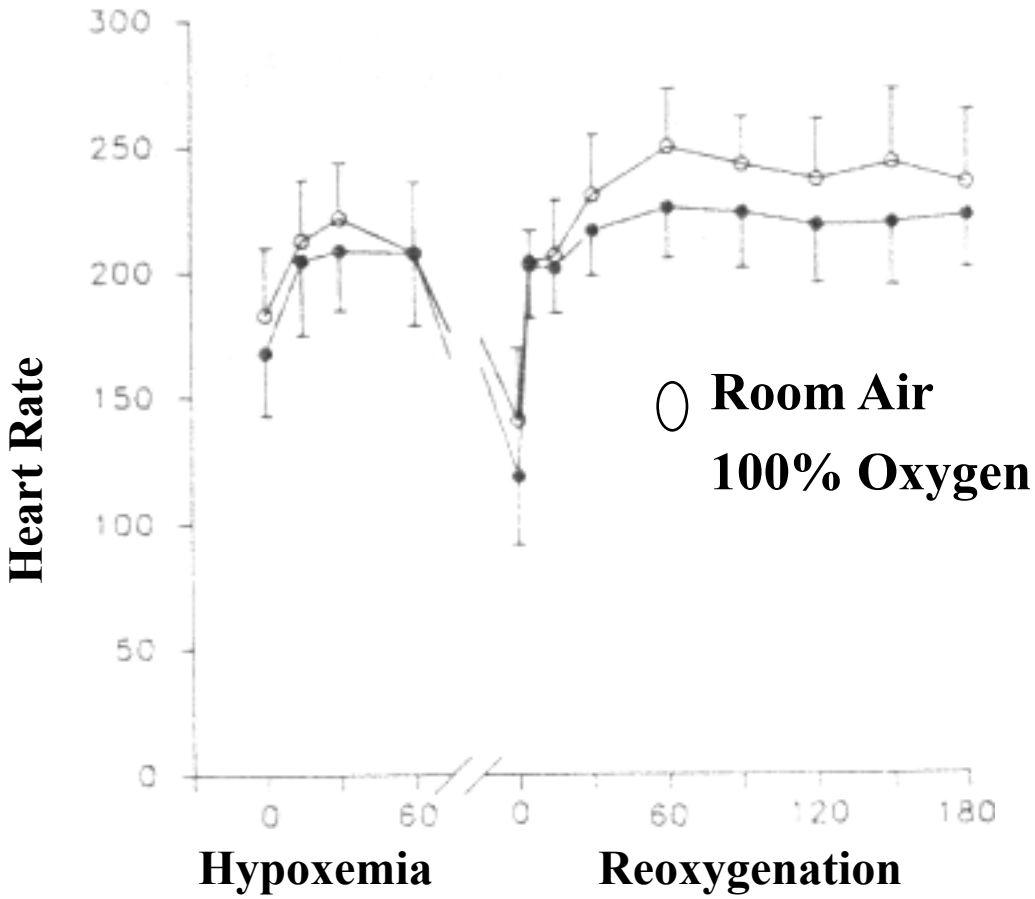
Hutchison, 1987

Blood Pressure During Resuscitation in Intact Animals



Rootwelt et al, 1992

Heart Rate During Resuscitation in Intact Animals



Rootwelt et al, 1992

PEDIATRICS Vol. 102 No. 1 July 1998, p. e1

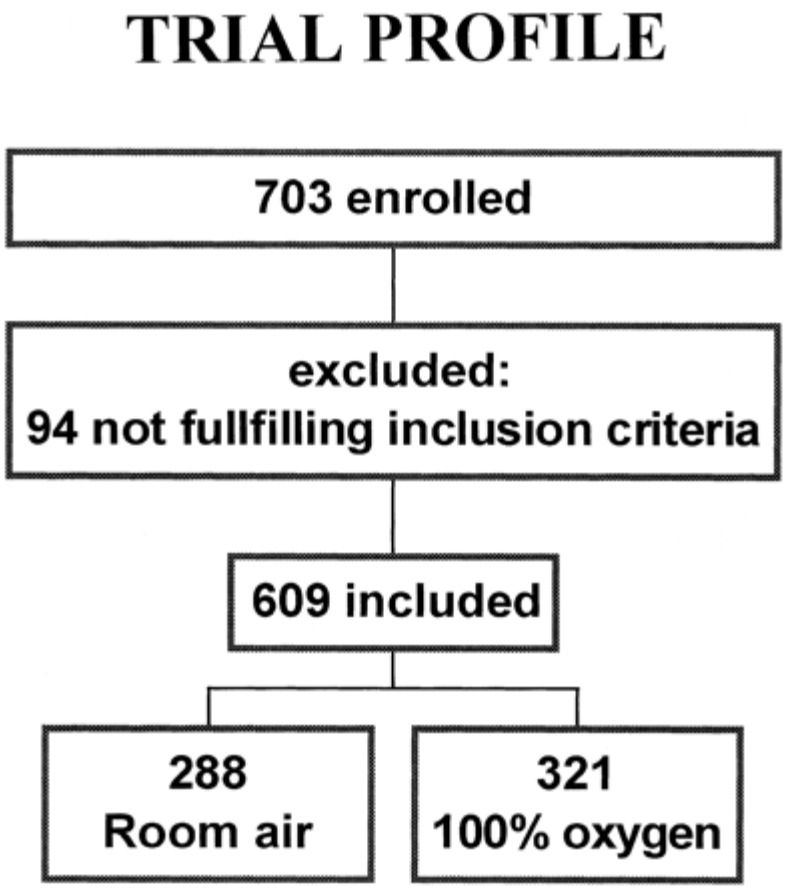
ELECTRONIC ARTICLE:

Resuscitation of Asphyxiated Newborn Infants With Room Air or Oxygen: An International Controlled Trial: The Resair 2 Study

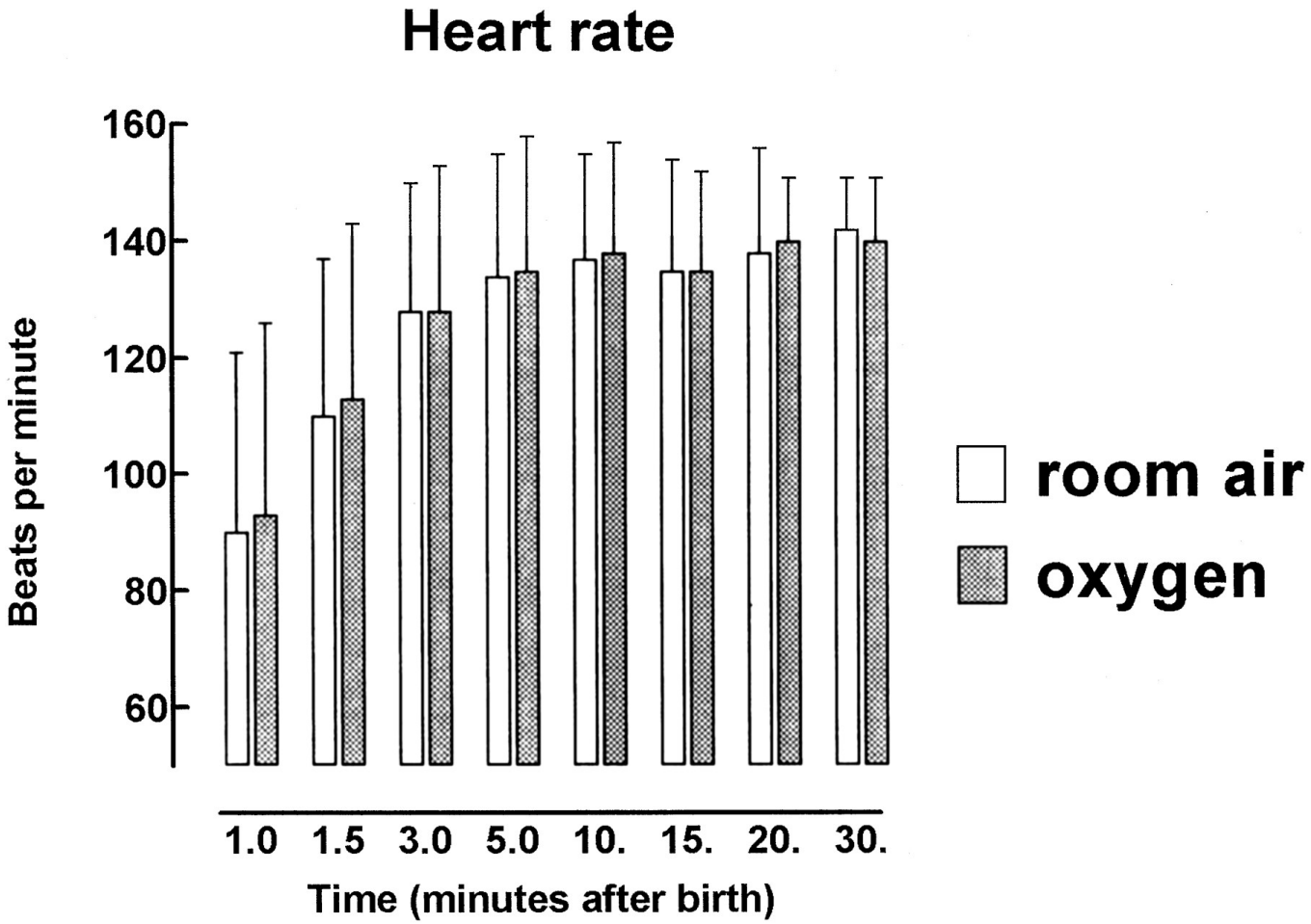
Ola Didrik Saugstad*, Terje Rootwelt*, and Odd Aalen

From the * Department of Pediatric Research, National Hospital, Oslo, Norway, and the Section of Medical Statistics, University of Oslo, Oslo, Norway.

Resair 2 Study



Resair 2 Study



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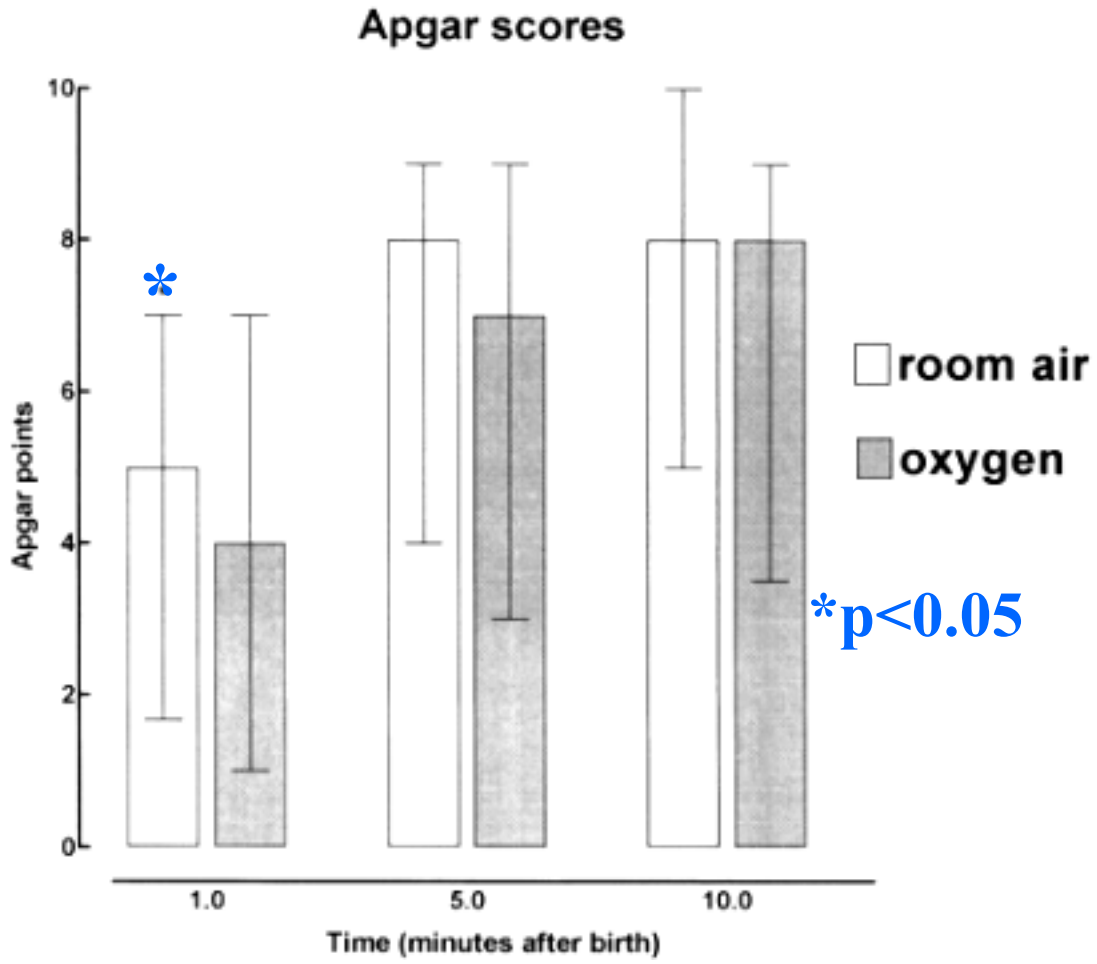

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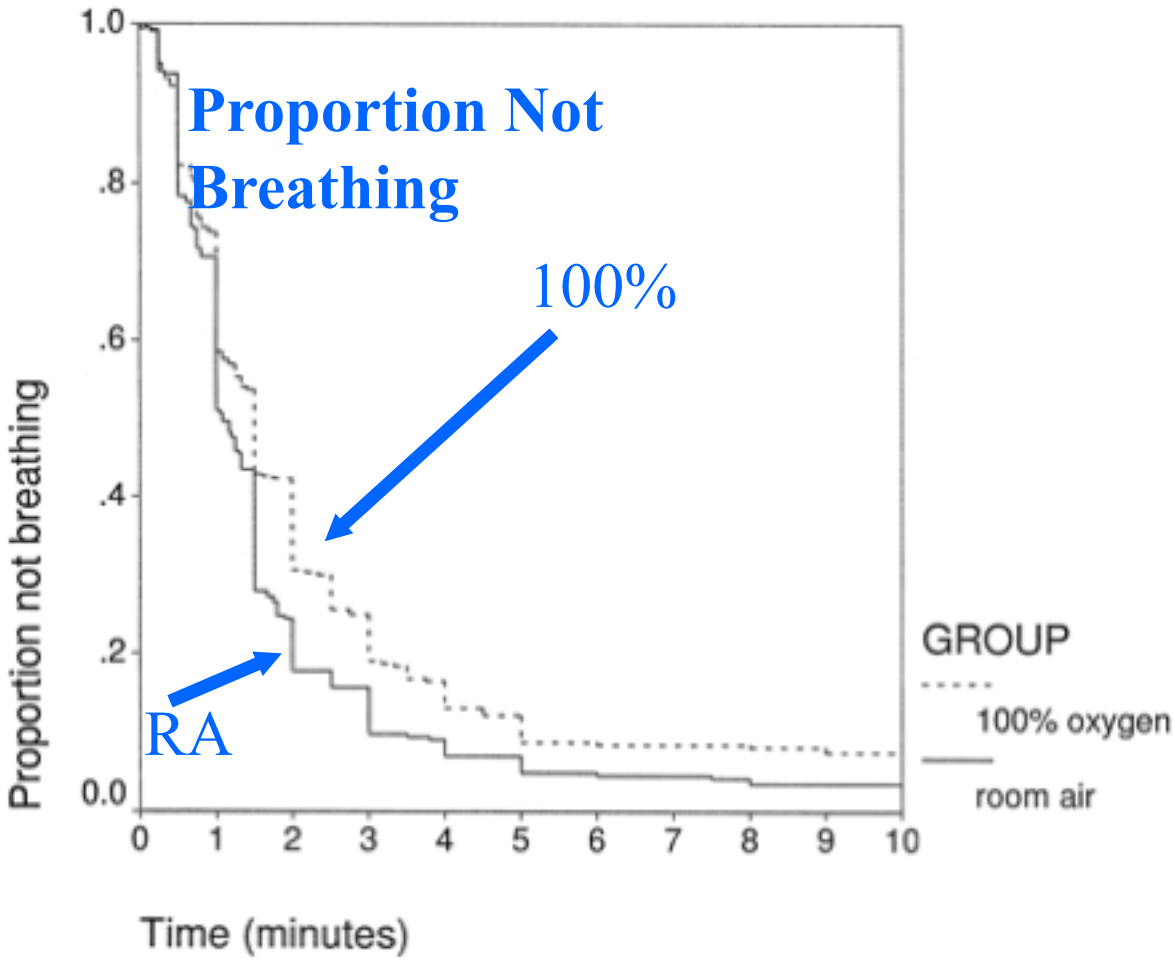


Resair 2 Study

TABLE 3

Number of Registered Infants With Adverse Outcome

Event	RA	O2
Death within 7 da	35/288 (12.2%)	48/321 (15.0%)
Death within 28 da	40/288 (13.9%)	61/321 (19.0%)
Death within 7 d or HIE grade II or IIIa	61/288 (21.2%)	76/321 (23.7%)
HIE grade II or IIIa	47/288 (16.3%)	55/321 (17.1%)

Room Air vs 100%

	Ramji (1993)[17]	Ramji (2003)[14]	Saugstad (1998)[11]	Vento (2001)[15]	Vento (2003)[16]
Participants					
n	84	431	609	40	151
Inclusion criteria	Birthweight >999 g with apnoea, HR < 80 bpm, or both	Birthweight >1000 g with HR <100 bpm, apnoeic, or both, and unresponsive to stimulation.	Birthweight 999 g with apnoea or gasping, HR <80 bpm, or both	Term infants with apnoea, hypotonia, unresponsive to stimuli and HR < 80 bpm, or both	Birth weight >999 g Term infants with apnoea, hypotonia, unresponsive to stimuli, HR < 80 bpm, and pH <7·05
Air group					
Birthweight (g)	2410 (540)	2529 (629)	2600 (1320-4078)*	3380 (318)	3160 (240)
Gestational age (weeks)	38·4 (1·9)	37·9 (2·9)	38 (32–42)*	38·6 (1·7)	38·9 (1·6)
Umbilical arterial pH	..	..	7·11 (0·14)	7·11 (0·04)	7·09 (0·07)
Oxygen group					
Birthweight (g)	2410 (540)	2529 (629)	2560 (1303-3900)*	3190 (245)	3220 (168)
Gestational age (weeks)	38·1 (2·6)	38·1 (2·6)	38 (32–42)*	40·2 (0·8)	40·5 (1·1)
Umbilical arterial pH	..	..	7·12 (0·18)	7·09 (0·04)	7·02 (0·3)
Methodology					
	Quasi-randomised unmasked	Quasi-randomised unmasked	Quasi-randomised unmasked	Randomised, masked to caregivers and assessors of outcome	Randomised, masked to caregivers and assessors of outcome
Long-term follow-up					
	No	No	Yes (paediatrician at 18–24 months to assess cerebral palsy and developmental milestones)	No	No

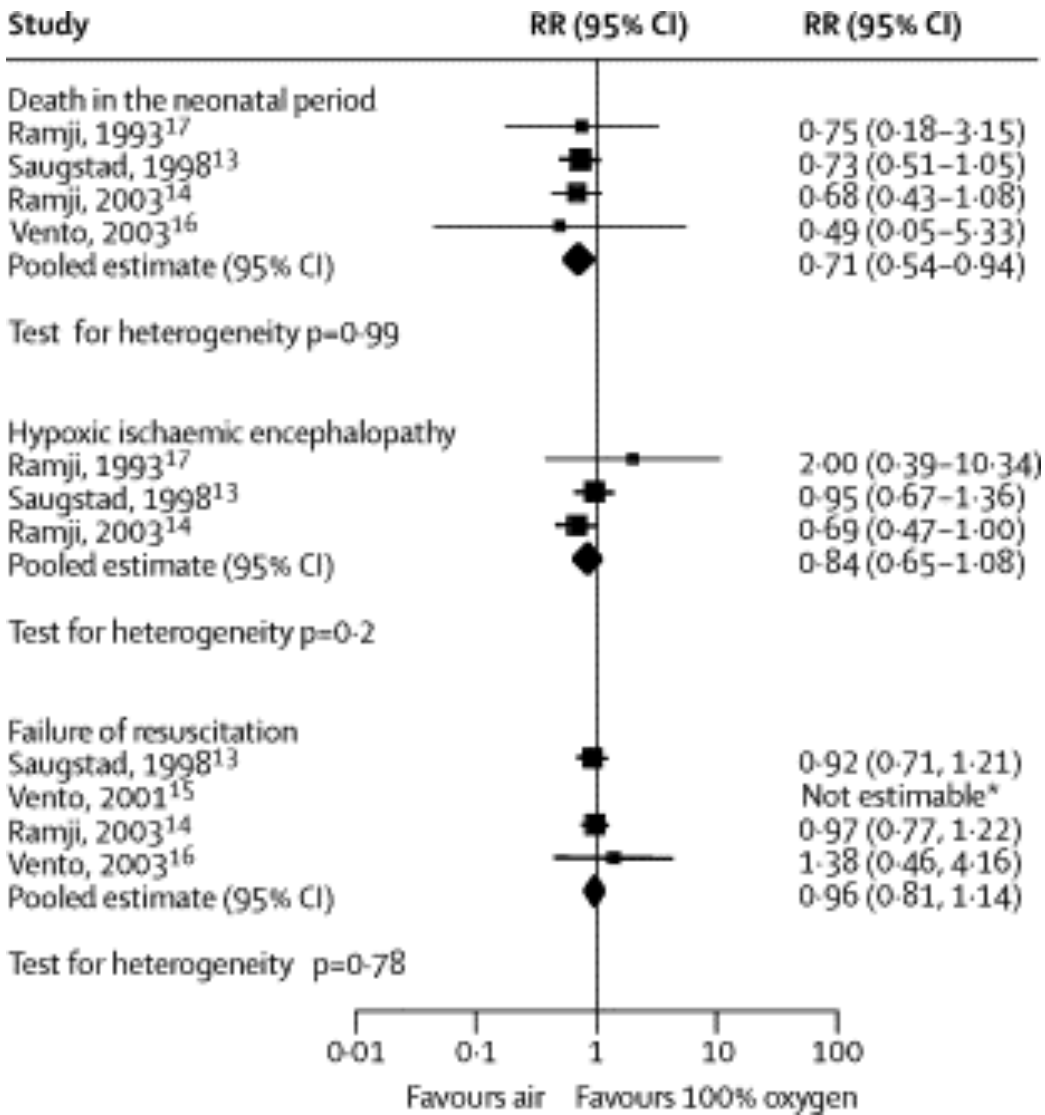
Data are mean (SD) unless otherwise indicated. HR=heart rate; bpm=beats per minute. *Median (95% CI).

Results of Trials

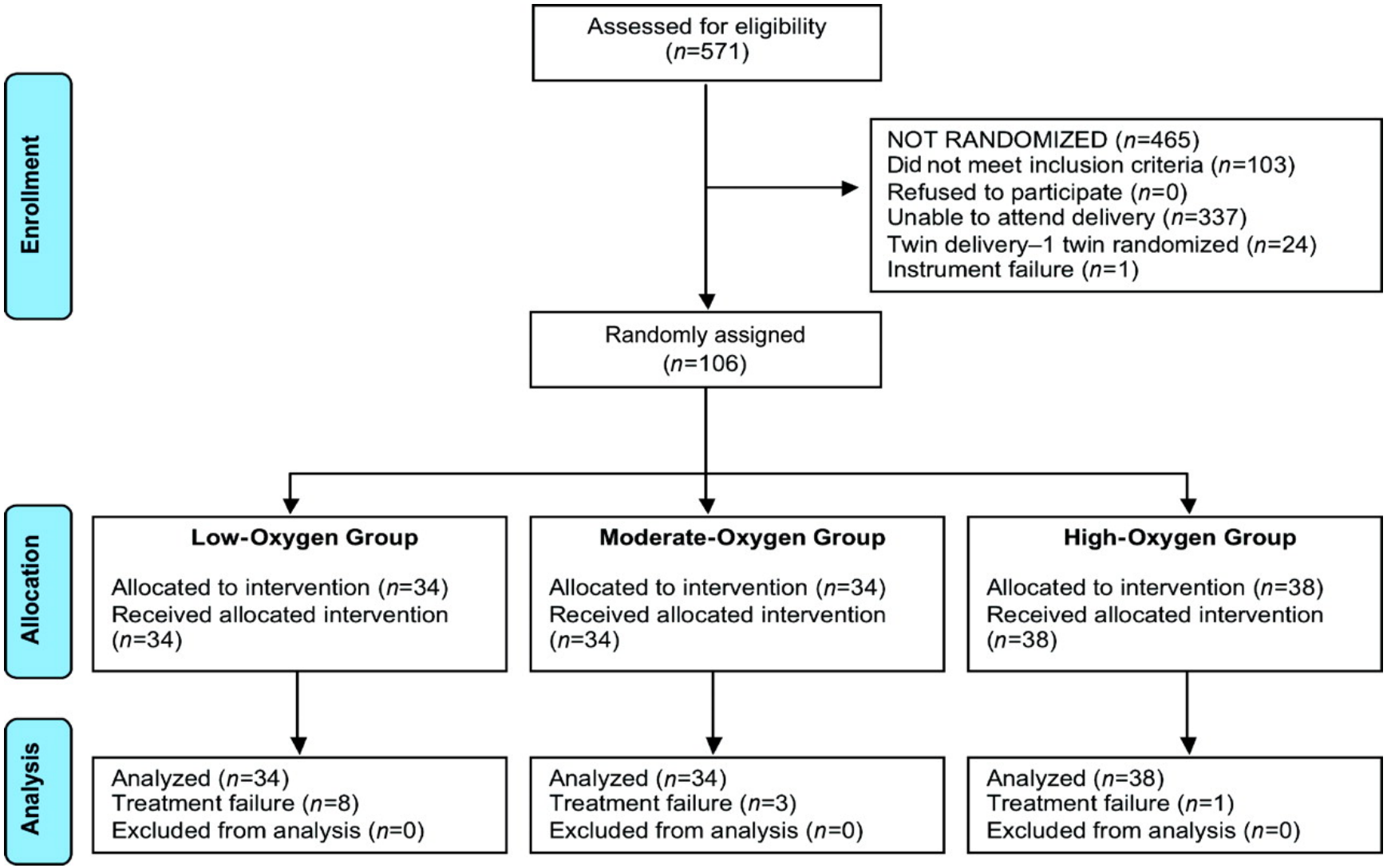
	Studies	Air	100% oxygen	RR (95% CI)	Risk difference (95% CI)	Number needed to treat
Death at latest follow-up*	4[13,14,16,17]	70/616	107/659	0·71 (0·54 to 0·94)	−0·05 (−0·08 to −0·01)	20
Death in first week	4[13,14,16,17]	65/616	94/659	0·75 (0·56 to 1·00)	−0·04 (−0·07 to 0·00)	
Cerebral palsy	1[19]	9/91	9/122	1·34 (0·55 to 3·24)	0·03 (−0·05 to 0·10)	
Not walking†	1[19]	10/91	13/122	1·03 (0·47 to 2·25)	0·00 (−0·08 to 0·09)	
No words†	1[19]	6/91	3/122	2·68 (0·69 to 10·44)	0·04 (−0·02 to 0·10)	
Abnormal development	1[19]	14/91	12/122	1·56 (0·76 to 3·22)	0·06 (−0·04 to 0·15)	
Time to first breath >3 minutes	1[13]	28/284	60/321	0·53 (0·35 to 0·80)	−0·09 (−0·14 to −0·03)	11
5-minute Apgar score <7	1[13]	71/288	102/321	0·78 (0·60 to 1·00)	−0·07 (−0·14 to 0·00)	
HIE Sarnat grade[8] 2 or 3	3[13,14,17]	87/540	112/584	0·84 (0·65 to 1·08)	−0·03 (−0·07 to 0·01)	
Failure of resuscitation	4[13,15,16,17]	162/593	182/638	0·96 (0·81 to 1·14)	−0·01 (−0·06 to 0·04)	

Data are number. HIE=hypoxic ischaemic encephalopathy. NNT=number needed to treat (calculated for significant results). *Deaths reported in first week[14,16,17] or in first 28 days of life.[13] †In those followed-up at 18–24 months.

Meta-analysis

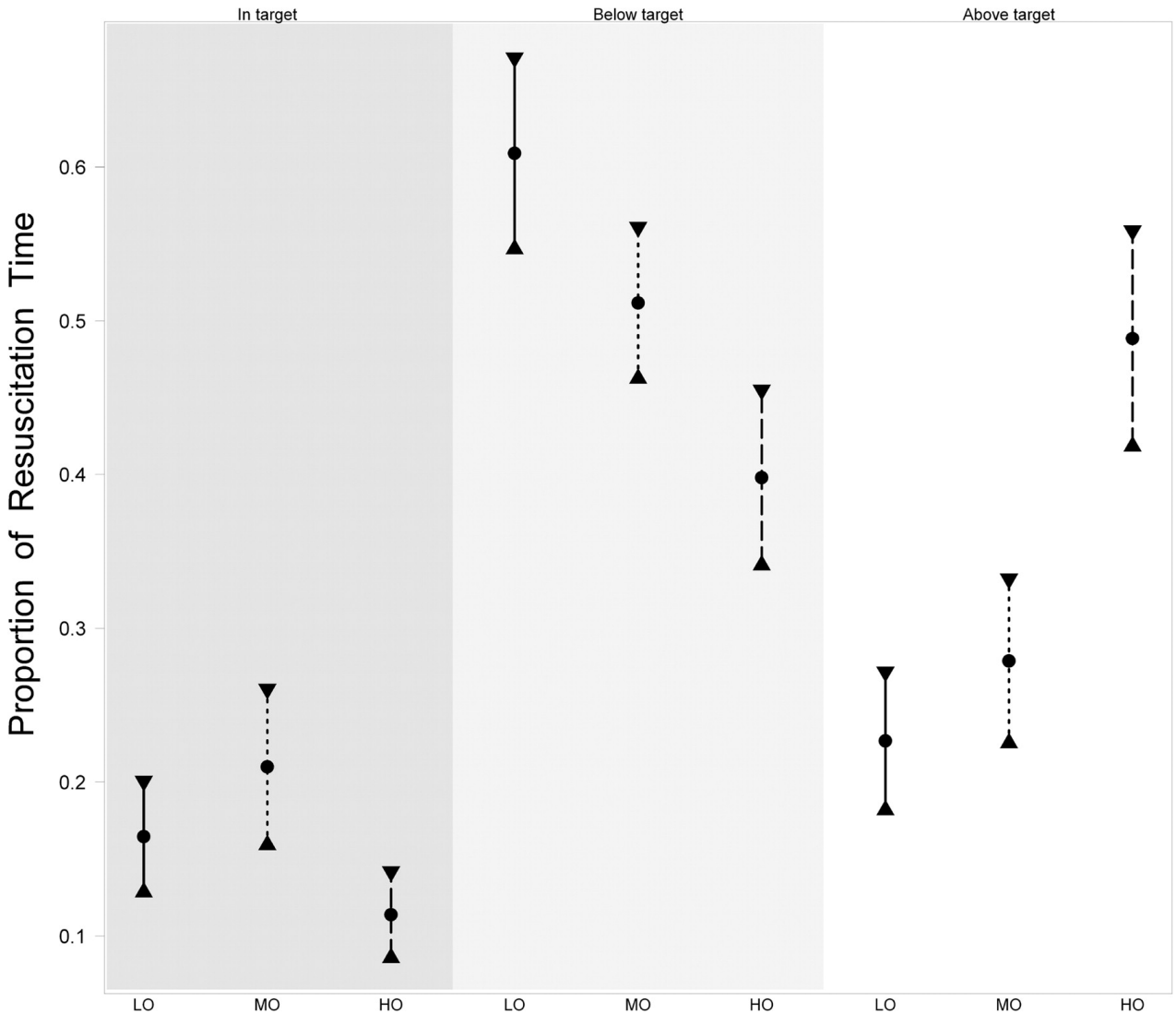


O2 Use in Premies



PEDIATRICS 128:Issue 2, 2011

O2 Use in Premies



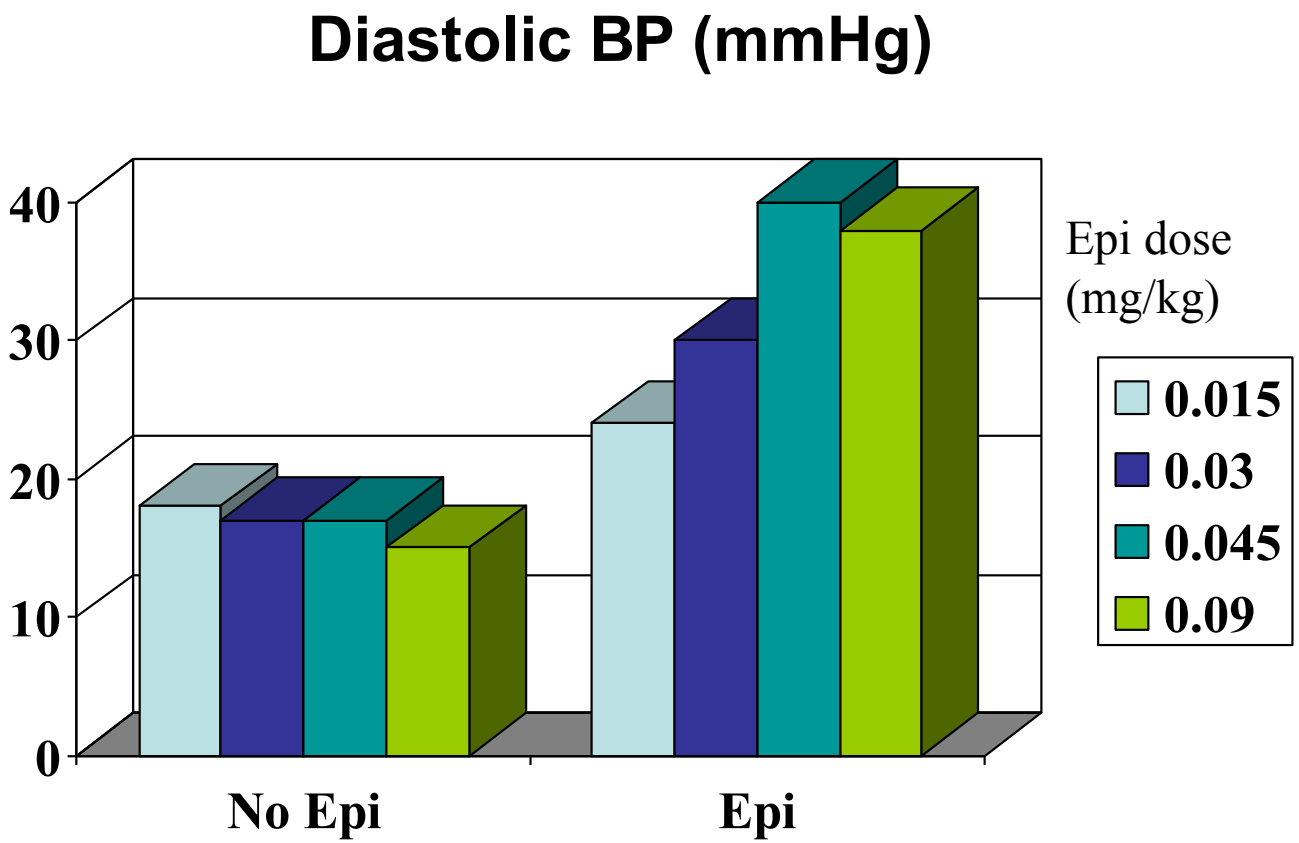
Origin of Present Dosage of Epinephrine

- Redding and Pearson originally used 1 mg in dogs weighing approximately 10 kg
  - Equates to 0.1 mg/kg
- Adult recommendations are 0.5-1.0 mg, possibly based on the dose used by Redding
  - In a 70 kg patient, this would equate to 0.007-0.014 mg/kg.
- Current dosage recommendation in neonates is 0.01-0.03 mg/kg, probably extrapolated from adult dosing guidelines.

Problem

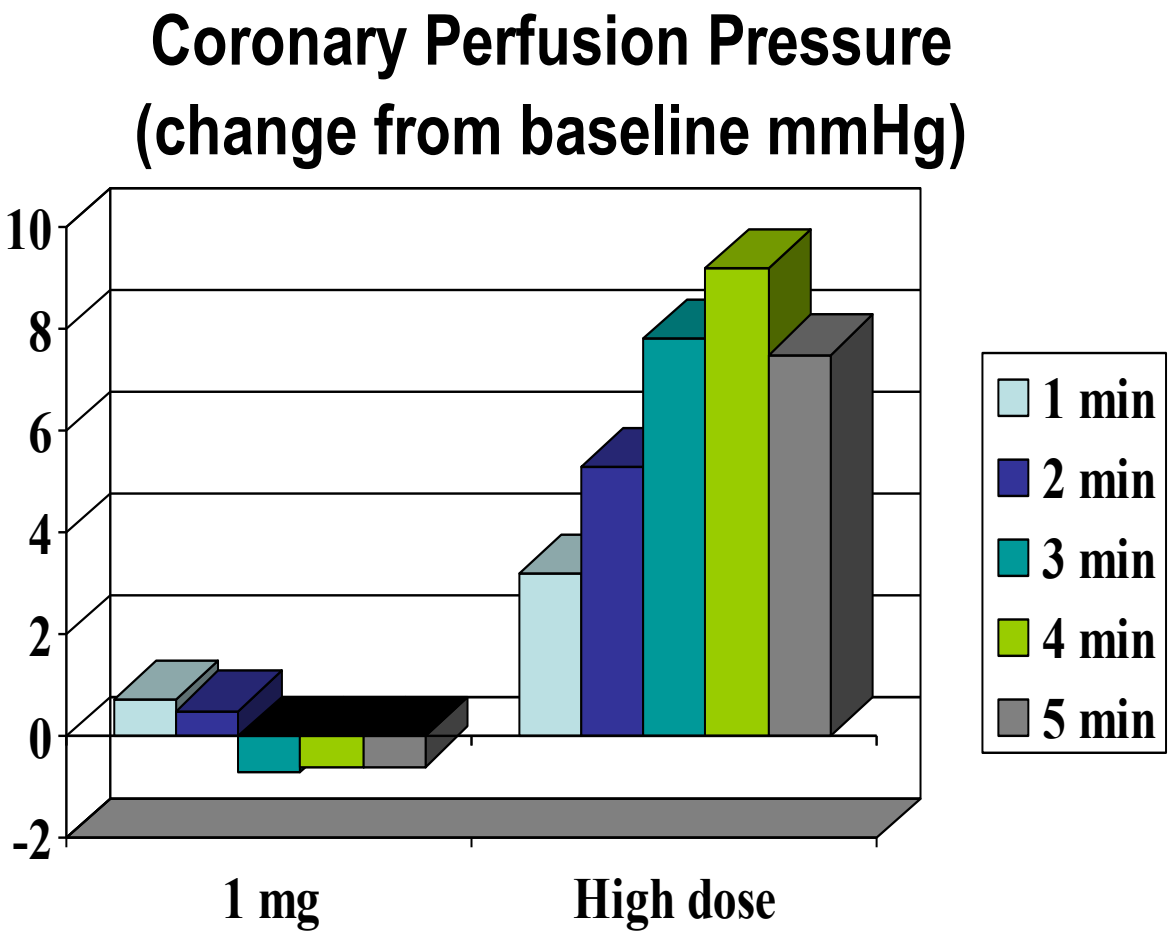
If the dose of epinephrine used by Redding et al has merit, then the current recommendations may lead to serious underdosing in adults and, by extrapolation, in children.

“Optimum” Dose of Epinephrine



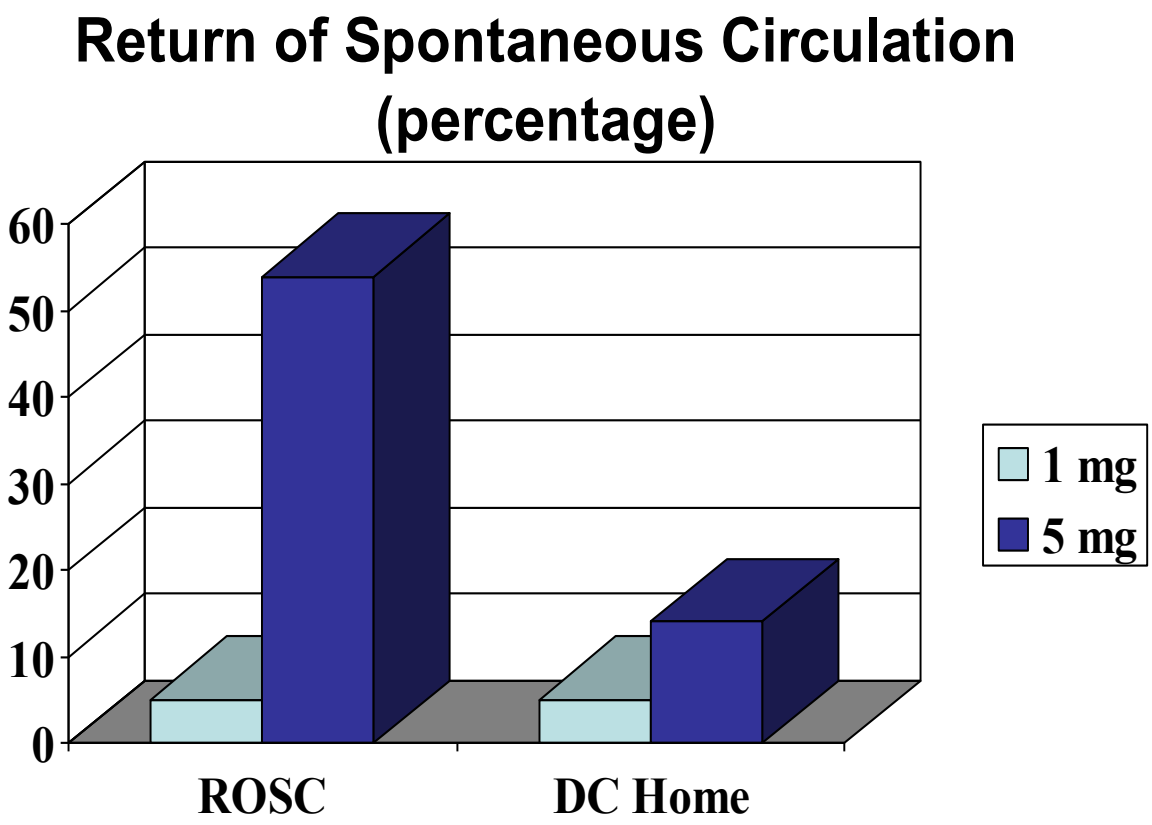
Linder et al: *Am J Emerg Med* 1991; 9:27-31

“Optimum” Dose of Epinephrine



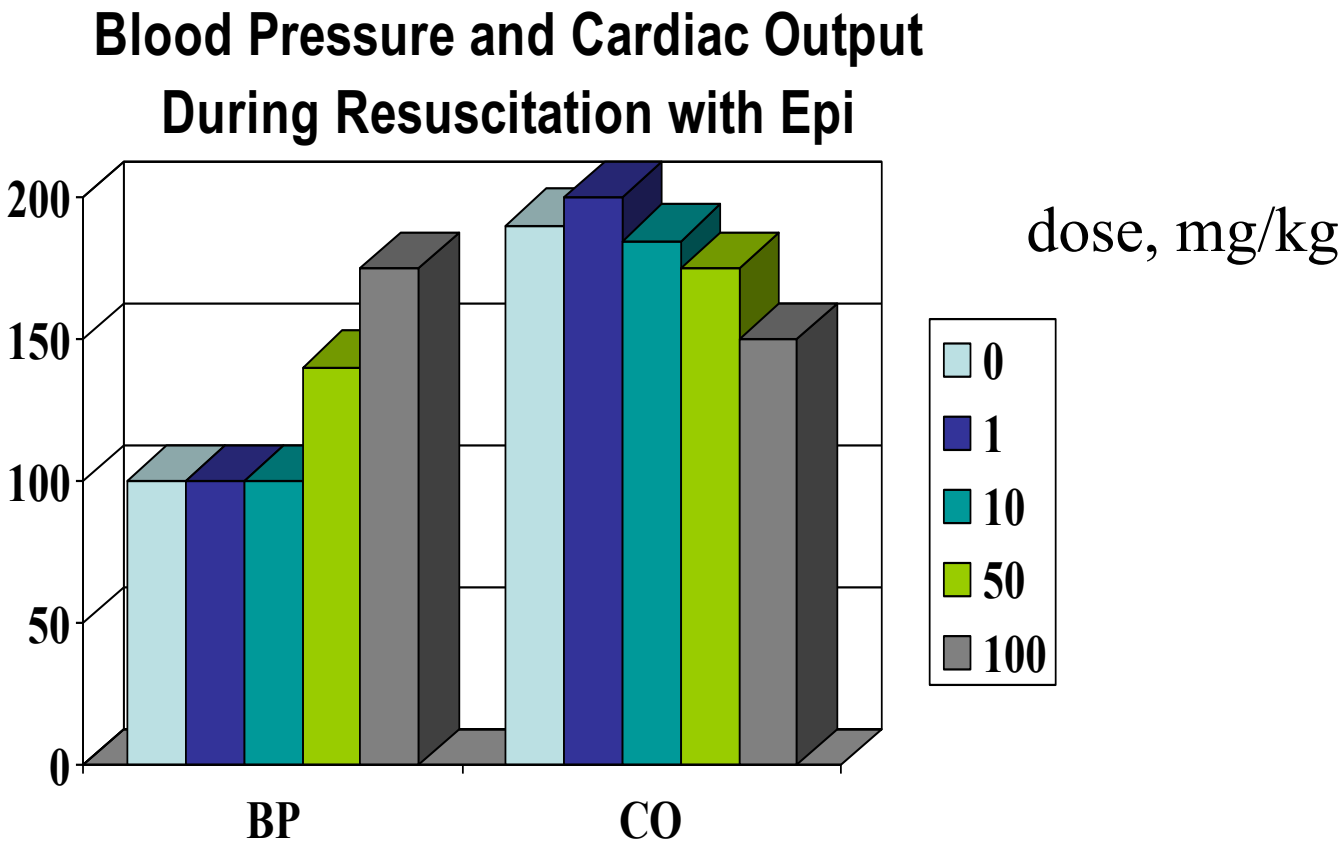
Paradis et al; *JAMA* 1991

“Optimal” Dose of Epinephrine



Linder et al: 1991 *Acta Anaesthesiol Scand*

“Optimal” Dose of Epinephrine



Burchfield et al *Resuscitation* 1993

Complications of Epinephrine in Neonatal Resuscitation

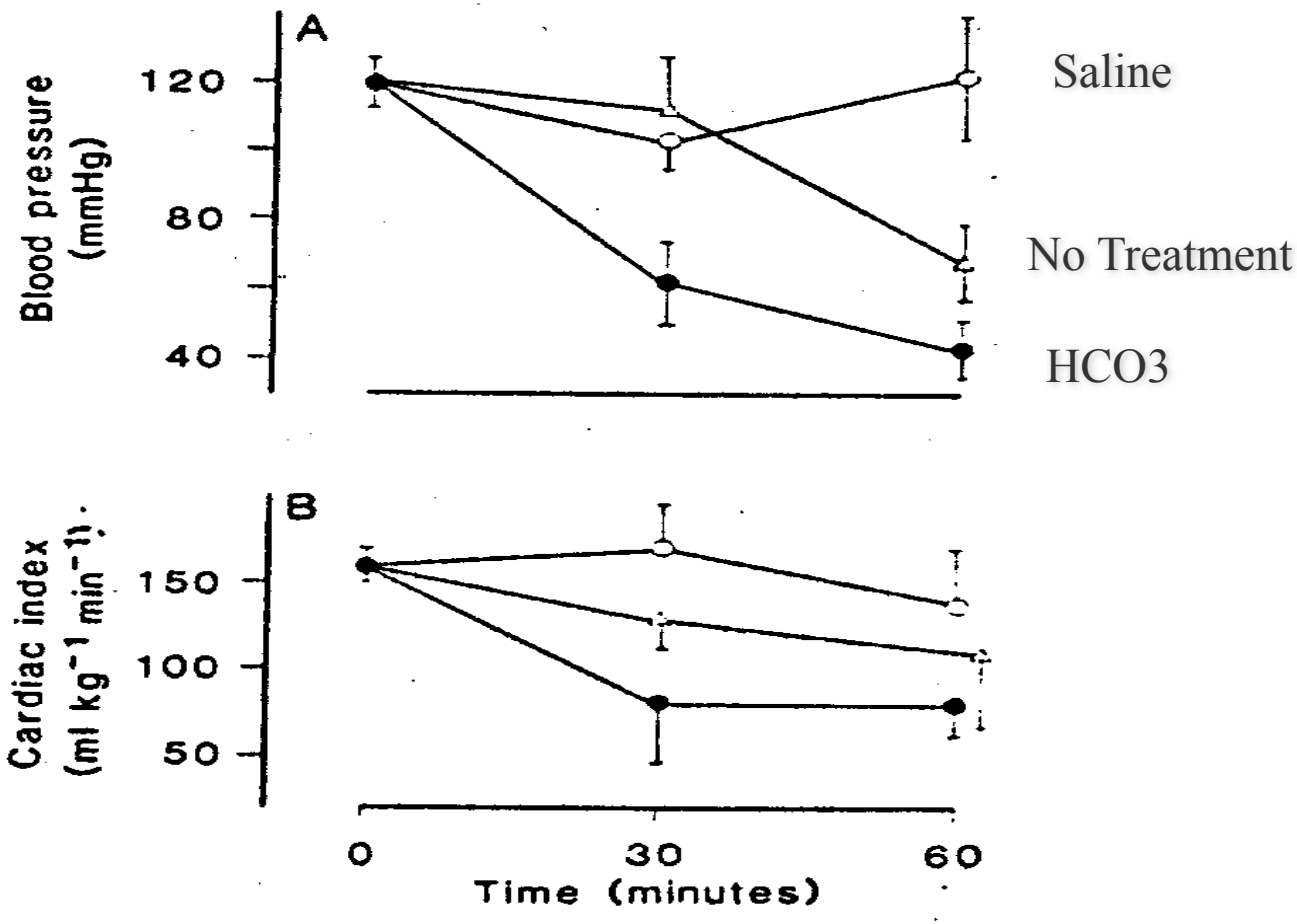
- Myocardial necrosis
- Mechanical injury to the mitral valve.
- Subendocardial hemorrhage
- Pulmonary edema
- Ischemic necrosis of the liver
- Cortical hemorrhage in the kidney
- Ischemic enterocolitis

Karch SB: *Am J Forensic Med Path* 1990

Present Recommendations for Epinephrine Use

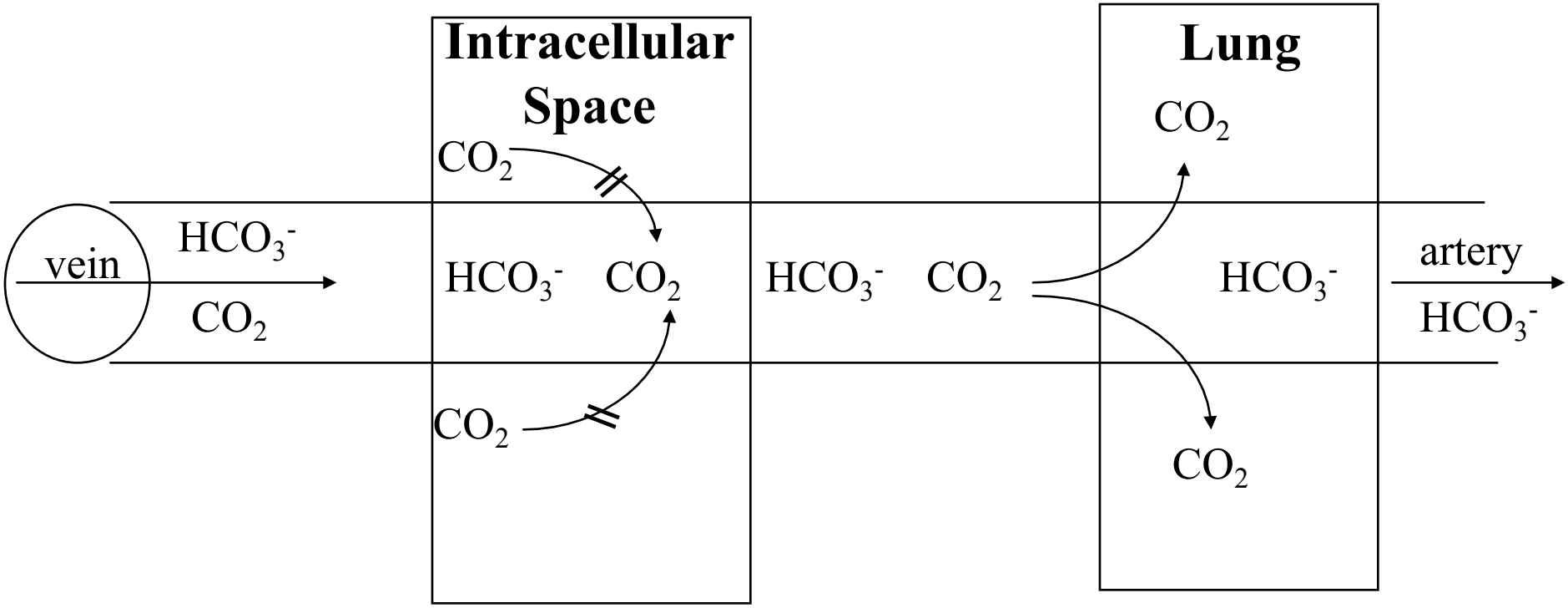
- Heart rate <60 beats per min despite 30 sec of CPR.
- Heart rate =0.
  - IV: 0.1-0.3 mL/kg of 1:10,0000 (0.01-0.03 mg/kg)
- Endotracheally, 1 mL/kg (max of 3 mL)
- Repeat every 3-5 min

Sodium Bicarbonate in Resuscitation



Graf et al, *Science* 227:745-756, 1985

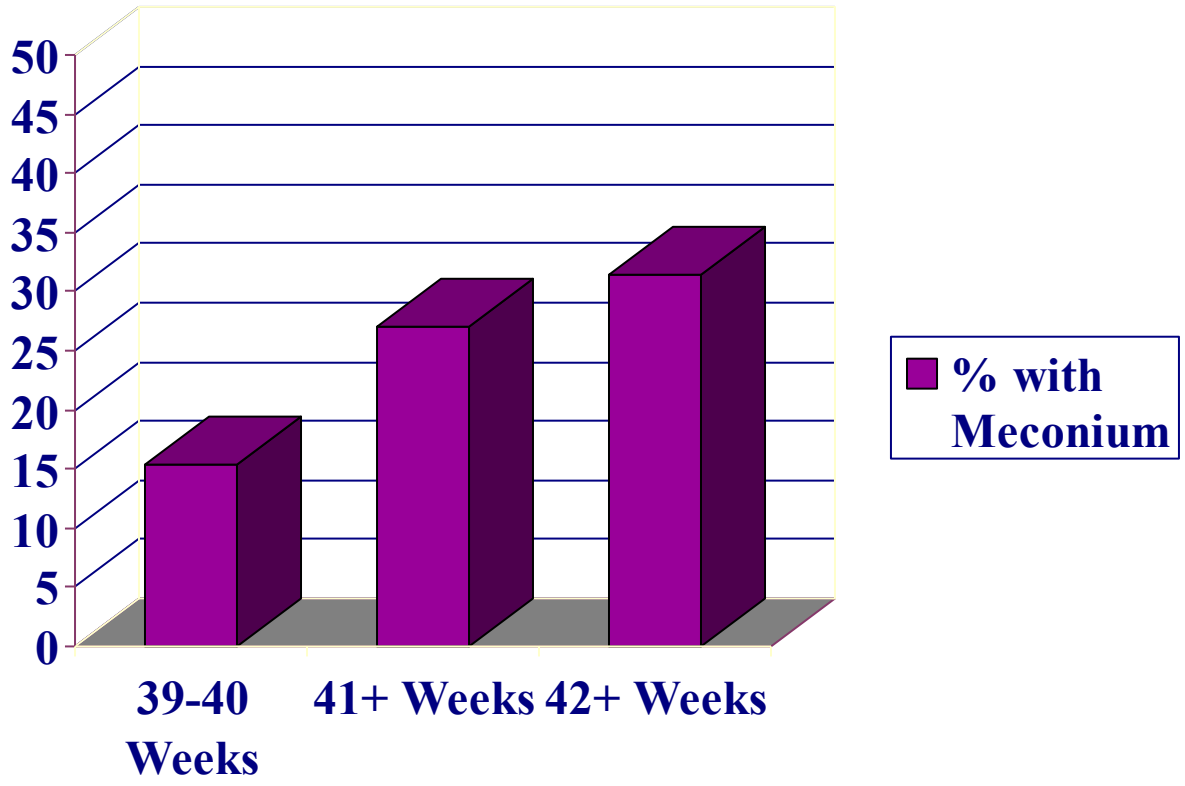
$$H^+ + HCO_3^- \leftrightarrow H_2CO_3 \leftrightarrow H_20 + CO_2$$



In-Utero Passage of Meconium

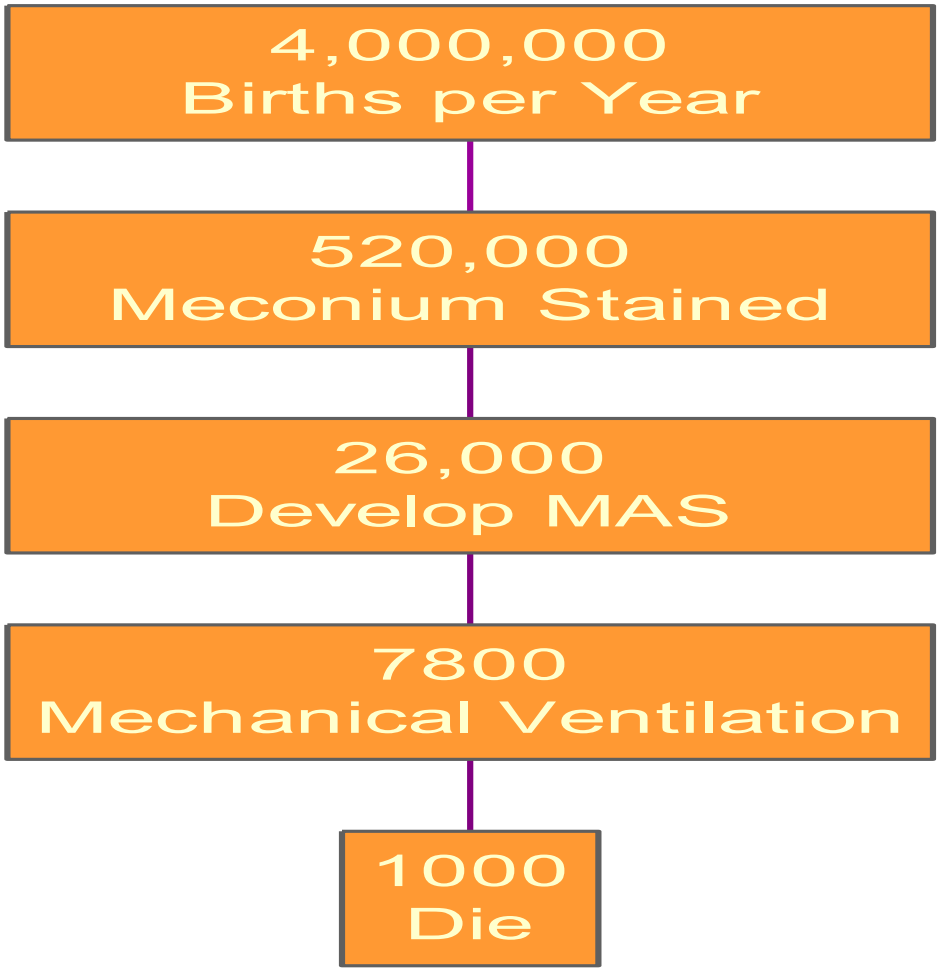
- **Associated with fetal hypoxia**
  - **Intestinal ischemia followed by hyperperistalsis (Van Liere, 1942)**
  - **Meconium and reduced umbilical venous oxygen (Walker, 1954)**
  - **Autopsy studies of fetal asphyxia showing no meconium in intestine (White, 1955)**

In-Utero Passage of Meconium Normal Physiology

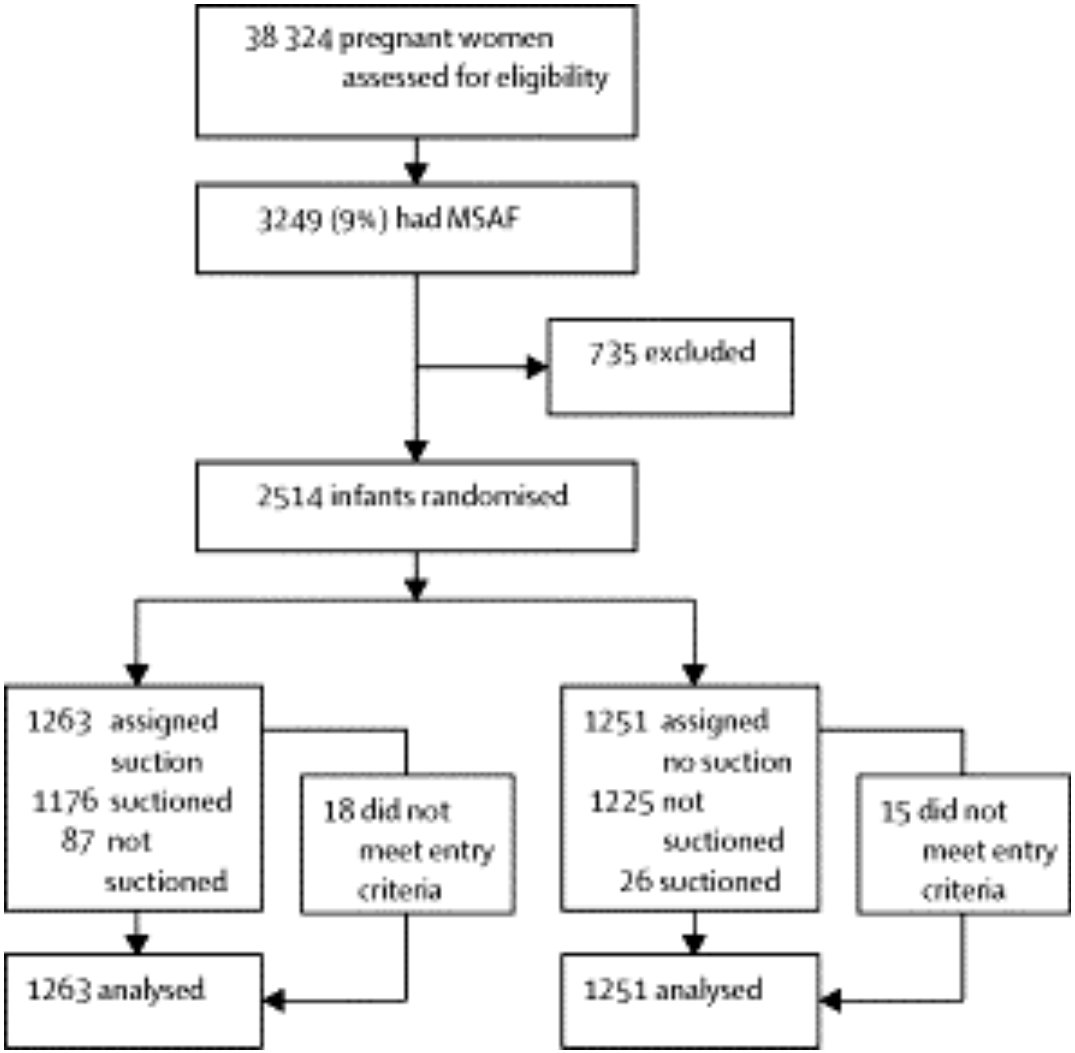


Usher, 1988

Meconium Aspiration Epidemiology



Suction on Perineum?

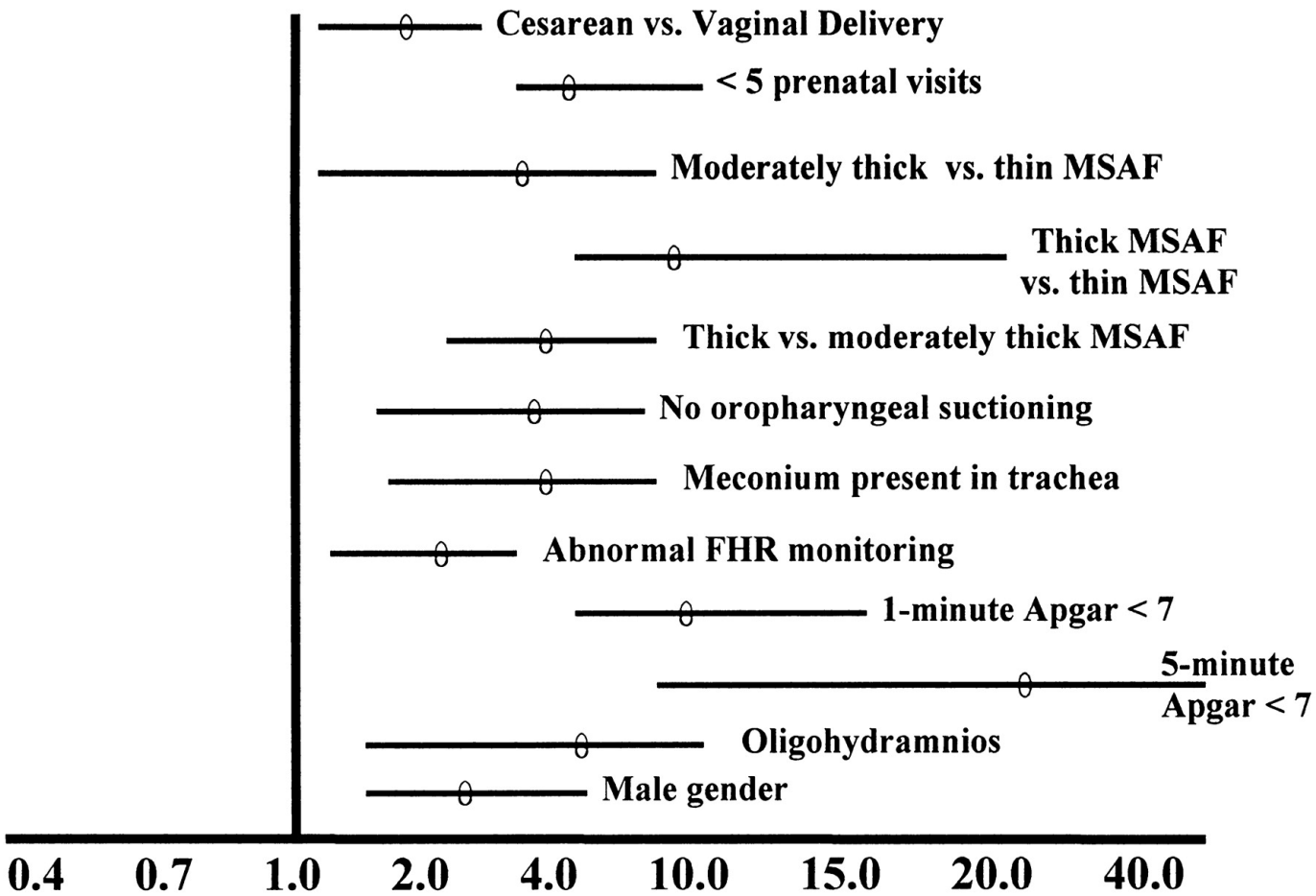


Results

	Suction (n=1263)	No suction (n=1251)	Relative risk (95% CI)	p*
MAS	52 (4%)	47 (4%)	0·9 (0·6–1·3)	··
Need for mechanical ventilation for MAS	24 (2%)	18 (1%)	0·8 (0·4–1·4)	··
Mortality	9 (1%)	4	0·4 (0·1–1·5)	··
Need for endotracheal intubation, suction and PPV in the delivery room	106 (8%)	113 (9%)	1·1 (0·8–1·4)	···
Other respiratory disorders	61 (5%)	79 (6%)	1·3 (0·9–1·8)	··
Pneumothorax	3	3	1·0 (0·2–5·0)	··
Range of 1-min Apgar scores				
0–3	22 (2%)	15 (1%)	··	0·29
4–6	65 (5%)	73 (6%)		
7–10	1174 (93%)	1163 (93%)		
Unknown	2	0		
Range of 5-min Apgar scores				
0–3	0	0	··	0·29
4–6	13 (1%)	5		
7–10	1230 (97%)	1231 (98%)		
Unknown	2	0		
Duration of oxygen threatment (days) in infants with MAS (mean, SD)	5·7, 8·8 (n=52)	5·1, 7·1 (n=47)	··	0·91
Duration of mechanical ventilation (days) in infants with MAS (mean, SD)	5·1, 4·9 (n=21)	4·2, 4·6 (n=14)	··	0·49
Duration of hospital care (days) in infants with MAS (mean, SD)	8·2, 10·7 (n=50)	9·0, 8·6 (n=43)	··	0·14

Lancet 2004, 364: 597-602

Risks for MAS

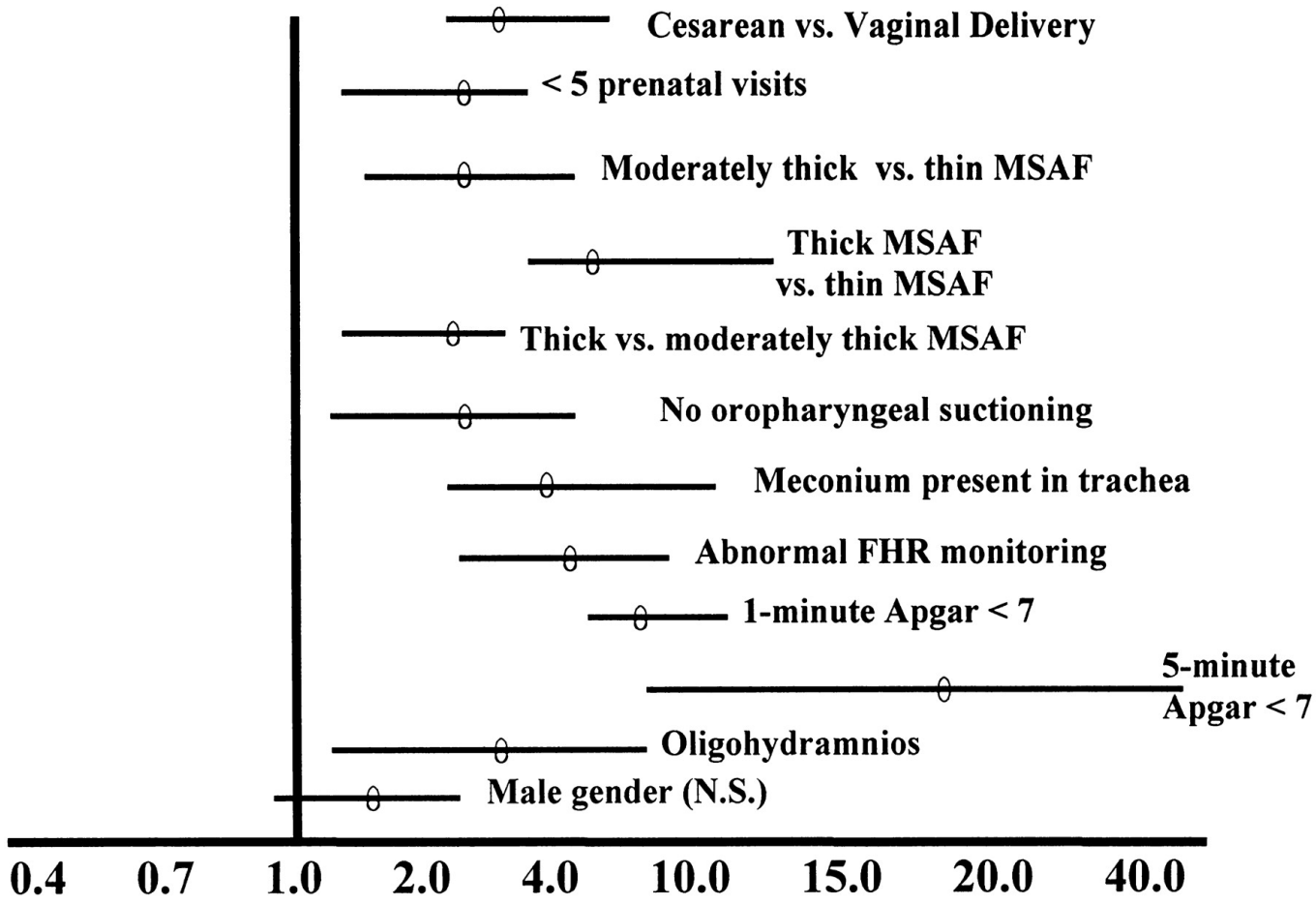


Odds Ratios and 95% Confidence Intervals

Wiswell, T. E. et al. Pediatrics 2000;105:1-7

PEDIATRICS®

Risks for all respiratory distress, not MAS



Odds Ratios and 95% Confidence Intervals

Wiswell, T. E. et al. Pediatrics 2000;105:1-7

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ET Suction of Meconium

TABLE 2
Infant Population Characteristics

	Intubate (n = 1051)	Expectant (n = 1043)	Significance
Racial background			
White	483 (46.0%)	483 (46.3%)	NS
Black	234 (22.3%)	251 (24.1%)	NS
Hispanic	253 (24.1%)	233 (22.3%)	NS
Asian	73 (6.9%)	68 (6.5%)	NS
Other	8 (0.8%)	8 (0.8%)	NS
Gender			
Male	530 (50.4%)	523 (50.1%)	NS
Female	521 (49.6%)	520 (49.9%)	NS
Range of 1-min Apgar scores			
1-3	36 (3.5%)	14 (1.3%)	P = .0018
4-6	139 (13.2%)	51 (4.9%)	P = .0001
7-10	876 (83.3%)	978 (93.8%)	P < .0001
Range of 5-min Apgar scores			
1-3	0 (0%)	0 (0%)	NS
4-6	14 (1.3%)	8 (0.8%)	NS
7-10	1037 (98.7%)	1035 (99.2%)	NS
Occurrence of MAS (n = 62)			
Overall	34/1051 (3.2%)	28/1043 (2.7%)	NS
Thin MSAF	5/447 (1.1%)	2/453 (0.4%)	NS
Moderately-thick MSAF	7/301 (2.3%)	6/307 (2.0%)	NS
Thick MSAF	22/303 (7.3%)	20/283 (7.1%)	NS
Occurrence of other respiratory disorders (n = 87)			
Overall	40/1051 (3.8%)	47/1043 (4.5%)	NS
Thin MSAF	6/447 (1.3%)	8/453 (1.8%)	NS

Wiswell, T. E. et al. Pediatrics 2000;105:1-7

Discontinuation of Resuscitation

- After 10 minutes of continuous and adequate resuscitative efforts, discontinuation of resuscitation may be justified if there are no signs of life (no heart beat and no respiratory effort).

Summary

- Newborn resuscitation has little direct evidence based practices
- NRP has been helpful in establishing guidelines "Everyone singing from the same sheet of music…"
- Because it is published in NRP **does not** mean that we should stop questioning and trying to improve