MASTER COMPLEMENTAIRE EN PEDIATRIE

MACCS 1ère et 2ème Années

3LS1 2023-2024

Detresses respiratoires

Ventilation

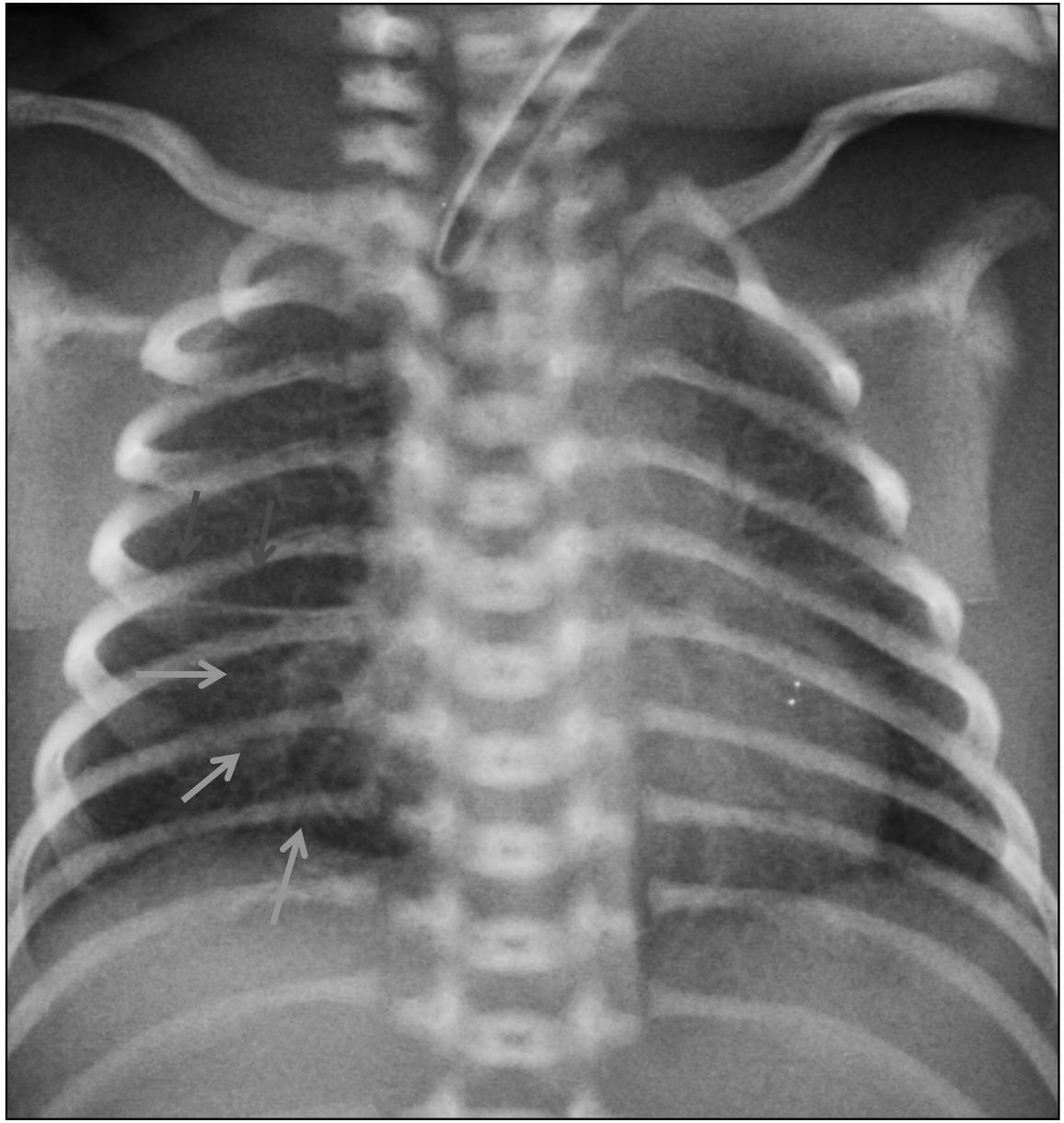
Olivier Danhaive

Tachypnée transitoire du nouveau–né (TTN)

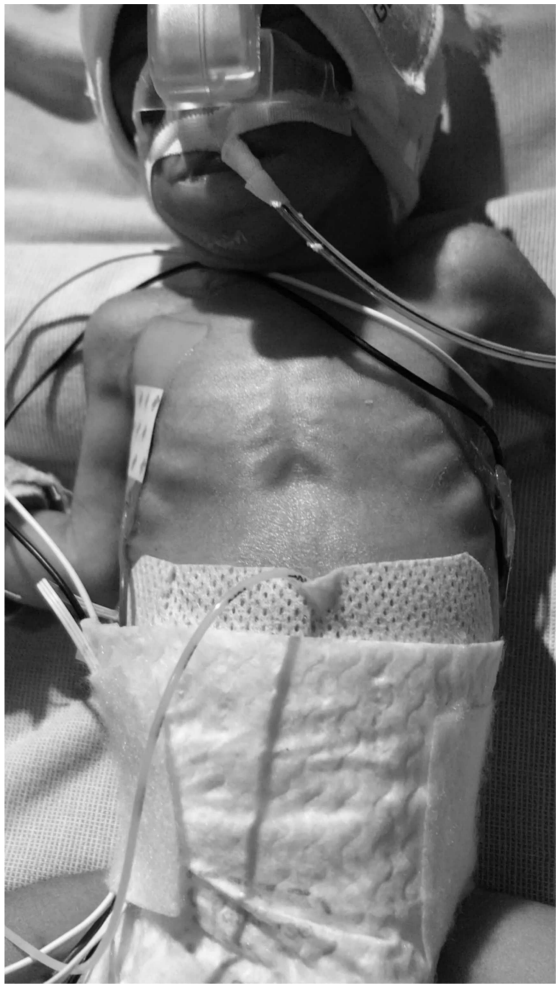
Mécanisme: persistence du liquide pulmonaire fetal

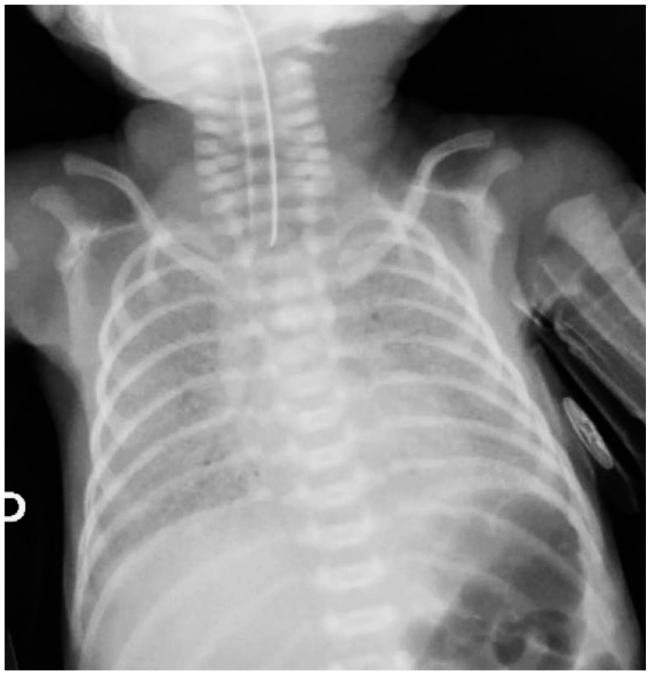
+ frequent chez prématurés tardifs (32-36 semaines)

- Volume pulmonaire normal à excessif
- Vascularisation périhilaire accentuée
- Liquide dans les scissures interlobaires
- Transitoire: se résout habituellement en <72h
- Traitement: support respiratoire



Syndrôme de détresse respiratoire (RDS)





RX:

- Opacité diffuse “en verre dépoli”
- Bronchogrammes aériques
- Volumes pulmonaires réduits

Pathophysiologie:

Déficit du surfactant lié à l’immaturité

+ frequent <28 semaines

Signes et symptômes:

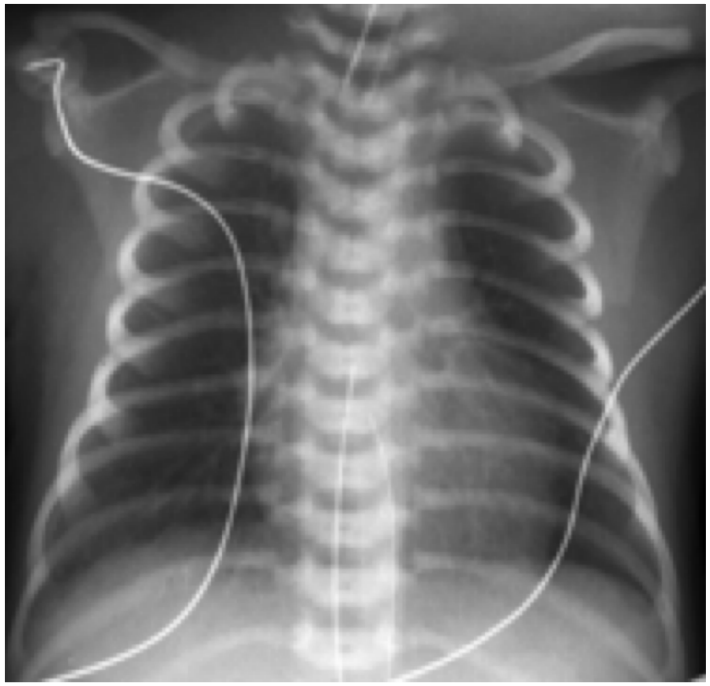
- Hypoxémie
- Hypercapnie
- Détresse respiratoire

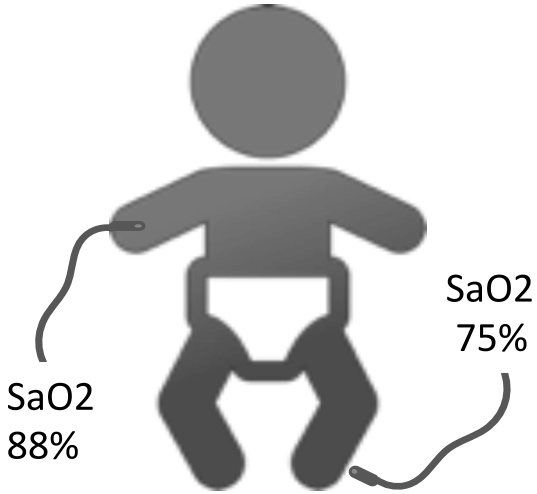
Traitement:

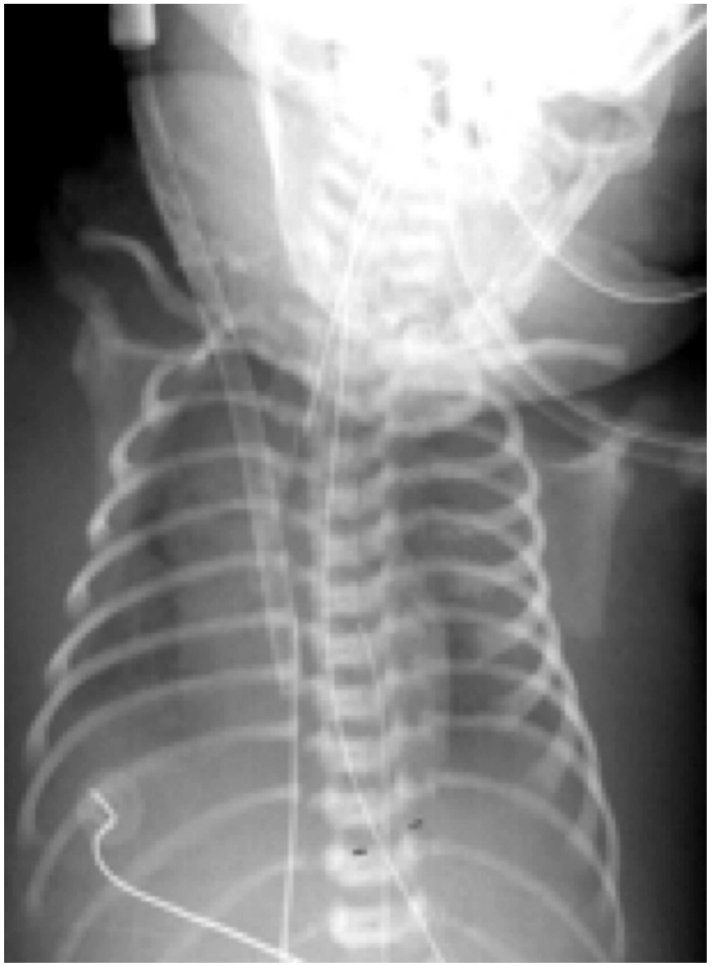
- Maturation pulmonaire fétale
  - betamethasone/dexamethasone 12mg x2 IM <7 jours de l’accouchement si <34 sem)
- Support respiratoire
- Surfactant
- Prévention des lésions pulmonaires secondaires:
  - Limiter oxygéne (Sat 92-95%)
  - Limiter pressions et volumes de la ventilation (hypercapnie persmissive tolérée – pCO_2 50-60)

Tatiana

Retard de croissance intrautérin- Césarienne 37w,
PN 2100g







Naissance: liquid meconial
Aspiration, ventilation, FiO2 100%,
SaO2 80:
H24: HFOV – FiO2 80% - iNO 20ppm

Echocardio: pression VD 60mmHg
Canal artériel shunt D>G

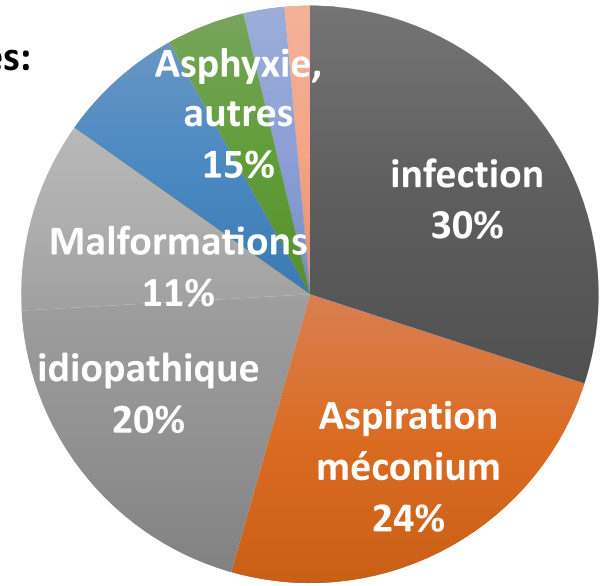
h120: ECMO

Hypertension artérielle pulmonaire (HTAP)

Persistent Pulmonary Hypertension of the Newborn in Late Preterm and Term Infants in California

Martina A. Steurer, MD, MAS,[a,b] Laura L. Jelliffe-Pawlowski, PhD, MS,[b,c] Rebecca J. Baer, MPH,[c,d] J. Colin Partridge, MD, MPH,[a] Elizabeth E. Rogers, MD,[a] Roberta L. Keller, MD[a]

Causes:



Steurer M et al. Pediatrics. 2017;139(1):e20161165

Incidence: 1-2 ‰

Mortalité: 7% (selon cause)

Présentation:

- hypoxémie réfractaire à l'oxygène
- Gradient de saturation pré/post-ductal

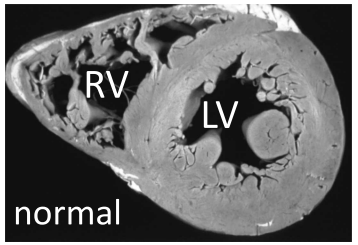
Facteurs de risque:

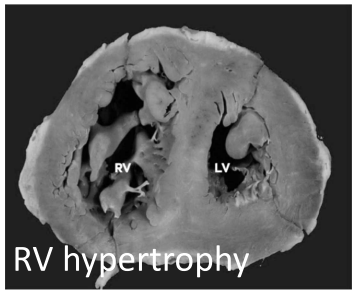
- Césarienne, absence de travail
- Prématurité, petit poids de naissance
- Insuffisance placentaire (retard de croissance intra-utérin, oligohydramnios, meconium…)
- Postmaturité ≥42 semaines
- Diabète maternel, poids de naissance excessif pour l'âge
- Tabac, drogues, médicaments (ISRS,AINS…)
- Infection (chorioamnionite, sepsis GBS…)

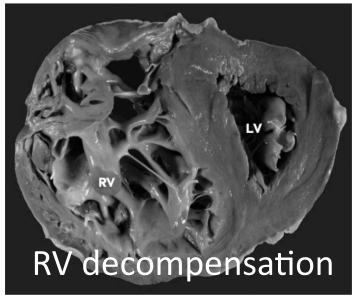
Traitement:

- Ventilation assistée
- Support hémodynamique
- Vasodilatateurs pulmonaires (oxide nitrique, sildenafil, epoprostenol, bosentan)

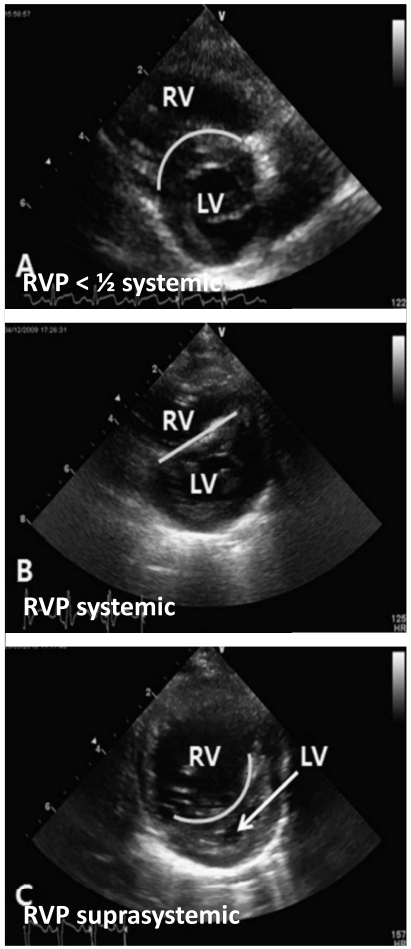
Echocardiography diagnosis of pulmonary hypertension in the newborn:

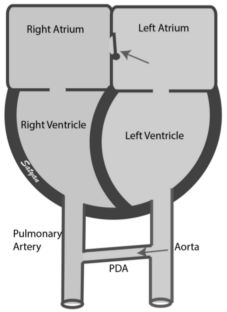


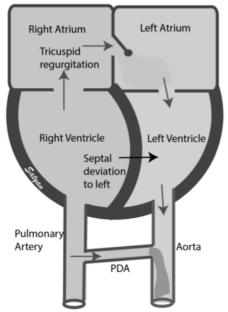




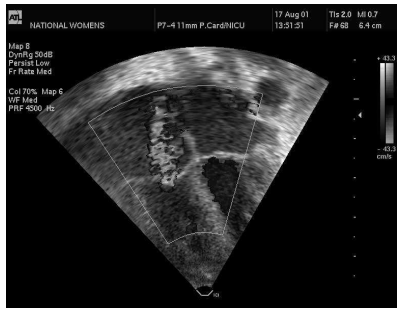
IV septum shape (2D)

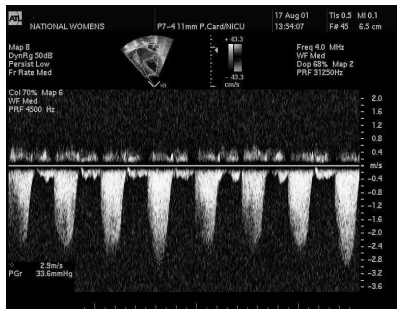




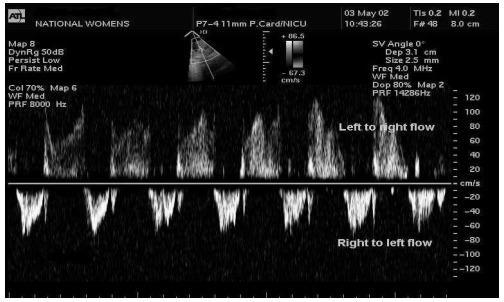


Tricuspid regurgitation





PDA flow



Kim GB. Korean J Pediatr 2010;53:688-93

Postnatal respiratory failure

Lung hypoplasia
Malformations

RDS

TTN

pneumonia

MAS

Pulmonary hemorrhage

neoARDS

Sepsis, NEC

asphyxia

aspiration

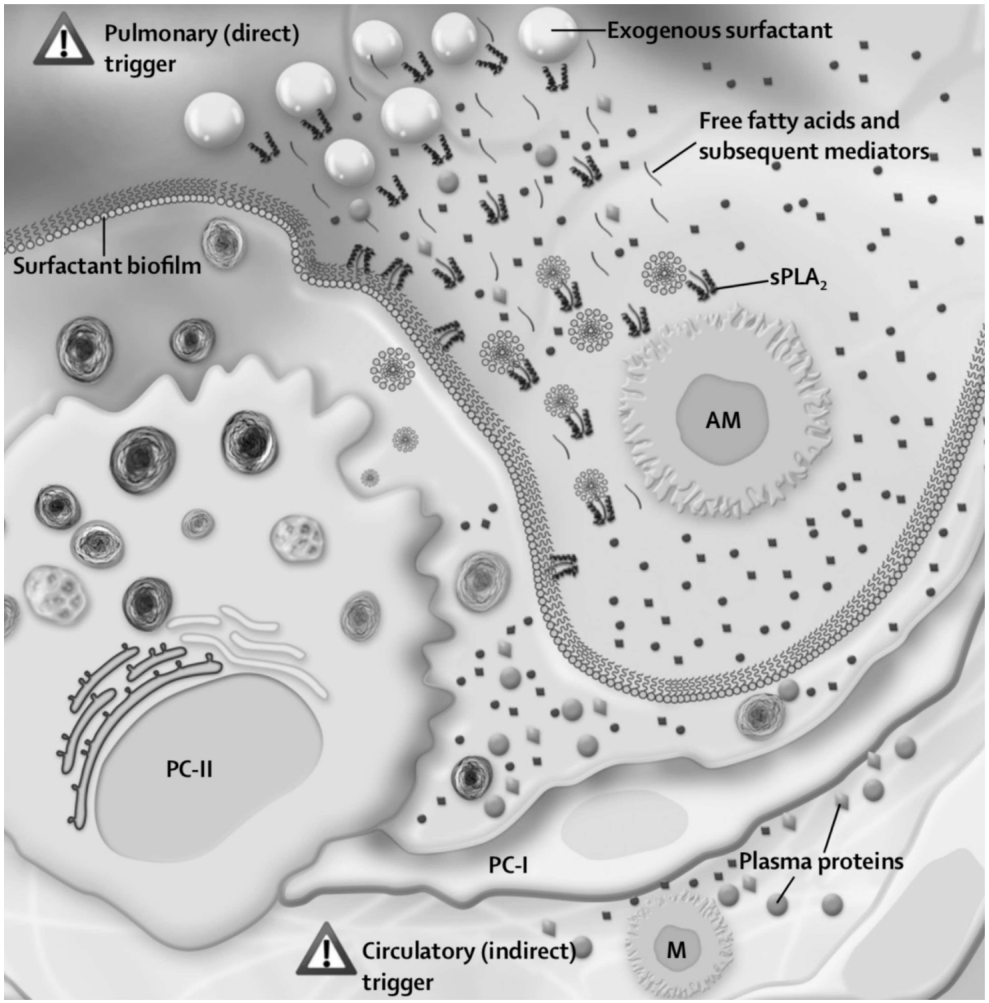
The Montreux definition of neonatal ARDS: biological and clinical background behind the description of a new entity

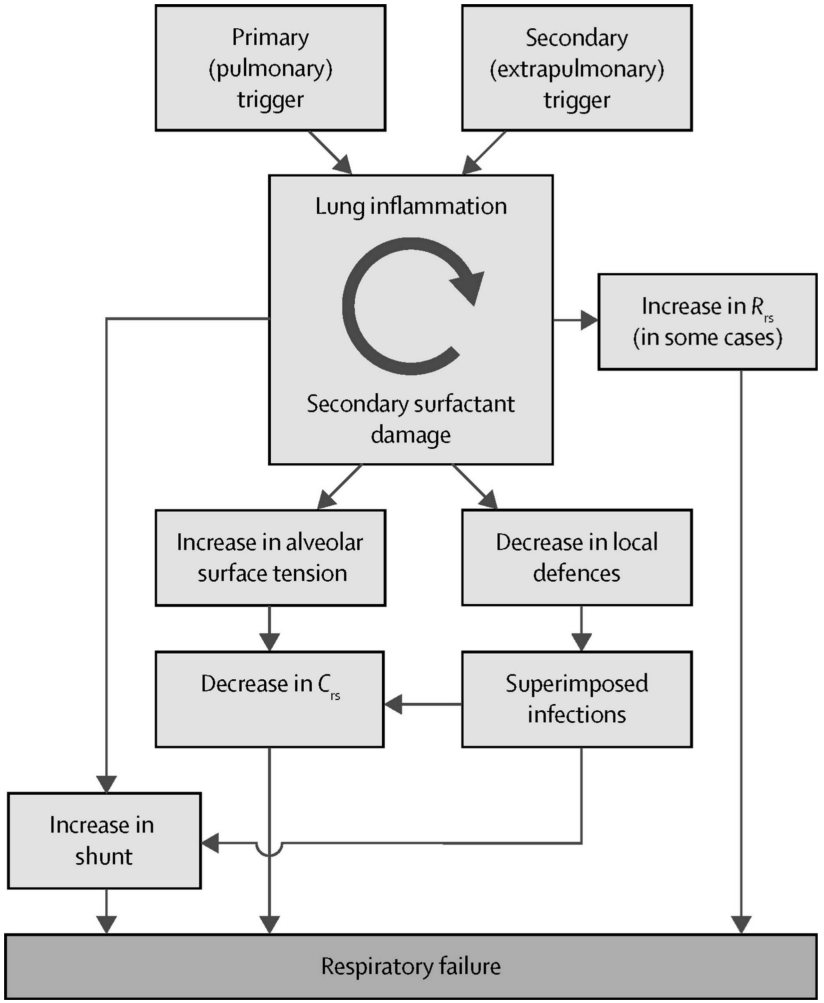
Daniele De Luca, Anton H van Kaam, David G Tingay, Sherry E Courtney, Olivier Danhaive, Virgilio P Carnielli, Luc J Zimmermann, Martin C J Kneyber, Pierre Tissieres, Joe Brierley, Giorgio Conti, Jane J Pillow, Peter C Rimensberger

Proposed criteria for nARDS	
Timeframe	Acute onset (ie, within one week) from a known or suspected clinical insult
Exclusion	RDS, TTN, or congenital anomalies as a primary current acute respiratory condition
Lung imaging	Diffuse, bilateral, and irregular opacities or infiltrates, or complete opacification of the lungs, which are not fully explained by local effusions, atelectasis, RDS, TTN, or congenital anomalies
Origin of oedema	Absence of congenital heart disease explaining the oedema (this includes ductus arteriosus with pulmonary overflow if no acute pulmonary haemorrhage exists). Echocardiography is needed to verify the origin of oedema.
Hypoxemia	Oxygenation deficit expressed as OI: • Mild ARDS: 4≤OI<8 • Moderate ARDS: 8≤OI<16 • Severe ARDS: OI≥16

De Luca et al. Lancet Respir Med 2017; 5: 657–66

Mechanism of disease



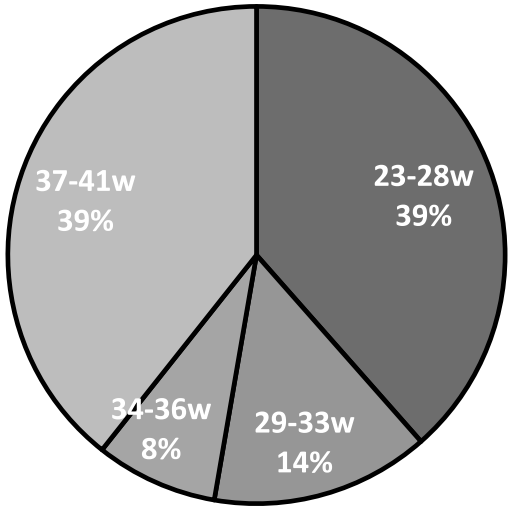


Similar to adult and pediatric ARDS

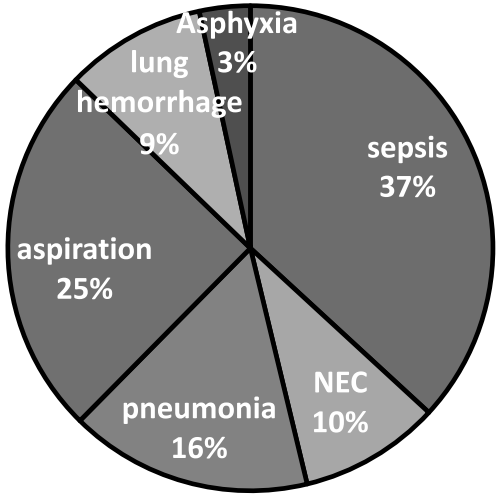
nARDS respiratory support: state of the art

- Prospective multicenter international cohort study
- 15,916 neonates admitted during the study period: prevalence of 1.5% (1-5%)
- 239 cases from 15 level III/IV NICUs 6/2015 - 5/2019

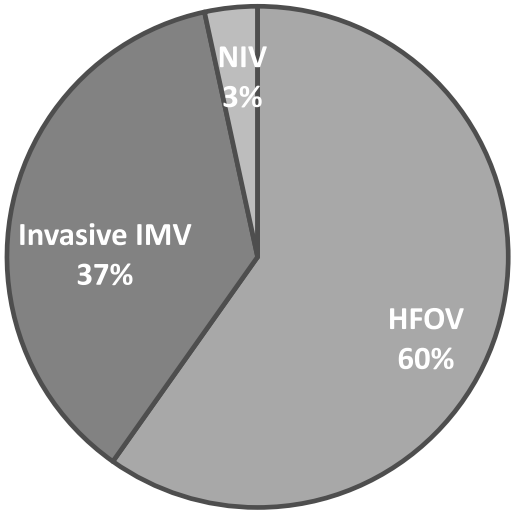
Gestational age



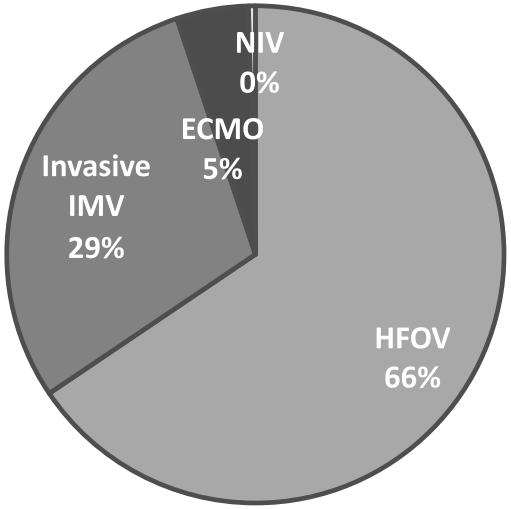
Cause/trigger



Initial ventilation



Peak ventilation



- Surfactant was used in 57% of infants (51% <28w,; 58% 28-32w; 63% 33-36w; 62% ≥37w)
- The study does not compare outcomes between the infants treated with surfactant and those not
- No conclusion can be drawn on surfactant efficacy in neoARDS

De Luca et al. Ped Crit Care Med 2022

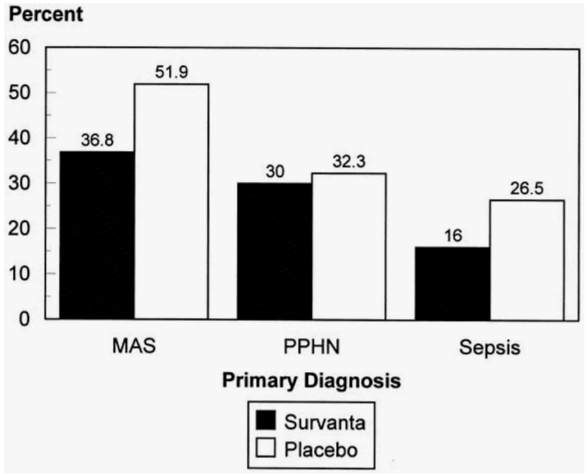
nARDS and surfactant

Multicenter study of surfactant (beractant) use in the treatment of term infants with severe respiratory failure

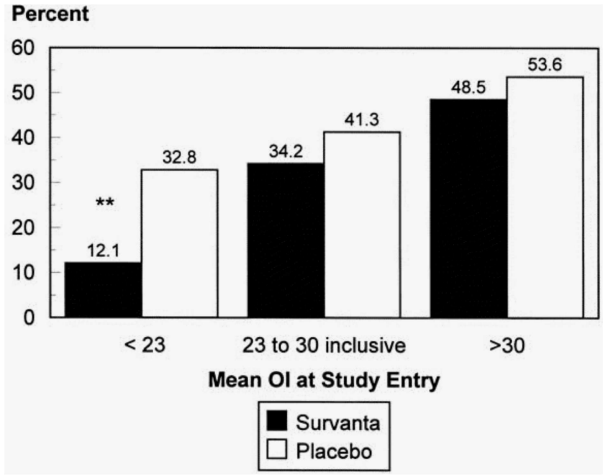
*Andrea Lotze, MD, Brian R. Mitchell, MS, Dorothy I. Bulas, MD, Elizabeth M. Zola, PharmD, Robert A. Shalwitz, MD, J. Harry Gunkel, MD, and the Survanta In Term Infants Study Group**

(J Pediatr 1998;132:40-7)

Need for ECMO by diagnosis

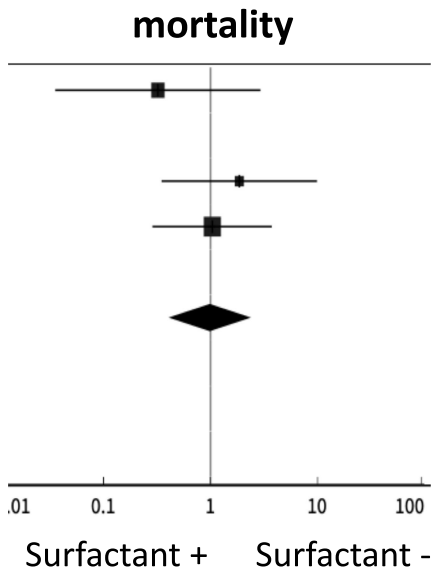


Need for ECMO by severity



Use of surfactant decreases the need for ECMO in the treatment of term newborns with respiratory failure, without increasing the risk of complications.

Surfactant for meconium aspiration syndrome in term and late preterm infants (Review)



4 studies 166 cases / 160 controls

Mortality: 0.98 [0.41,2.39]
ECMO: 0.64 [0.46,0.91]
Air leaks: 1.04 [0.23,4.71]
Ventilation: 0.6 [-0.41,1.62]
Oxygen: 0.4 [-2.83,3.64]
CLD: 0.47 [0.12,1.8]
IVH: 0.67 [0.31,1.46]

El Shahed AI et al. Cochrane 2014

nARDS and iNO

Gebistorf F et al. *Cochrane Database of Systematic Reviews* 2016, Issue 6. Art. No.: CD002787

Analysis 5.1. Comparison 5 PaO_2/FiO_2 (mm Hg): INO versus control, Outcome 1 PaO_2/FiO_2 up to 24 hours.

Study or subgroup	INO N	INO Mean(SD)	Control N	Control Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Total ***	**348**		**266**			**100%**	**15.91[8.25,23.56]**

Heterogeneity: Tau^2=36.89; Chi^2=13.34, df=10(P=0.21); I^2=25.02%

Test for overall effect: Z=4.07(P<0.0001)

Test for subgroup differences: Chi^2=0, df=1 (P=0.98), I^2=0%

Favours control -100 -50 0 50 100 Favours INO

Analysis 4.1. Comparison 4 Complications during the in-patient stay: INO versus control, Outcome 1 Renal impairment: INO vs control.

Study or subgroup	INO n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
4.1.1 Trials with overall high risk of bias					
Lundin 1999	28/93	12/87		23.41%	2.18[1.19,4.02]
Subtotal (95% CI)	**93**	**87**		**23.41%**	**2.18[1.19,4.02]**

Favours experimental 0.01 0.1 1 10 100 Favours control

Analysis 1.3. Comparison 1 Mortality: INO versus control group, Outcome 3 Mortality: subgroup analysis, paediatric vs adult population.

Study or subgroup	INO n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
1.3.1 Paediatric					
Bronicki 2015	2/24	8/29		3.2%	0.3[0.07,1.29]
Day 1997	1/12	2/12		0.88%	0.5[0.05,4.81]
Dobyns 1999	22/53	24/55		10.41%	0.95[0.61,1.47]
Subtotal (95% CI)	**89**	**96**		**14.49%**	**0.78[0.51,1.18]**

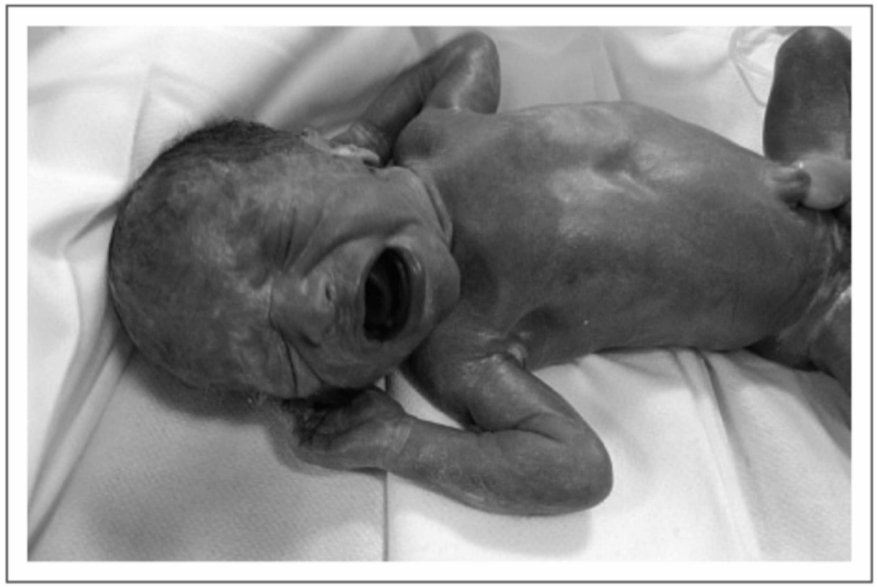
Favours experimental 0.01 0.1 1 10 100 Favours control

No strong evidence is available to support the use of INO to improve survival of adults and children with acute respiratory failure and low blood oxygen levels. We found no beneficial effects: despite signs of oxygenation and initial improvement, INO does not appear to improve survival and might be hazardous, as it may cause kidney function impairment.

Oxygène

Pression arterielle en oxygène

- Fetus: 35-46 mmHg
- Nouveau-ne: 50-80 mmHg
- Adulte: 70-90 mmHg



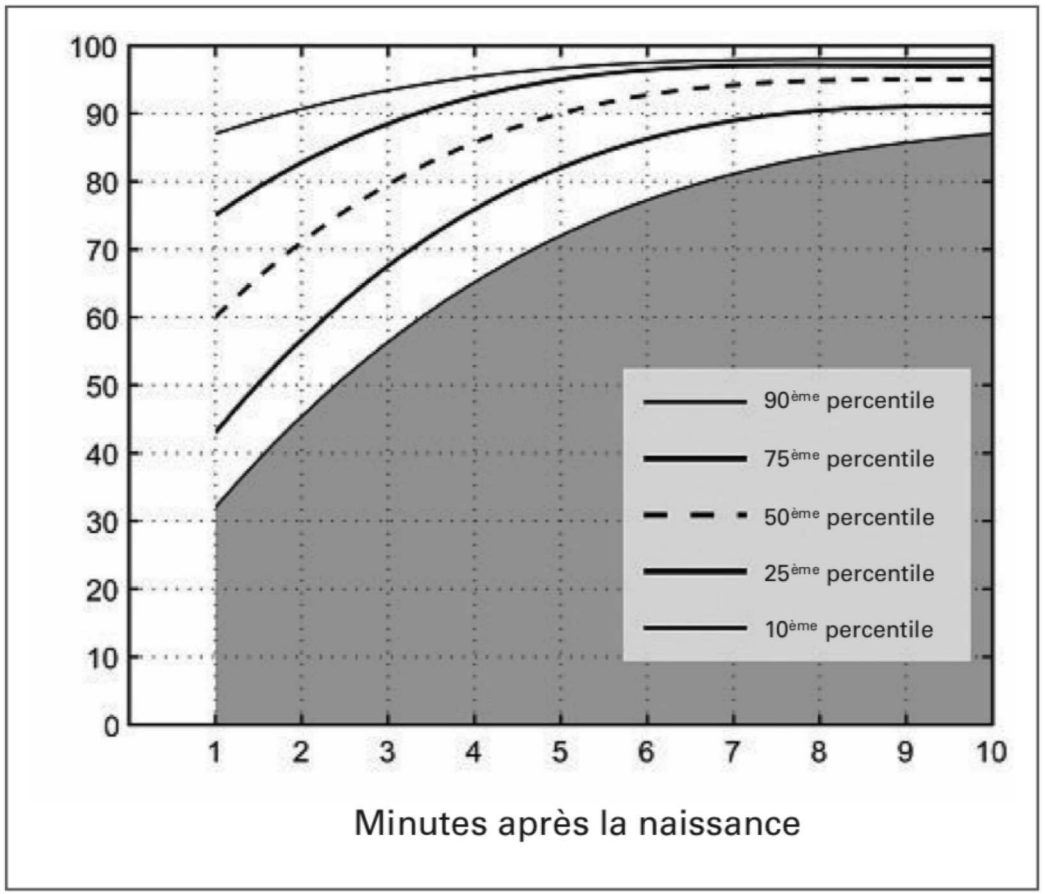


Figure 2
Saturation en oxygène au cours des 10 premières minutes après la naissance (mesure par oxymétrie de pouls à la main droite, c.-à-d. préductale) (d'après [4]).

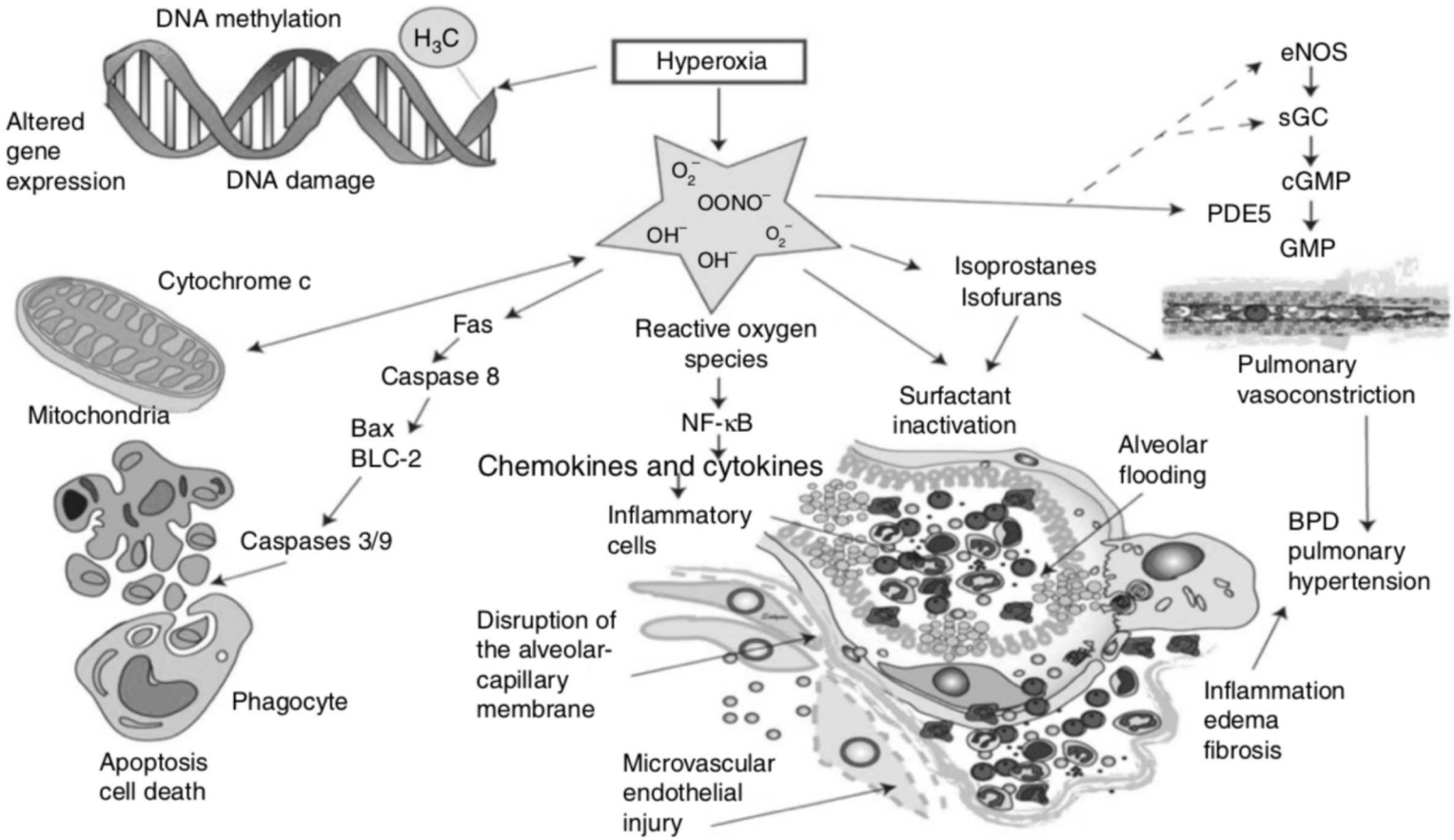
Risks of hypoxemia

- Delivery room:
  - hypoxic ischemic encephalopathy,
  - periventricular leukomalacia,
  - multi-organ dysfunction,
  - adverse neurodevelopmental outcomes
- NICU:
  - increased mortality (SUPPORT)
  - Increased death or developmental delay (BOOST II)
  - Necrotizing enterocolitis

Risks of hyperoxia

- Retinopathy of prematurity
- Bronchopulmonary dysplasia
- Lung alveolar and vascular damage
- 3x increase risk of leukemia (DR exposure at term)
- Decreases
- Neuronal cell death, neurodevelopmental delay, CP
- Decreases inflammatory responses, increases susceptibility to infection

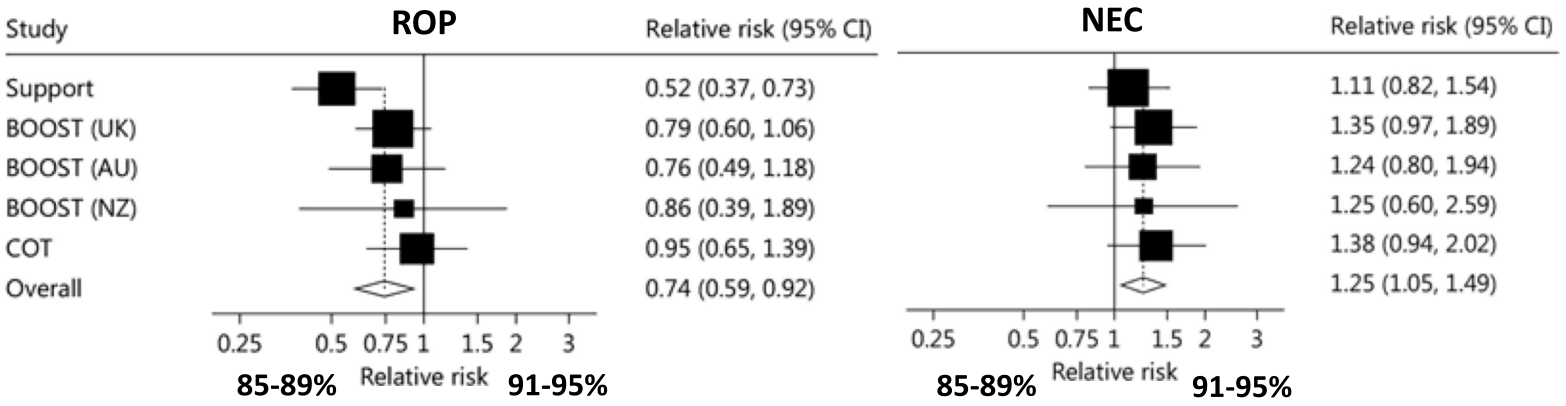
Toxicité de l'oxygène



At birth:

- 100%vs 21% O2 does not improve vital prognosis in term infants
  - Generates free radicals
  - DNA damage
  - Increase risk of cancer

Oxygen targets during postnatal course:

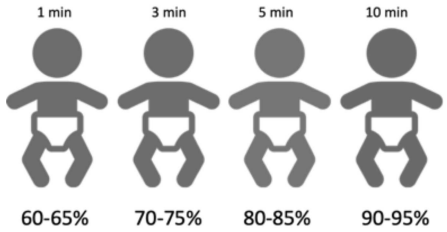


IN THE DELIVERY ROOM

>32w: Start at 21%

<32w: Start at 30%

Adjust gradually for target:



European Consensus Guidelines on the Management of Respiratory Distress Syndrome 2019 Update

Sweet D.G. · Carnielli V. · Greisen G. · Hallman M. · Ozek E. · te Pas A. · Plavka R. · Roehr C. · Saugstad O.D. · Simeoni U. Speer C.P. · Vento M. · Visser G.H.A. · Halliday H.L.

Recommendations

1 Delay clamping the umbilical cord for at least 60 s to promote placento-fetal transfusion (**A1**).

2 In spontaneously breathing babies, stabilise with CPAP of at least 6 cm H_2O via mask or nasal prongs (**B1**). Do not use SI as there is no long-term benefit (**B1**). Gentle positive pressure lung inflations with 20–25 cm H_2O peak inspiratory pressure (PIP) should be used for persistently apnoeic or bradycardic infants.

3 Oxygen for resuscitation should be controlled using a blender. Use an initial FiO_2 of 0.30 for babies <28 weeks' gestation and 0.21–0.30 for those 28–31 weeks, 0.21 for 32 weeks' gestation and above. FiO_2 adjustments up or down should be guided by pulse oximetry (**B2**).

4 For infants <32 weeks' gestation, SpO_2 of 80% or more (and heart rate >100/min) should be achieved within 5 min (**C2**).

5 Intubation should be reserved for babies not responding to positive pressure ventilation via face mask or nasal prongs (**A1**). Babies who require intubation for stabilisation should be given surfactant (**B1**).

Neonatology 2019;115:432–450

Gas du sang:

Valeurs normales (adulte)

- PaO2: 65-100 mmHg
- PaCO2: 35-45 mmHg
- pH: 7.35-7.45

PvO2: 40-50 mmHg

PvCO2: 40-50 mmHg

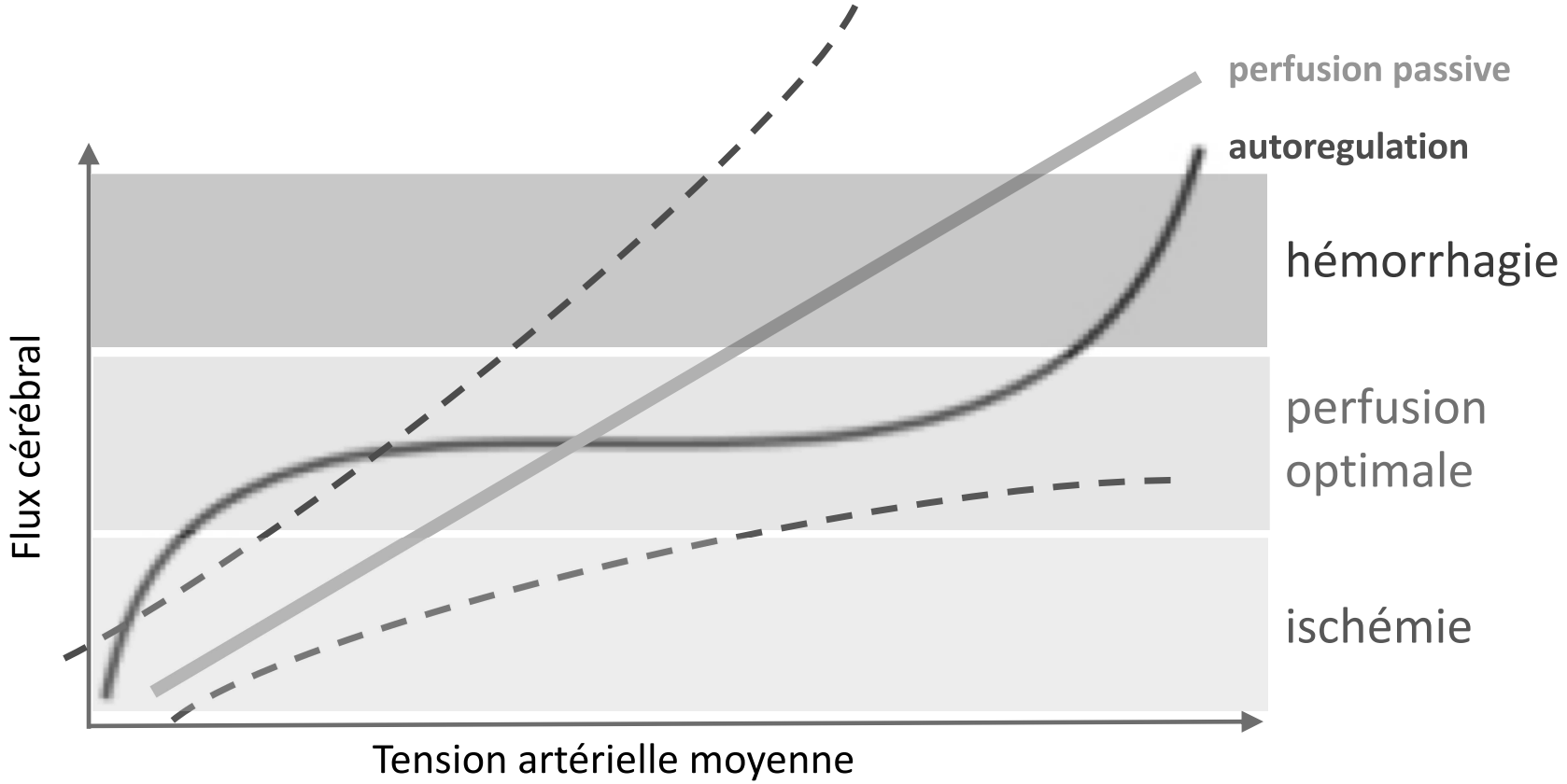
Nouveau-né: valeurs permissives

- PaO2: 60-80 mmHg
- PaCO2: 40-60 mmHg
- pH: 7.25-7-40

Autoregulation de la perfusion cérébrale

CO2 ↑

CO2 ↓



<u>Absence d'autorégulation:</u>

- Prématurité
- Asphyxie
- Sepsis

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Recommendations

1 After stabilisation, MV should be used in babies with RDS when other methods of respiratory support have failed (**A1**). Duration of MV should be minimised (**B2**).
2 The primary choice of ventilation mode is at discretion of clinical team; however, if conventional MV is used, targeted tidal volume ventilation should be employed (**A1**).
3 When weaning from MV, it is reasonable to tolerate a modest degree of hypercarbia provided the pH remains above 7.22 (**B2**).

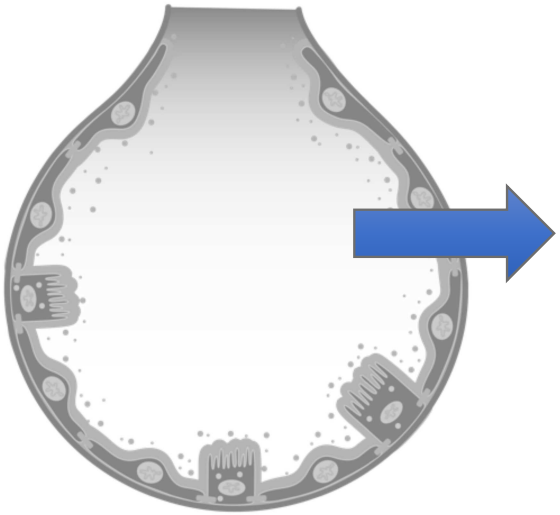
Adjust about caffeine

Neonatology 2019;115:432–450

Principe de base des échanges gazeux alvéolaires

Oxygene: diffusion lente

-> proportionnel à la surface



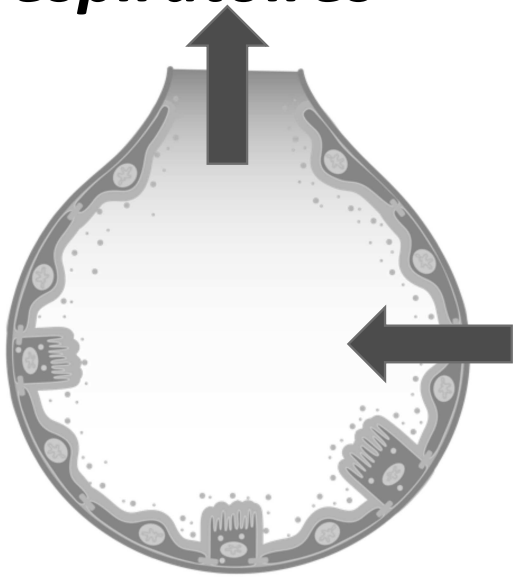
Pour augmenter l'oxygénation:

↑ FiO2

↑ pression de base (PEEP)

CO2: diffusion rapide

-> proportionnel aux cycles respiratoires

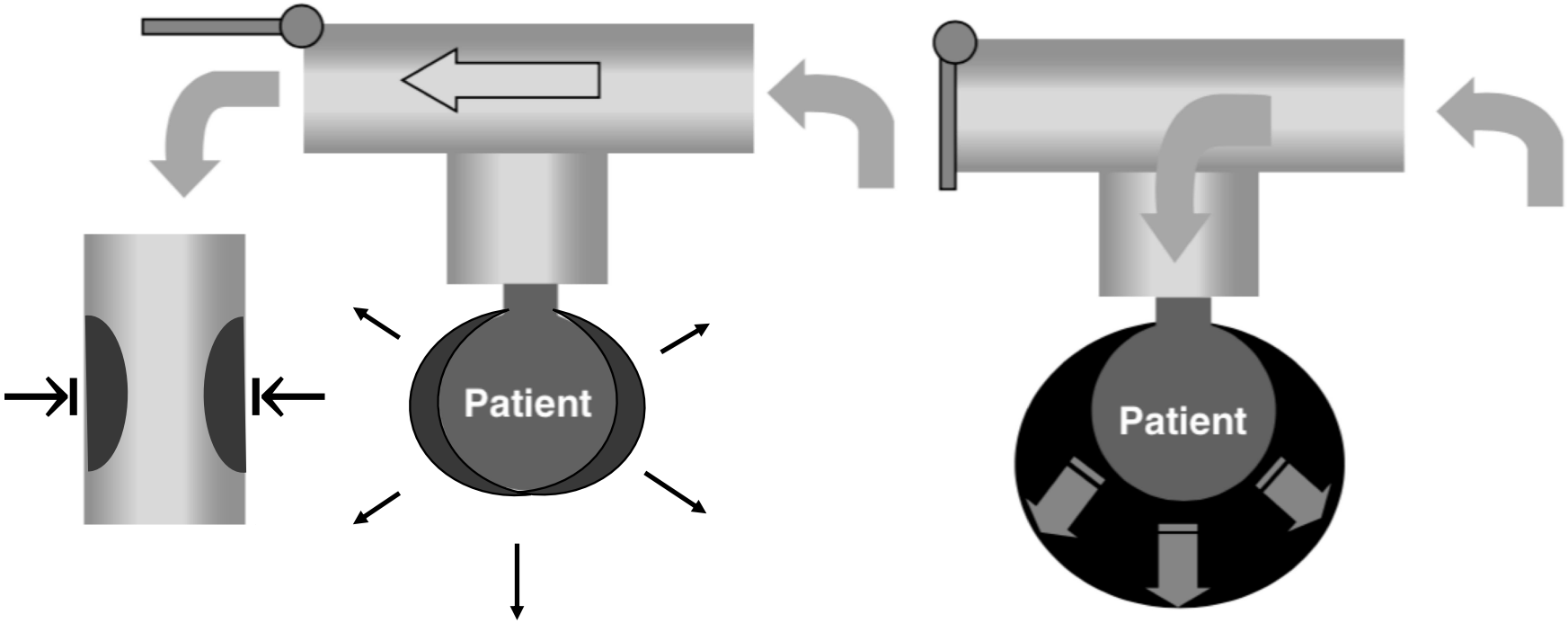


Pour éliminer le CO2:

↑ fréquence respiratoire

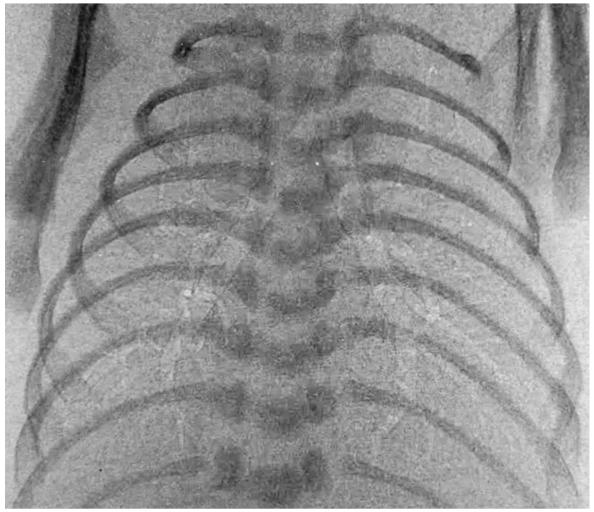
↑ pression inspiratoire (PIP)

Principe de la ventilation à pression positive intermittente néonatale

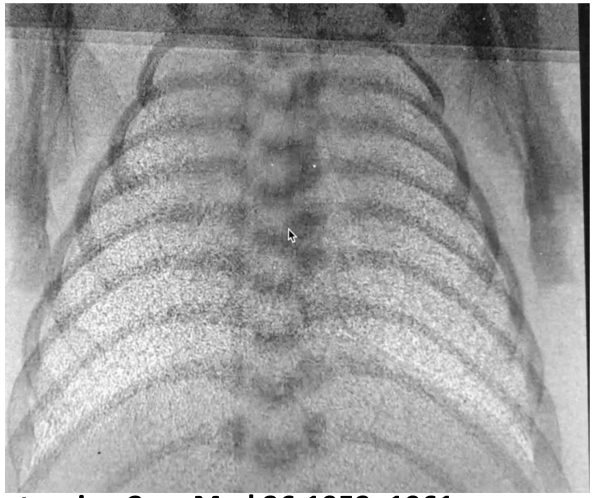


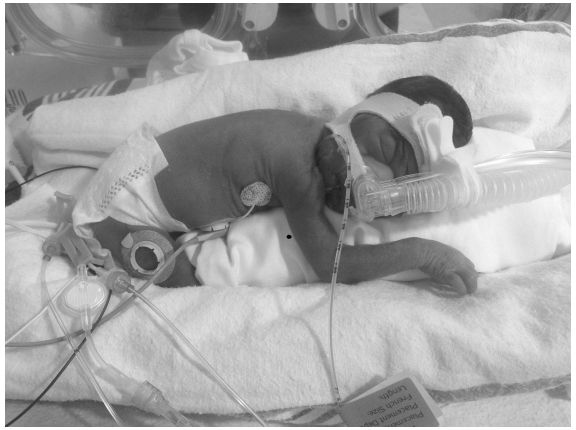
Pression positive continue (CPAP)

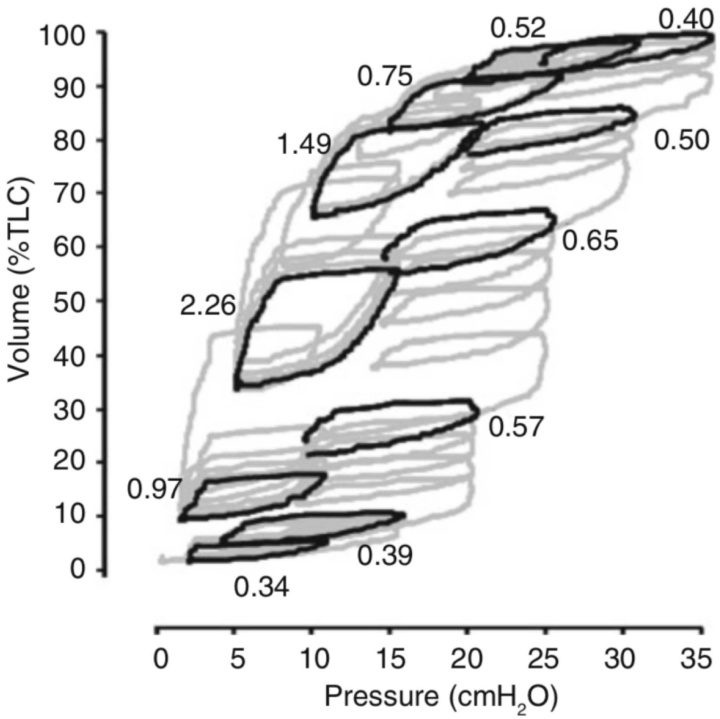
PEEP = 0

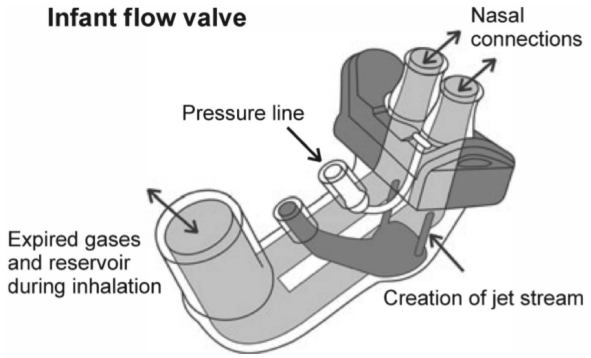


PEEP = 5



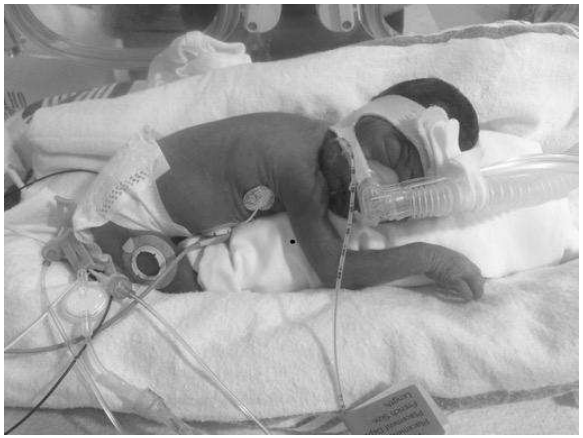


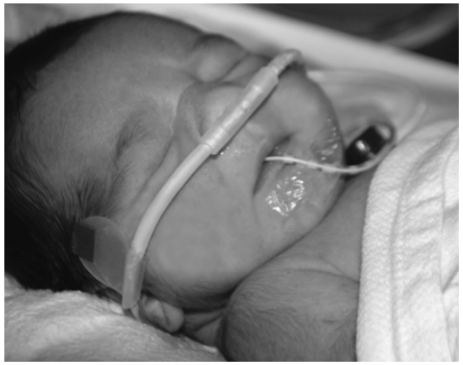


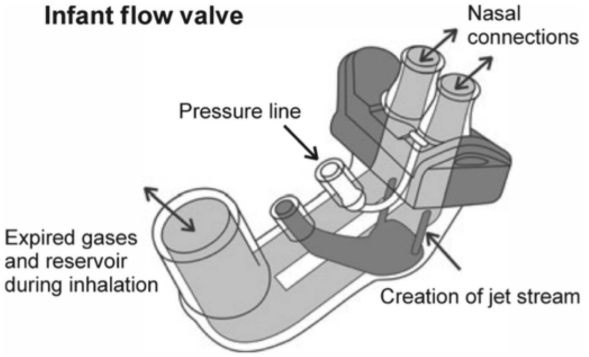


Dargaville PA. Intensive Care Med 36:1953–1961

How to optimize **alveolar recruitment**? *Positive pressure*







Mask or prong CPAP:

- Connected to a ventilator
- Efficient for maintaining lung volumes in preemies
- May be combined with tidal ventilation (IMV) but difficult to synchronize
- Side effects (nose injury)

RAM cannula CPAP:

- Connected to a ventilator or to bubble system
- Efficient for maintaining lung volumes in preemies
- May be combined with tidal ventilation (IMV) but cannot be synchronized
- More simple
- Sometimes better tolerated (ask the baby!)

SiPAP (biphasic CPAP)

- Connected to a specific machine (Infant Flow)
- Cannot ventilate but varies in real time between Insp and Exp
- Efficient in tachypnea
- Efficient for controlling CO2 retention (BPD)
- Usually well tolerated

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

FROM THE AMERICAN ACADEMY OF PEDIATRICS

Organizational Principles to Guide and Define the Child Health Care System and/or Improve the Health of all Children

POLICY STATEMENT

Respiratory Support in Preterm Infants at Birth

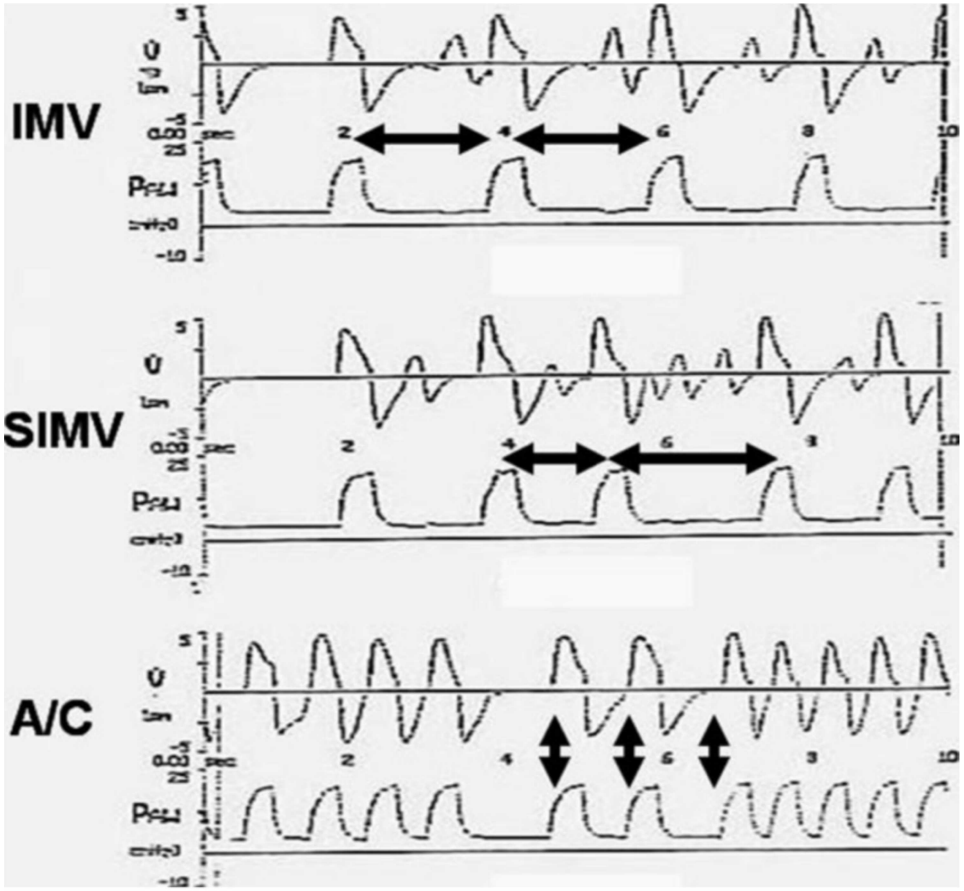
COMMITTEE ON FETUS AND NEWBORN

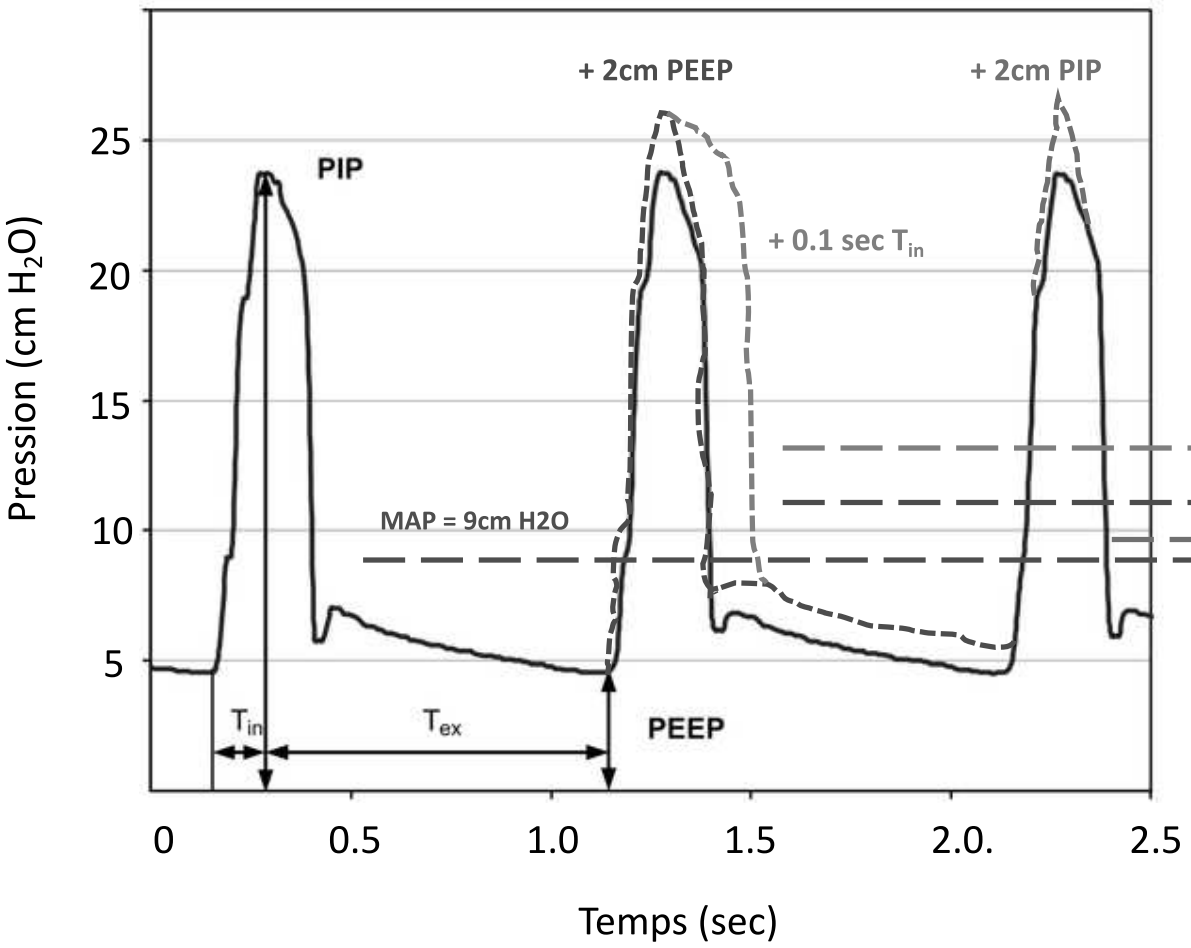
Using CPAP immediately after birth with subsequent selective surfactant administration may be considered as an alternative to routine intubation with prophylactic or early surfactant administration in preterm infants (Level of Evidence: 1, Strong Recommendation).

If it is likely that respiratory support with a ventilator will be needed, early administration of surfactant followed by rapid extubation is preferable to prolonged ventilation (Level of Evidence: 1, Strong Recommendation).

PEDIATRICS Volume 133, Number 1, January 2014

Ventilation intermittente (“conventionnelle”)





MAP = 13 cm H2O

MAP = 11 cm H2O

MAP = 9.5 cm H2O

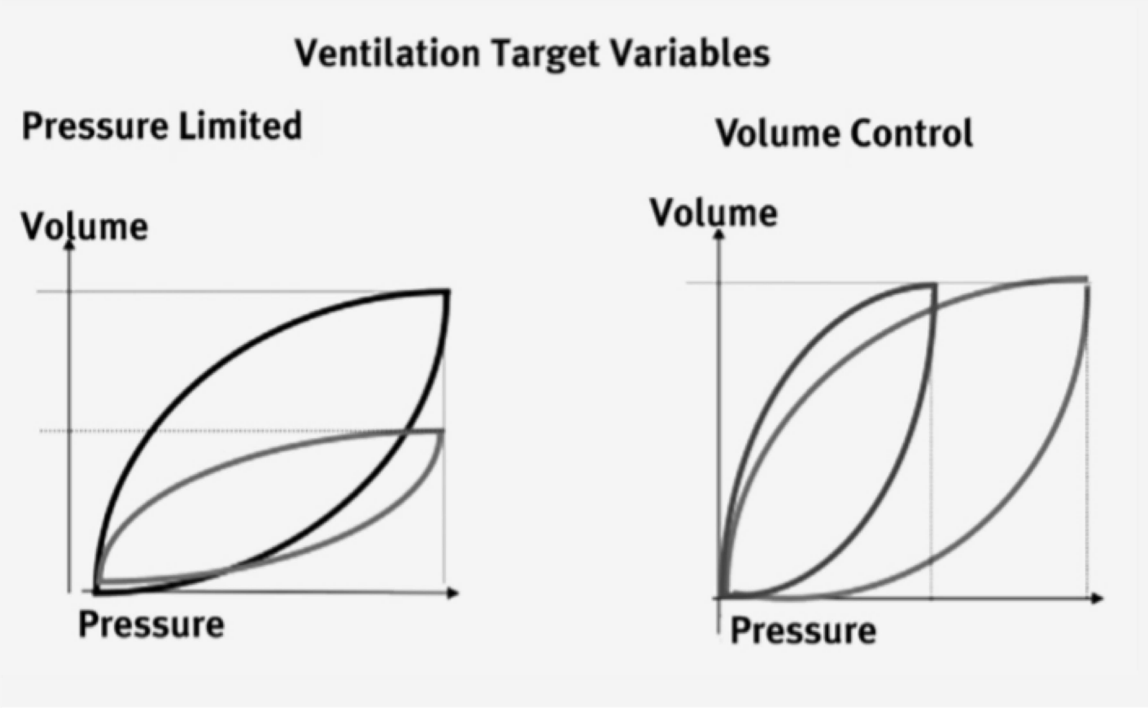
Oxygenation (↑ SaO_2):

- ↑ PEEP
- ↑ Tin (temps inspiratoire)
- ↑ FiO_2

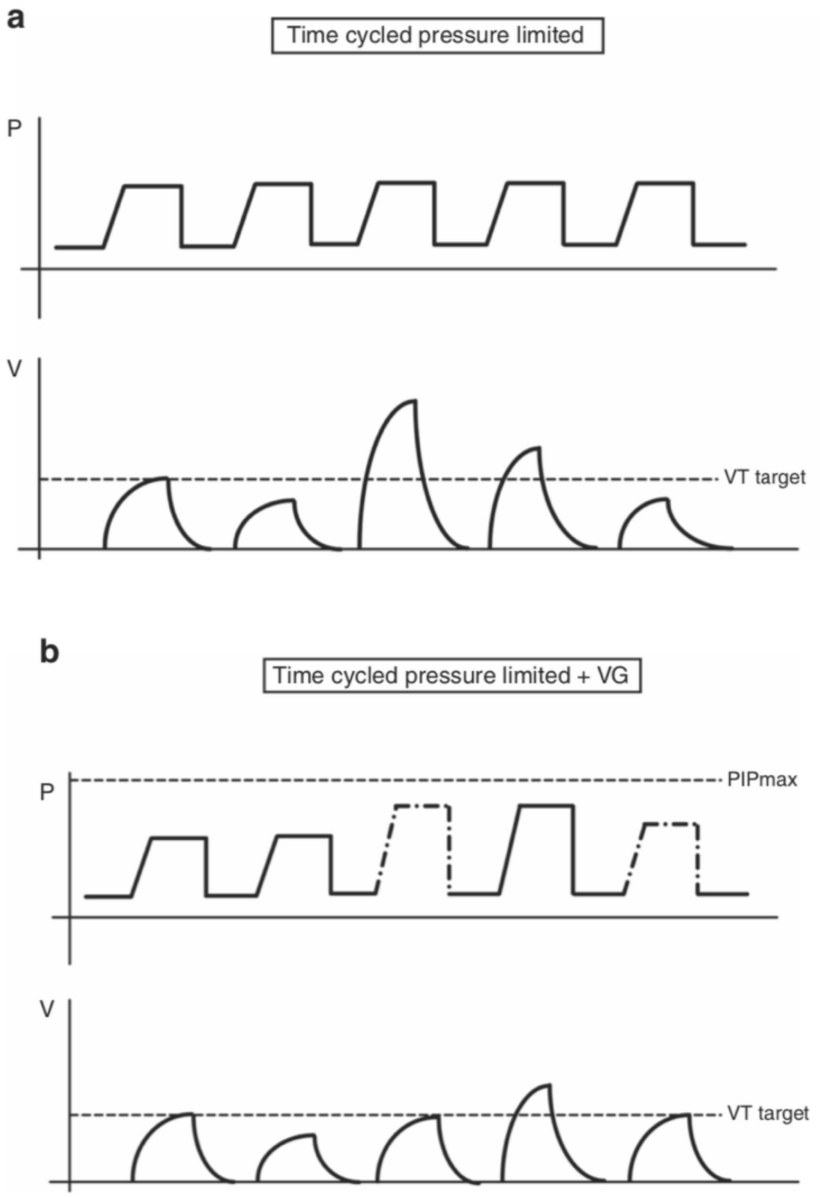
Ventilation (↓ pCO_2):

- ↑ PIP
- ↑ fréquence

pressure control ou volume control?



advantage of PTV: limitation of the risk of “barotrauma”



Pressure support (=aide inspiratoire)

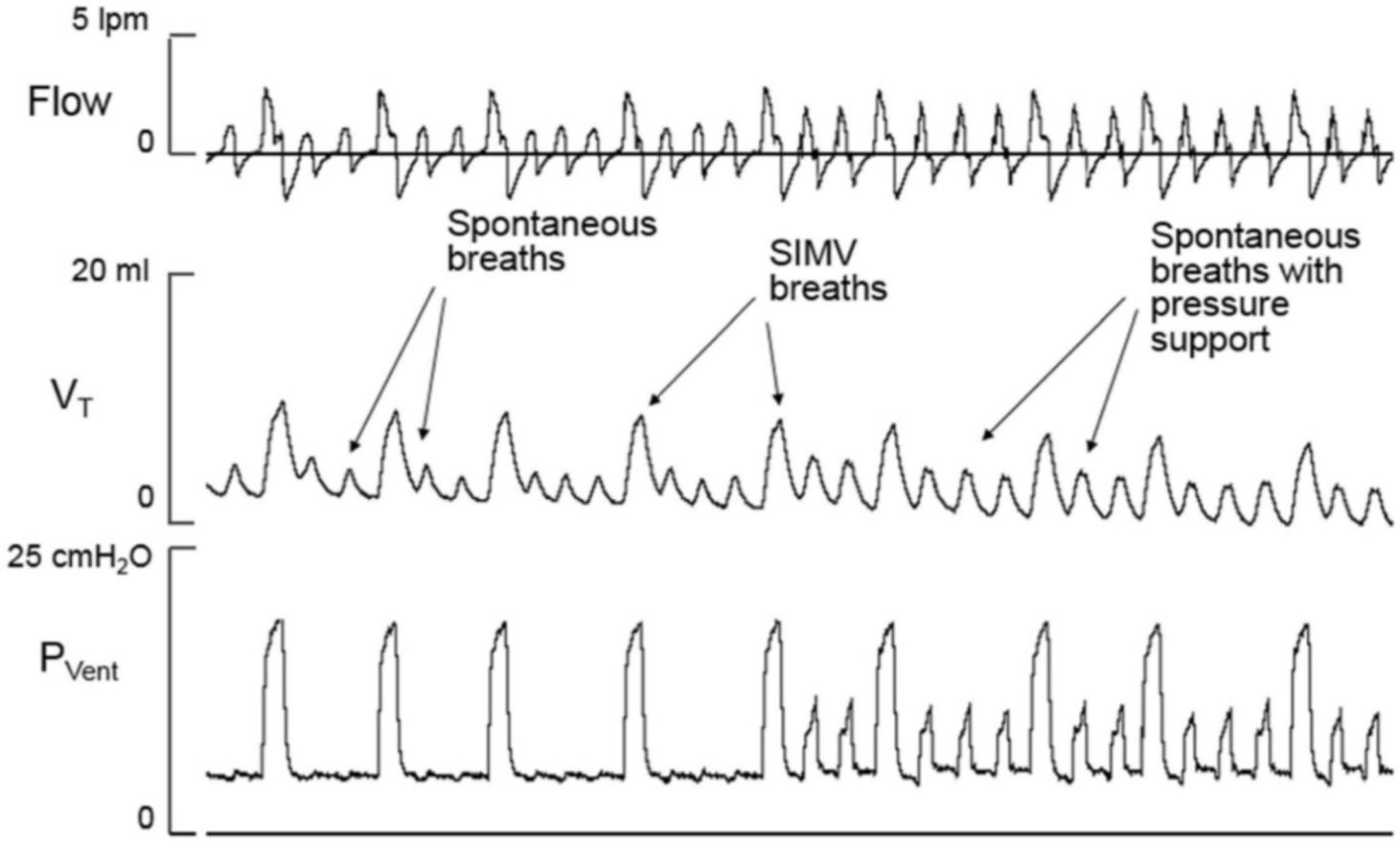
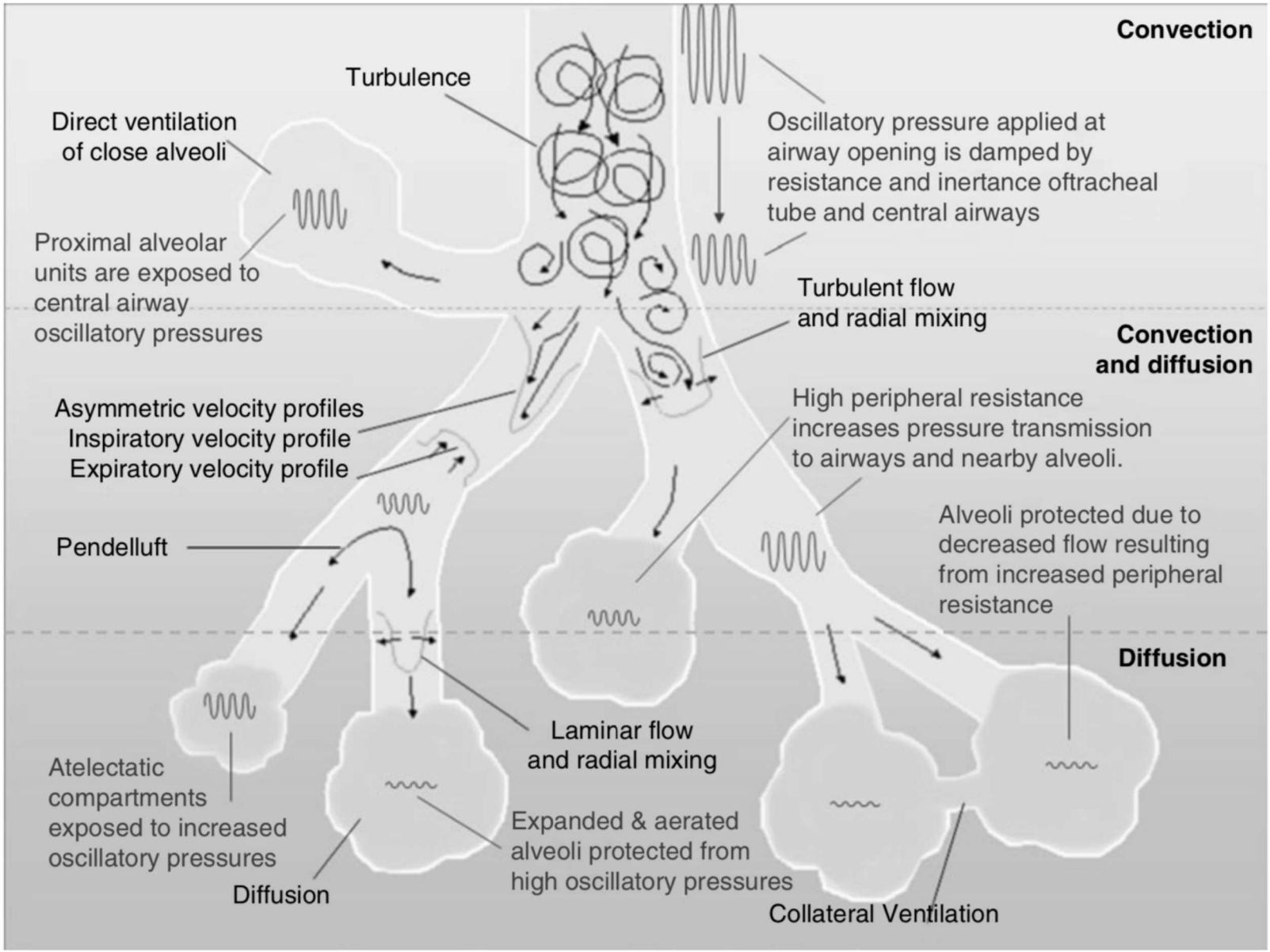
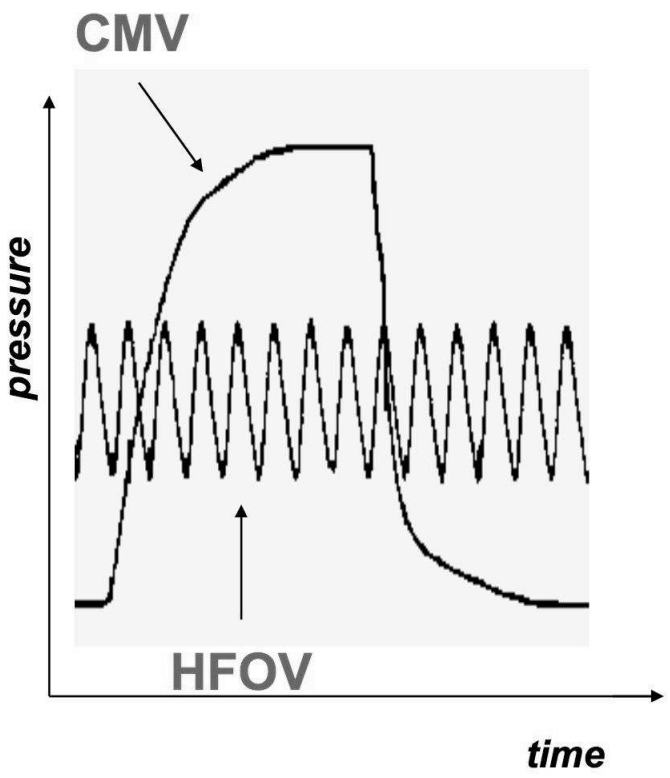


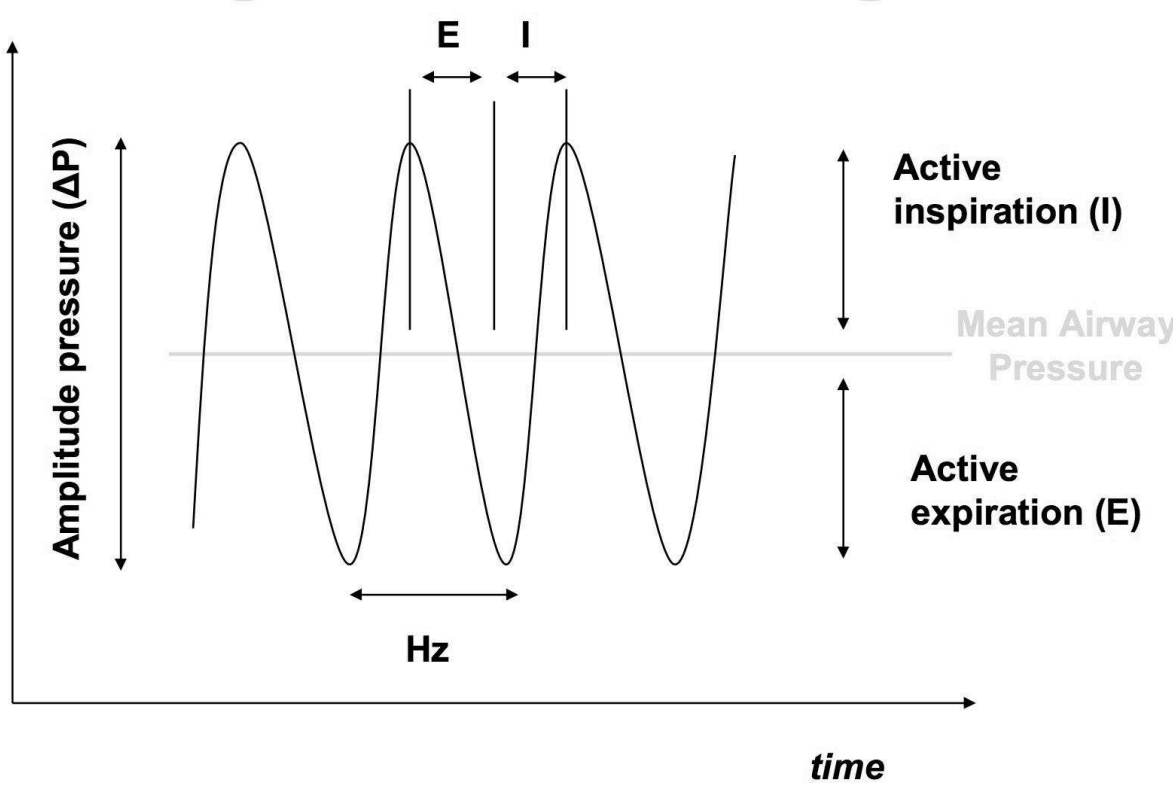
Figure 2 Synchronized intermittent mandatory ventilation combined with pressure support. Tracings of flow, tidal volume (V_T) and ventilator pressure (P_{Vent}) obtained from a premature infant switched from SIMV to SIMV combined with pressure support. The tidal volume from spontaneous breaths assisted by pressure support is larger than the tidal volume from non-assisted spontaneous breaths between SIMV cycles.

Bancalari and Claure. Maternal Health, Neonatology, and Perinatology (2015) 1:13

HFOV: principes des échanges gazeux




CMV
pressure
HFOV
time


E
I
Amplitude pressure (ΔP)
Active inspiration (I)
Mean Airway Pressure
Active expiration (E)
Hz
time

Comment régler l'oxygénation en HFOV

- FiO2
- Pression moyenne = MAP

Comment régler la ventilation en HFOV

- Élimination du C02 proportionnelle à Vt x fréquence
- Volume courant : il est produit par le mouvement de va et vient d'une membrane ou d'un piston → **expiration active**
- Amplitude du mouvement de la membrane = pic à pic = deltaP
- Fréquence avec laquelle la membrane vibre

synchronization

Asynchrony may result in patient discomfort, less effective oxygenation and ventilation, high airway pressure, pneumothorax, and an increased risk of intraventricular hemorrhage. Randomized trials have shown that synchronization reduces duration of ventilation compared with non-synchronized ventilation. However, synchronized ventilation does not appear to reduce mortality or BPD.

Flow trigger

+ Located at the Y piece
+ More sensitive (threshold determination)
+ Detects initiation and termination of inspiration
+ Short response time
- Increases dead space
- Sensitive to condensation
- Influenced by leaks

Pressure trigger

+ More distant on circuit
+ Not influenced by leaks
+ No condensation interference
- Higher trigger threshold
- Does not sync with end of expiration

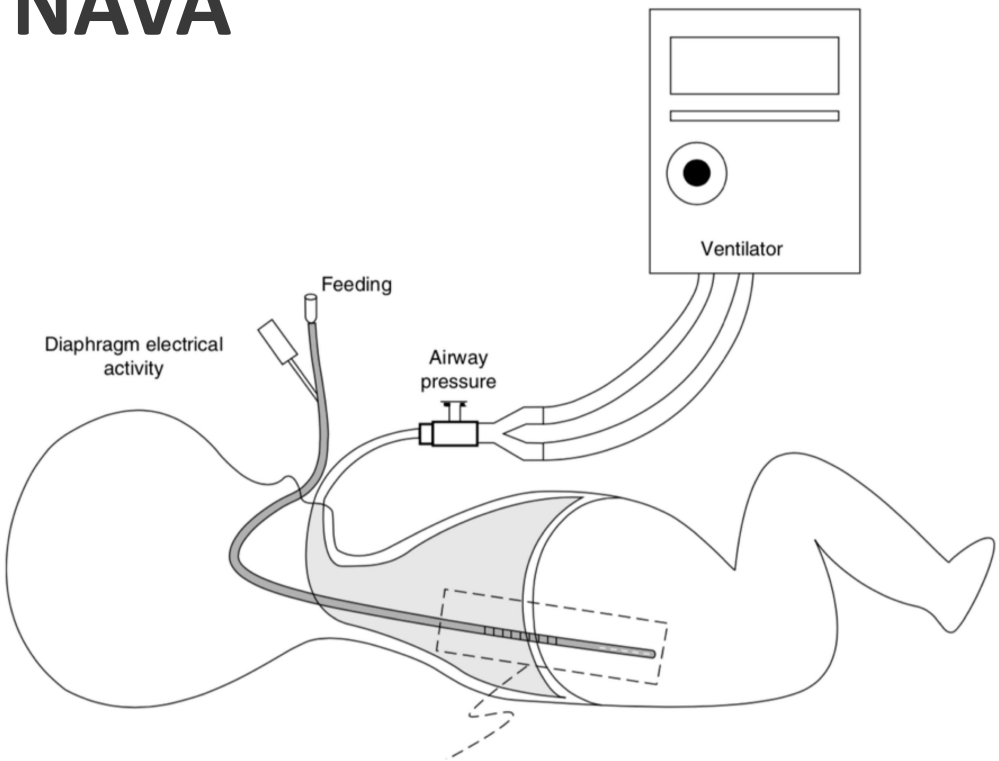
Pneumatic capsule

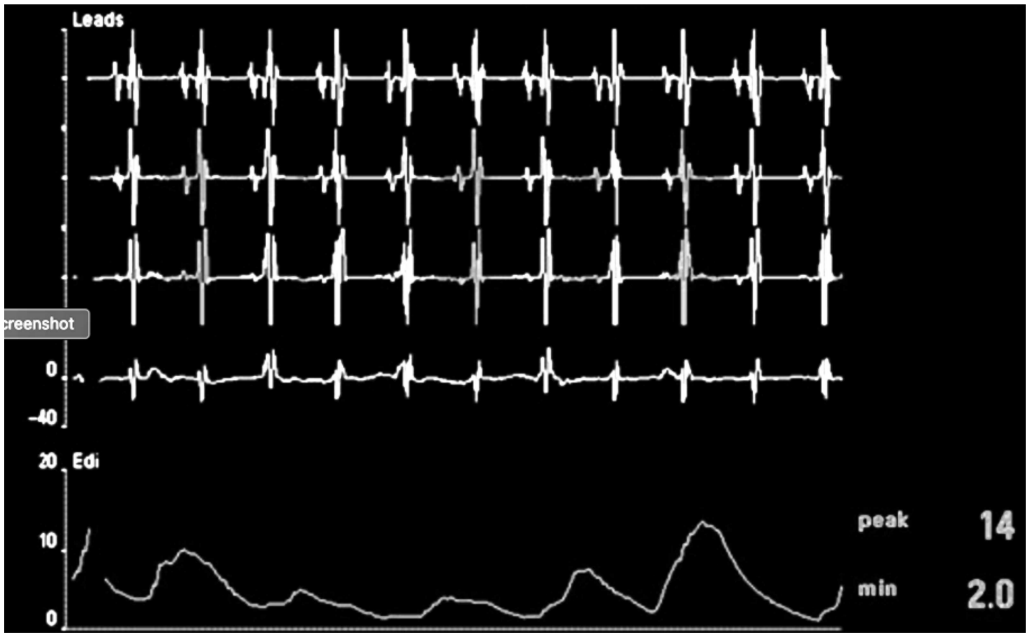
+ Placed on baby's body
+ Fast response
- Older technology
- Poor sensitivity
- Threshold not adjsutable

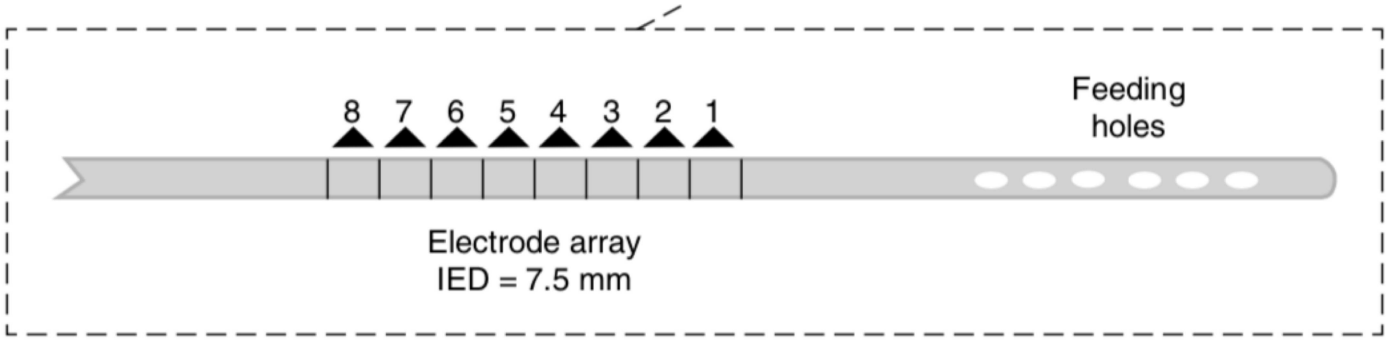
NAVA

+ Captor incorporated in nasogastric tube
+ Uses the electrical activity of the diaphragm (EAdi)
+ Fast detection of initiation and termination of inspiration
+ Less affected by artifacts

NAVA





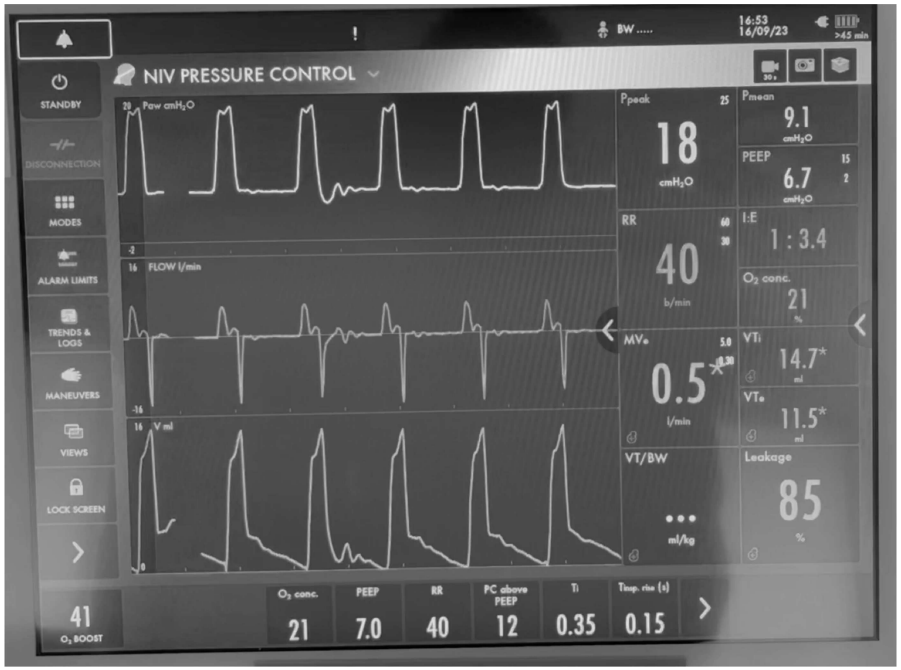


Positioning of the Edi probe:

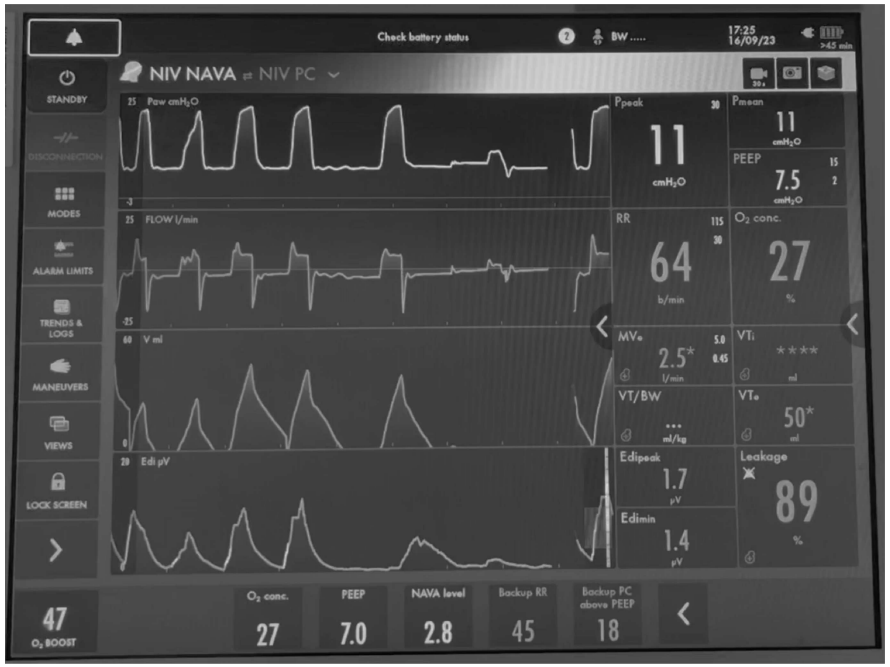
- Decreasing ECG signal towards the bottom tracings
- Adequate Edi signal

Why NAVA?

Baby Emmanuel - 23 2/7 weeks – day 0, after UVC and LISA
Non-invasive Pressure Control mode



Baby Celestine – 26 weeks triplet – day 7 – skin-to-skin
Non-invasive NAVA

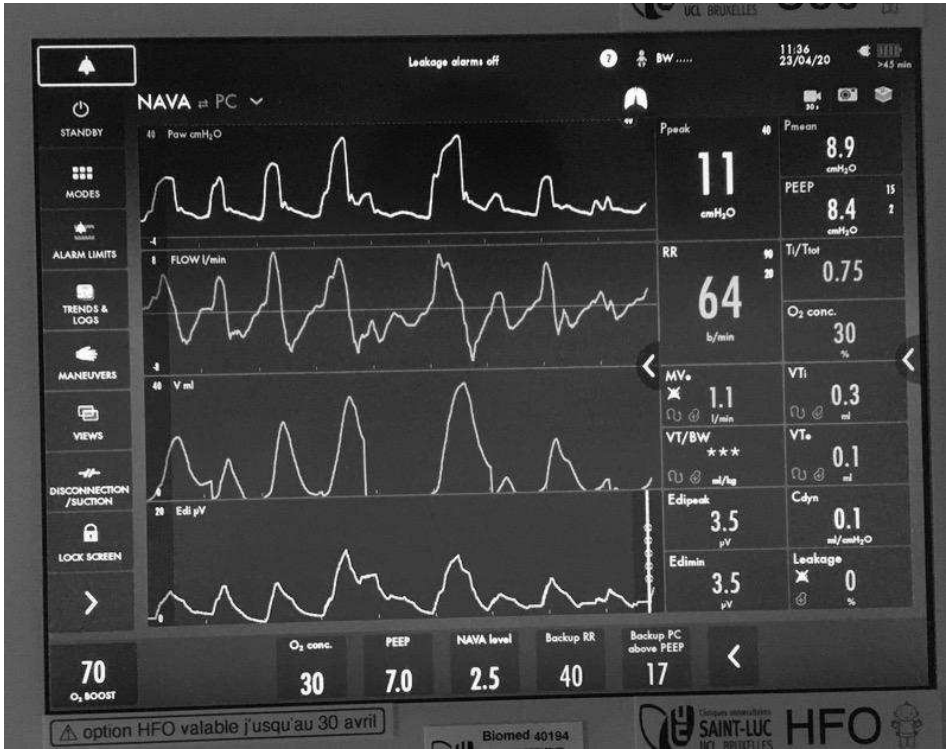


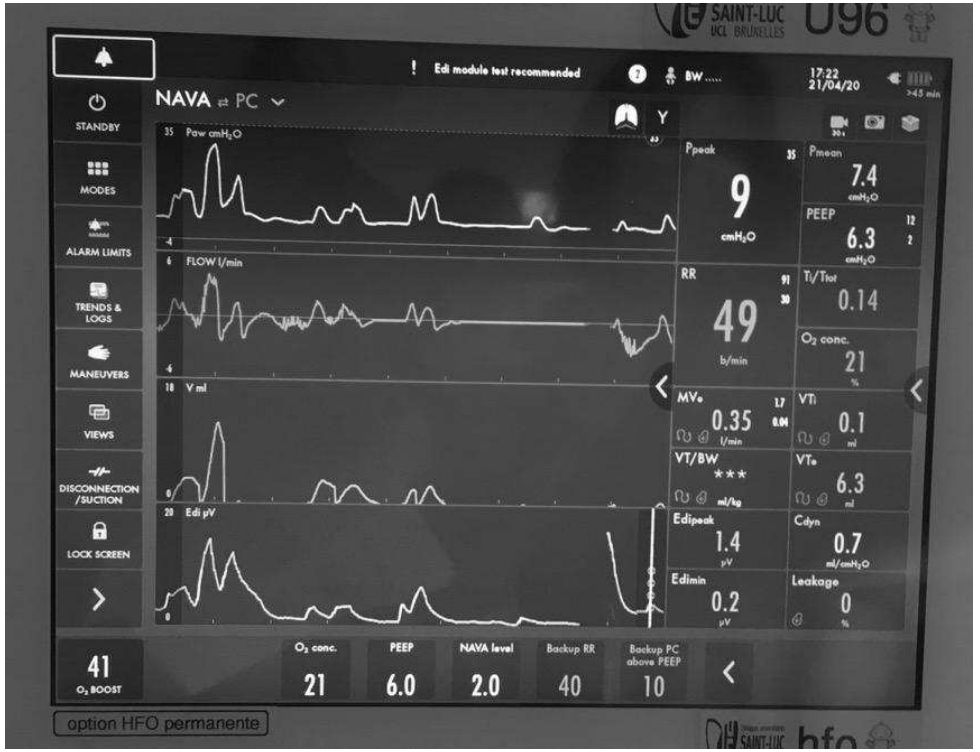
NAVA – quels réglages ?

- Ventilation en NAVA :
  - Niveau NAVA : 0,5-3
  - PEEP
  - FiO2
  - Limites de pressions (alarmes)
- Ventilation back –up :
  - Pression inspiratoire
  - PEEP
  - Ti
  - Fréquence respiratoire
  - Temps d’apnée après lequel la ventilation back-up prend le relais

NAVA – limites chez le nouveau-nés prématurés

- Le syndrome brady-apnéique -- > réglage optimal de la ventilation back-up en cas d'apnée





Que surveiller en NAVA ?

- Edi peak : entre 5-15 µV
  - Si Edi peak trop bas : diminuer le niveau NAVA et/ou diminuer la ventilation back-up
  - Si edi peak trop haut : majorer le niveau NAVA et/ou majorer la ventilation back-up
- Edi min : <1 µV
  - Si Edi min trop haut : majorer la PEEP

How to adjust NAVA?

Pressure/volume adjustments happen spontaneously breath-to-breath. The support will decrease/increas as the infant makes less/more effort

Edi Peak monitors the effort: should be between 5 and 15 µV

- Edi Peak too low : too much ventilator help
  - Decrease NAVA level and backup
- Edi Peak too high: too much infant's effort
  - Increase NAVA level and backup

Edi Min monitors the diaphragm tone between cycles : should be <1 µV

- Edi Min too high: increase PEEP

Approaches to Noninvasive Respiratory Support in Preterm Infants: From CPAP to NAVA

Walid A. Hussain, MD,* Jeremy D. Marks, PhD, MD*†

	APPROACHES	BENEFITS	RISKS
Nasal continuous positive airway pressure	Monitored and controlled positive pressure through nonrestrictive nasal prongs	Improves V/Q mismatch Improves oxygenation Maintains FRC Reduces atelectasis Decreases work of breathing	Nasal trauma Air leak syndromes Gastric distention
High-flow nasal cannula	Heated, humidified flow of supplemental oxygen through small-bore nasal cannula	Parental acceptance Ease of nursing care Reduced gastric distention	Distending pressure is unmonitored and can be dangerously high or ineffective
Nasal intermittent mandatory ventilation	Pressure-regulated, time-cycled positive pressure delivery through restrictive or nonrestrictive nasal prongs Synchronized or nonsynchronized	Improves gas exchange Improves oxygenation Decreases work of breathing Maintains FRC Decreases need for invasive ventilation	Nasal trauma Gastric distention Air leak syndromes
Neurally adjusted ventilatory assist	Diaphragm activity-controlled and regulated pressure delivery	Improves patient-ventilator synchrony Improves patient comfort Reduces peak inspiratory pressures	Limited data regarding efficacy Limitations in extremely premature infants with immature respiratory rhythm

JAMA | Original Investigation

Association of Noninvasive Ventilation Strategies With Mortality and Bronchopulmonary Dysplasia Among Preterm Infants

A Systematic Review and Meta-analysis

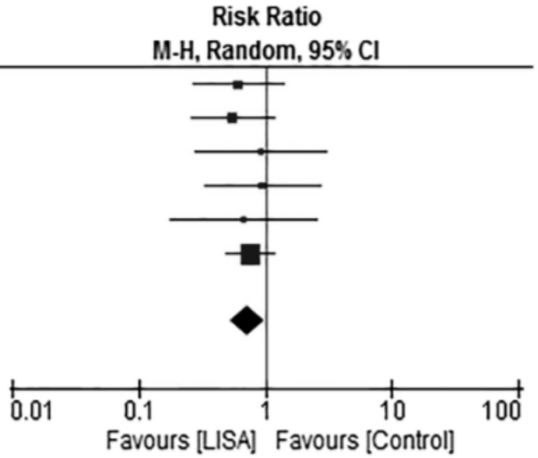
Tetsuya Isayama, MD, MSc; Hiroko Iwami, MD; Sarah McDonald, MD, FRCSC, MSc; Joseph Beyene, PhD

Mortalité ou BPD

	LISA		Control			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI
Gopel 2011	8	101	14	107	14.0%	0.61 [0.27, 1.38]
Kanmaz 2013	9	84	17	87	16.9%	0.55 [0.26, 1.16]
Mirnia 2013	5	64	5	59	6.7%	0.92 [0.28, 3.02]
Bao 2015	6	46	6	43	8.6%	0.93 [0.33, 2.68]
Mohammadizadeh 2015	3	18	4	16	5.3%	0.67 [0.18, 2.54]
Kribs 2015	25	97	31	92	48.5%	0.76 [0.49, 1.19]
Total (95% CI)		**410**		**404**	**100.0%**	**0.72 [0.53, 0.97]**
Total events	56		77			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.16$, $df = 5$ ($P = 0.95$); $I^2 = 0\%$

Test for overall effect: $Z = 2.13$ ($P = 0.03$)



CONCLUSIONS AND RELEVANCE Among preterm infants, the use of LISA was associated with the lowest likelihood of the composite outcome of death or BPD at 36 weeks' postmenstrual age. These findings were limited by the overall low quality of evidence and lack of robustness in higher-quality trials.

JAMA. 2016;316(6):611-624. doi:10.1001/jama.2016.10708

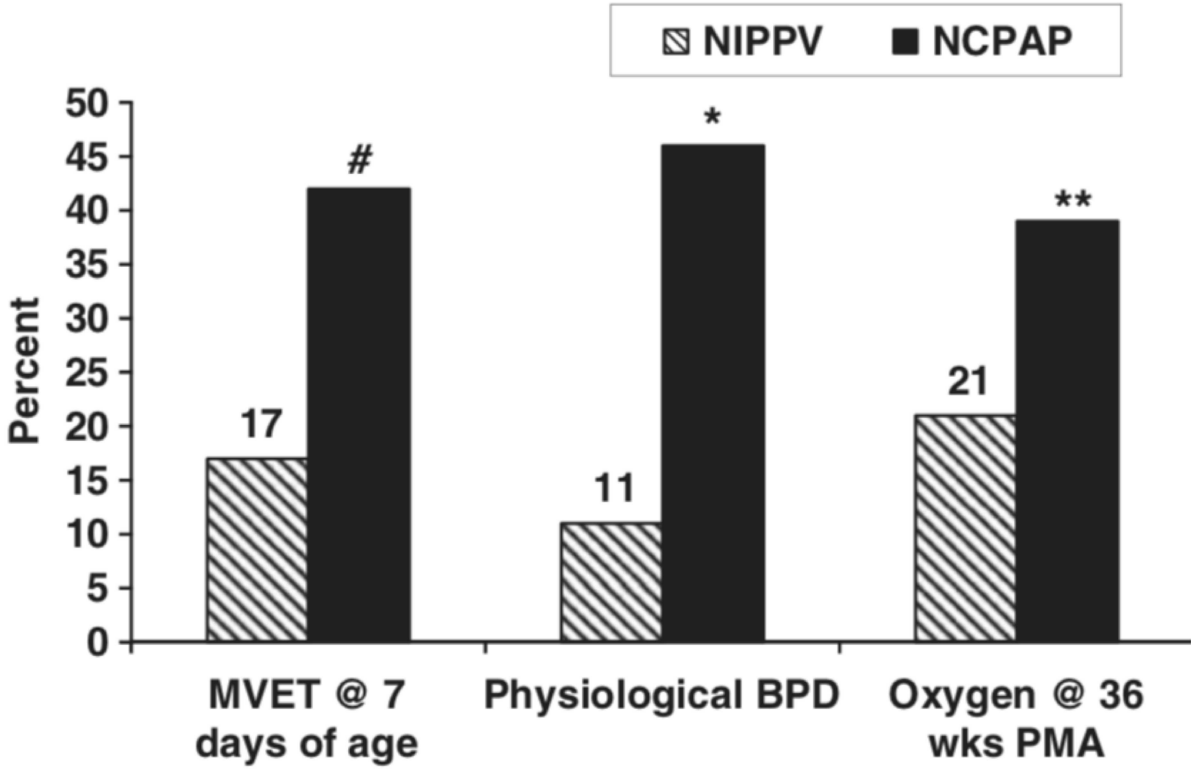
Journal of Perinatology (2012) 32, 336–343

www.nature.com/jp

Nasal intermittent positive pressure ventilation after surfactant treatment for respiratory distress syndrome in preterm infants <30 weeks' gestation: a randomized, controlled trial

R Ramanathan[1], KC Sekar[2], M Rasmussen[3], J Bhatia[4] and RF Soll[5]

Multicenter, randomized, controlled trial. A total of 57 infants were randomized within 120 min of birth to NCPAP (BW 1099 g and GA 27.8 weeks) and 53 infants to NIPPV (BW 1052 g, and GA 27.8 weeks). Infants were stabilized on NCPAP at birth and were given poractant alfa combined with MVET within 60 min of age. When stabilized on MVET, they were extubated within the next hours or days to NCPAP or NIPPV.



European Consensus Guidelines on the Management of Respiratory Distress Syndrome 2019 Update

Sweet D.G. · Carnielli V. · Greisen G. · Hallman M. · Ozek E. · te Pas A. · Plavka R. · Roehr C. Saugstad O.D. · Simeoni U. Speer C.P. · Vento M. · Visser G.H.A. · Halliday H.L.

Recommendations

1 CPAP should be started from birth in all babies at risk of RDS, such as those <30 weeks' gestation who do not need intubation for stabilisation (**A1**).

2 The system delivering CPAP is of little importance; however, the interface should be short binasal prongs or mask with a starting pressure of about 6–8 cm H_2O (**A2**). Positive end-expiratory pressure (PEEP) can then be individualised depending on clinical condition, oxygenation and perfusion (**D2**).

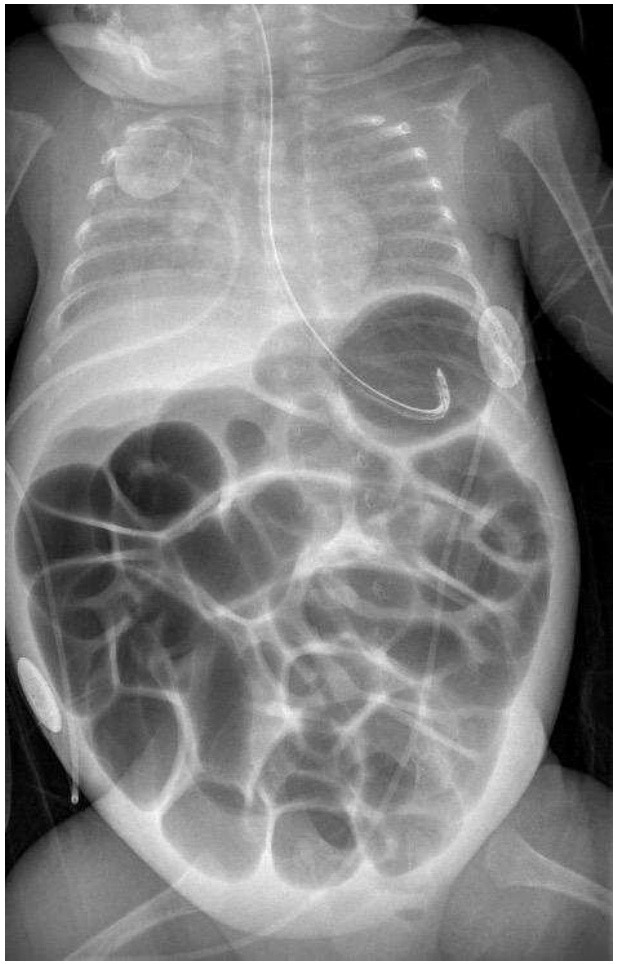
3 CPAP with early rescue surfactant is considered optimal management for babies with RDS (**A1**).

4 Synchronised NIPPV, if delivered through a ventilator rather than BIPAP device, can reduce extubation failure but may not confer long-term advantages such as reduction in BPD (**B2**).

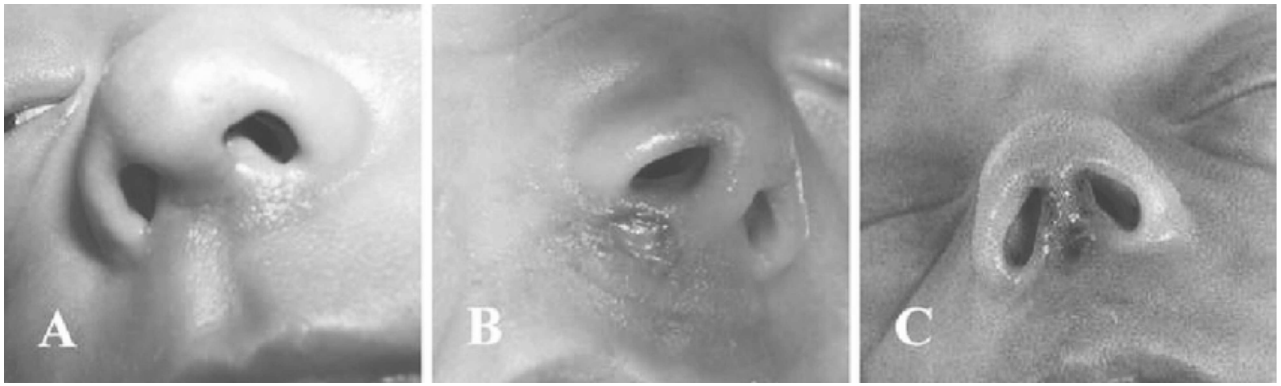
5 During weaning, HFNC can be used as an alternative to CPAP for some babies with the advantage of less nasal trauma (**B2**).

Neonatology 2019;115:432–450

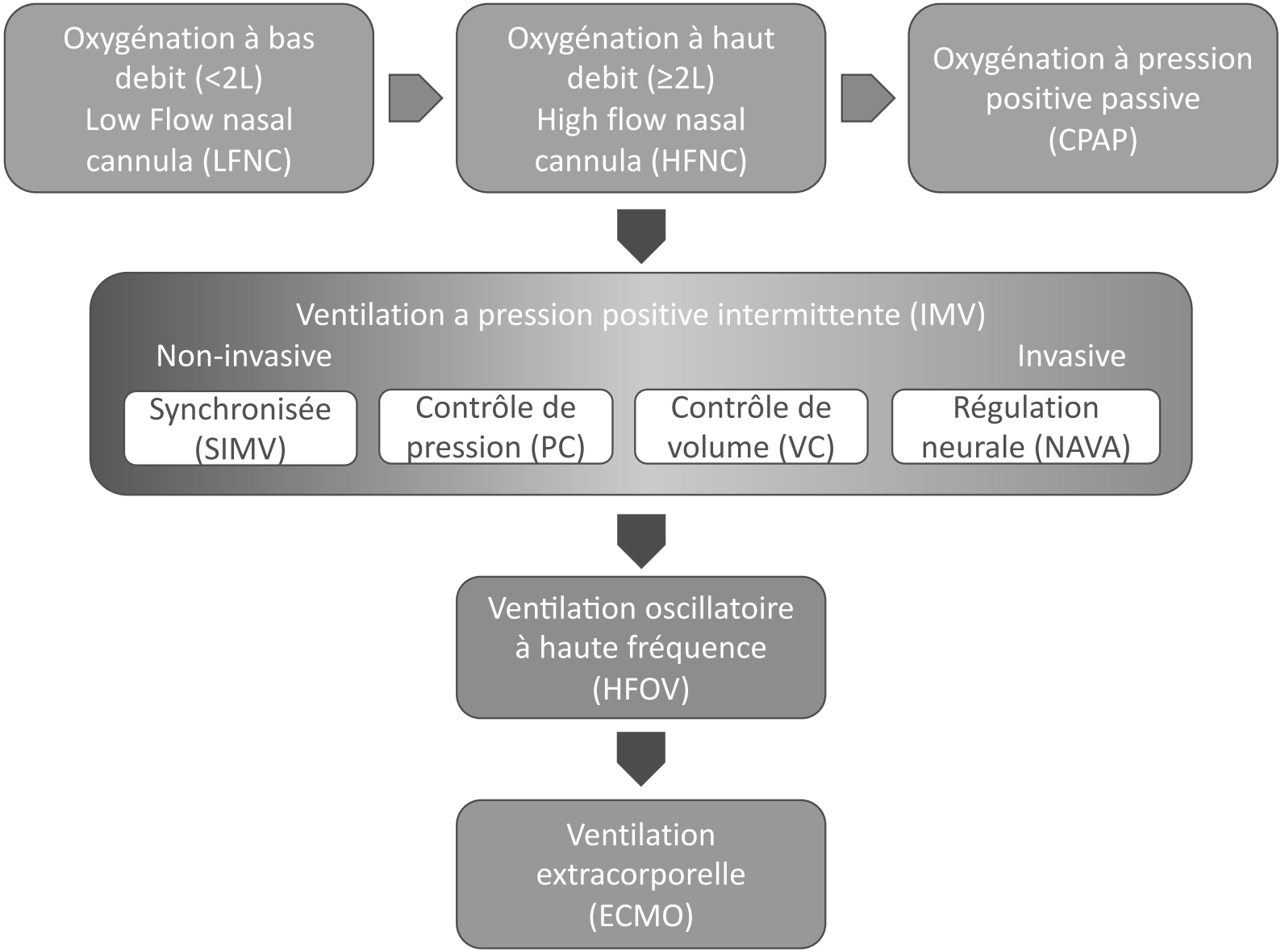
Complications de la ventilation non-invasive:



- Hypoxie/hypercapnie (nécessité d'intubation pour pressions plus élevées)
- Distension abdominale ("CPAP belly")
- Plaies nasales
- Condensation excessive ("washout")



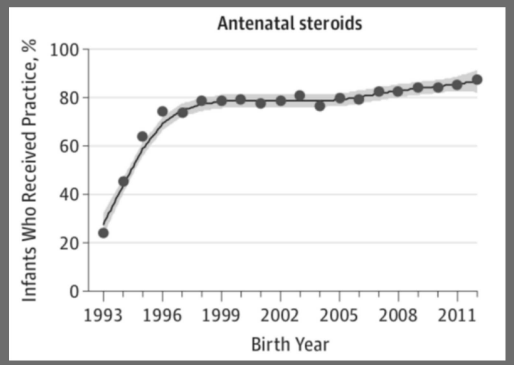
Conclusion: Modes de support respiratoire

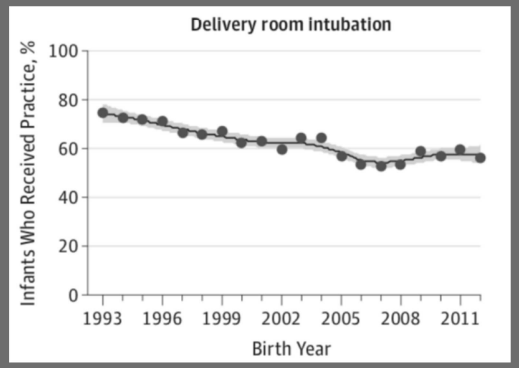


Traitement par surfactant

Quand?

<2013:
Usage **prophylactique** chez enfants “à risque de RDS” prématurés <32 semaines





>2013:
usage **thérapeutique précoce** chez les enfants avec signes cliniques de RDS persistants après stabilisation en CPAP

Quel surfactant?

Animal

porcin	Poractant α	Curosurf®	+++
bovin	calfactant	Infasurf®	++
	beractant	Survanta®	+

Artificiel

1ère gen	colfosceryl	Exosurf®	-
3ème gen (PL+SPB/C)	CHF5633	Alisurf®	?++

Quelles indications?

- Prematurés <32 semaines FiO2 ≥30%
- Prématurés moyens/tardifs ≥32 semaines
  Prématurés intubés ≥1 semaine
- Insuffisance respiratoire secondaire (neoARDS)
- Véhicule medicaments (ex. budésonide)

LISA: Administration non-invasive du surfactant

Thin soft catheter (gastric tube)
(Cologne method)

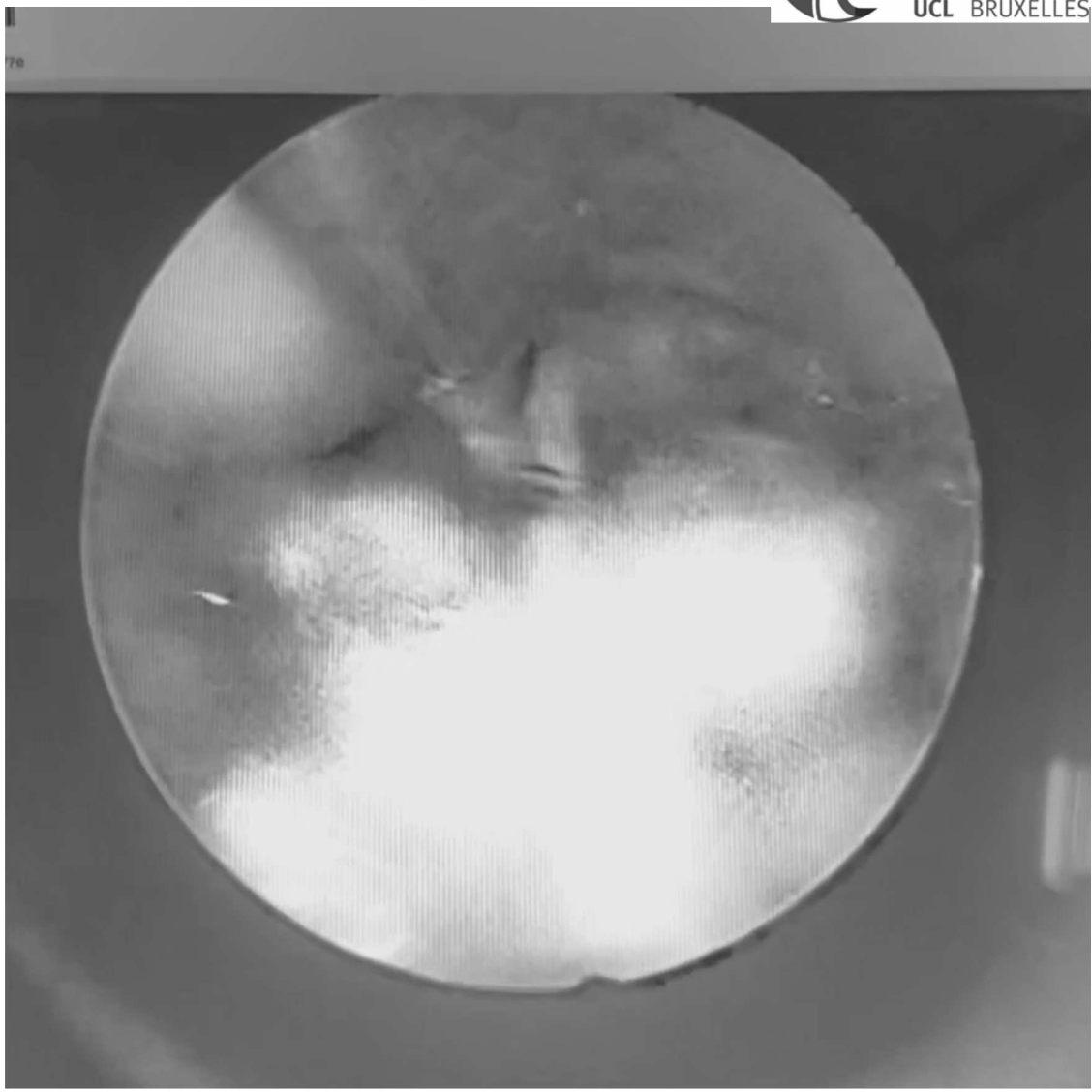
- Nasal or oral route
- Magill forceps

Thin rigid catheter (Hobart method)

- Oral route ± forceps
- LISACath: straight
- SurfCath: angled
- Other vascular catheters

Placement under video-laryngoscopy

- Helps preventing misplacement
- Favors trainees practice



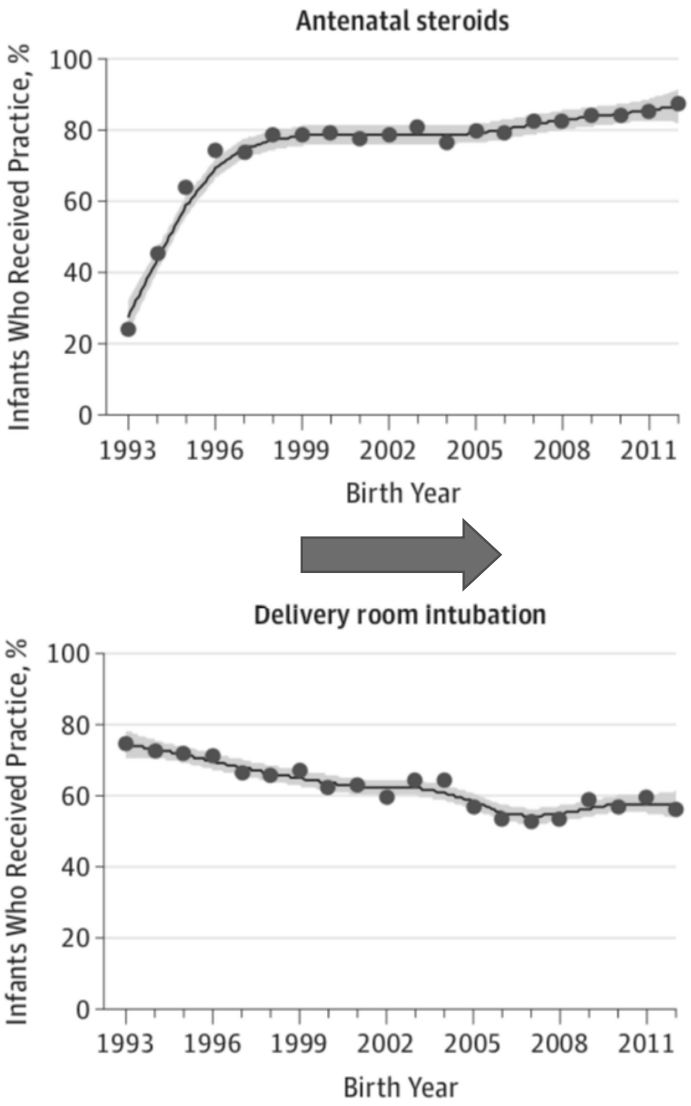
When?

Cochrane Soll, Morley 2001

- *8 studies*
- *<30-32 weeks "at risk of RDS"*
- *No routine CPAP*

"Prophylactic surfactant improves clinical outcome compared to selective use of surfactant in infants with established RDS"

- *Lower mortality*
- *Less BPD or death*
- *Less pneumothorax*
- *Less interstitial emphysema*



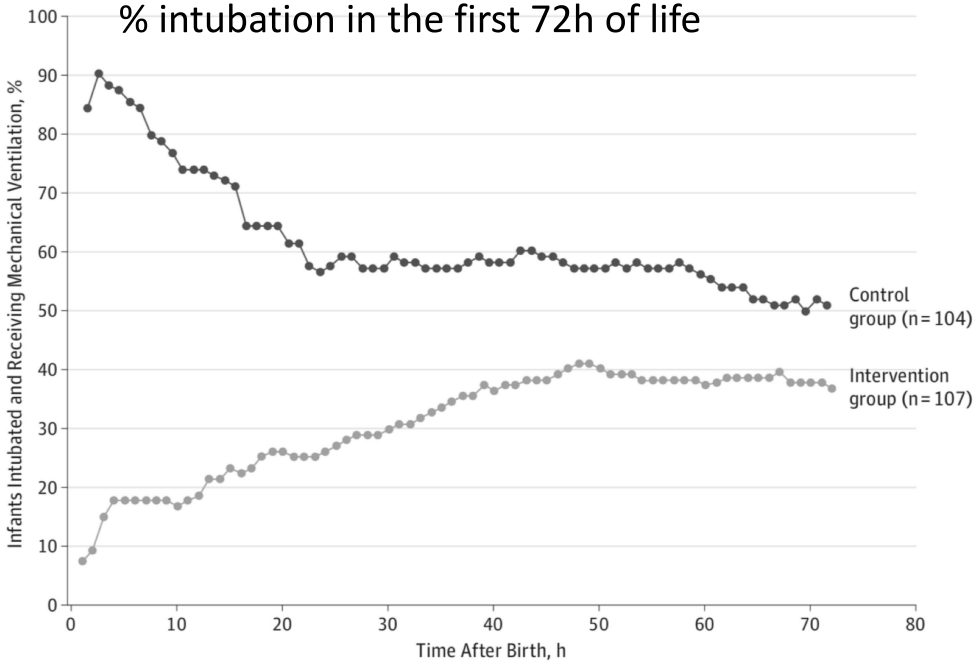
Stoll BJ et al. **Trends in Care Practices, Morbidity, and Mortality of Extremely Preterm Neonates, 1993-2012.** JAMA. 2015 Sep;314:1039-51

Cochrane Rojas-Reyes, Soll, Morley 2012

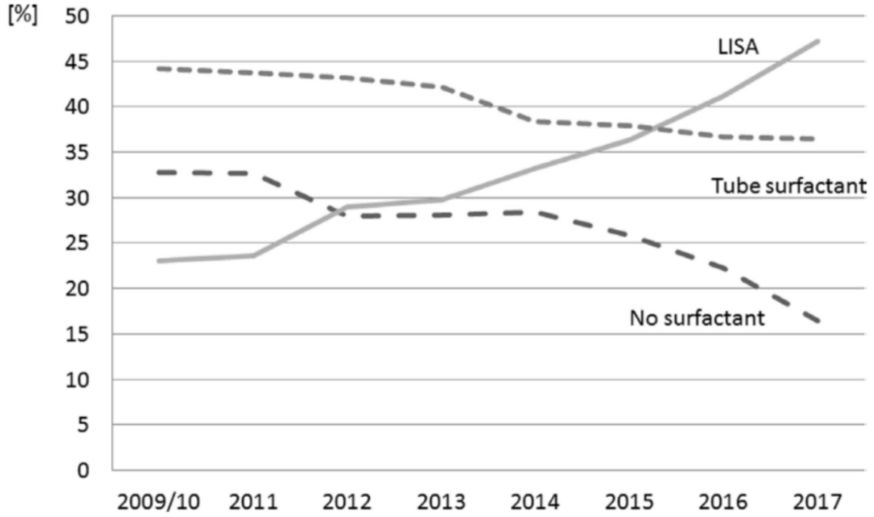
- 11 studies (previous + 3 large RCT's)
  - 9 with no routine CPAP
  - 2 with routine CPAP

"recent large trials demonstrate better clinical outcomes when using early stabilization on CPAP with selective surfactant administration in infants requiring intubation compared to prophylaxis"

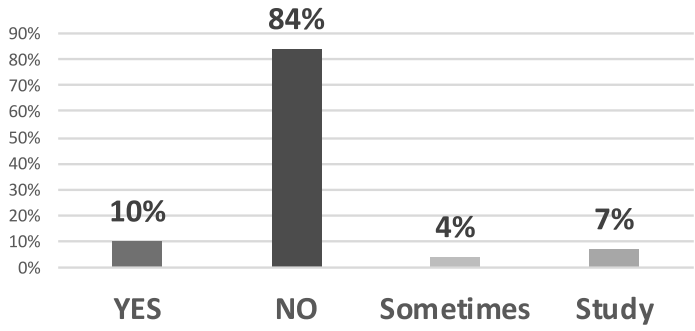
- No more benefits of prophylaxis
- Less BPD or death with selective surfactant



Multicenter RCT 2009-2012. 211 preterm infants 23.0-26.8 weeks randomized for surfactant administration vis LISA vs. ET tube. Kribs A et al. JAMA Pediatr. 2015;169(8):723-730



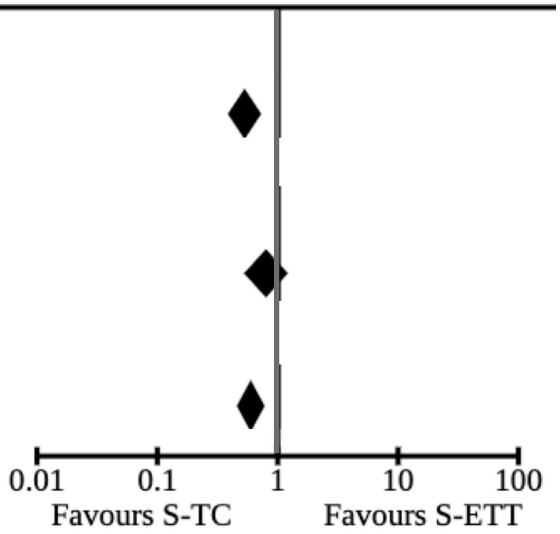
Mode of surfactant administration ≤30 weeks of gestation in the German Neonatal Network. Herting E et al. *Arch Dis Child Fetal Neonatal Ed* 2019;**104**:F655–F659.



Use of LISA in the US (AAP 2018 survey – 472 neonatologists) Kurepa D. et al. Journal of Perinatology (2019) 39:426–432

LISA/MIST
Surfactant therapy via thin catheter with spontaneous breathing

Study or Subgroup	Surfactant via catheter Events	Total	Surfactant via ETT Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.1.1 S-TC vs INSURE						
Subtotal (95% CI)		555		558	75.2%	0.52 [0.40 , 0.68]
1.1.2 S-TC vs surfactant via ETT with delayed extubation						
Subtotal (95% CI)		107		104	24.8%	0.79 [0.55 , 1.13]
Total (95% CI)		662		662	100.0%	0.59 [0.48 , 0.73]



16 RCT – 2164 infants

- 12 LISA/MIST vs. INSURE
- 2 LISA/MIST vs. intubation/ventilation
- 1 LISA/MIST vs. prolonged CPAP + rescue intubation
- 1 LISA/MIST with vs. without sedation

- Fewer intubations in first 72 hours
- Fewer deaths and BPD at 36 weeks
- Fewer air leaks
- Fewer severe IVH (grade III-IV)

Abdel-Latif ME et al. Cochrane Database of Systematic Reviews 2021, Issue 5. Art. No.: CD011672.

European Consensus Guidelines on the Management of Respiratory Distress Syndrome – 2019 Update

Sweet DG et al. Neonatology 2019;115:432–450

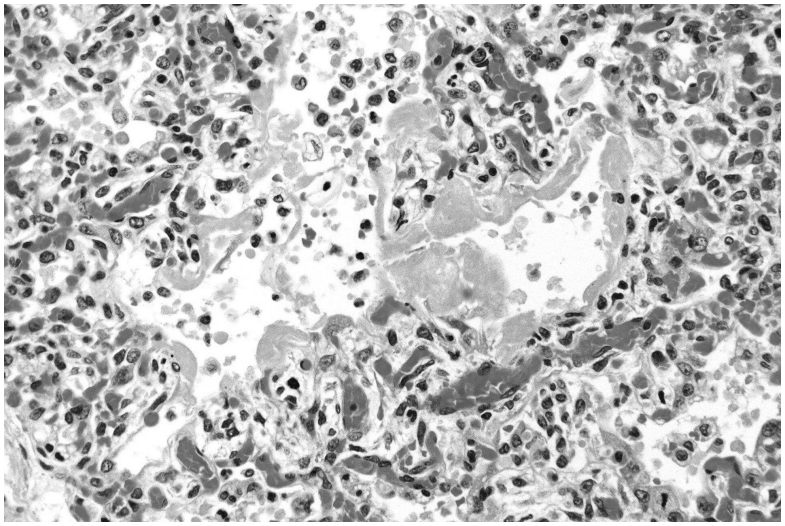
- Babies with RDS should be given an animal-derived surfactant preparation (**A1**).
- A policy of early rescue surfactant should be standard (**A1**), but there are occasions when surfactant should be given in the de- livery suite, such as when intubation is needed for stabilization (**A1**).
- Babies with RDS should be given rescue surfactant early in the course of the disease. A suggested protocol would be to treat babies who are worsening when FiO2 >0.30 on CPAP pressure of at least 6 cm H2O (**B2**).
- Poractant alfa at an initial dose of 200 mg/kg is better than 100 mg/kg of poractant alfa or 100 mg/kg of beractant for rescue therapy (**A1**).
- LISA is the preferred mode of surfactant administration for spontaneously breathing babies on CPAP, provided that clinicians are experienced with this technique (**B2**).
- A second and occasionally a third dose of surfactant should be given if there is ongoing evidence of RDS such as persistent high oxygen requirement and other problems have been excluded (**A1**).

There are no evidence-based recommendations for surfactant use in late preterm (LPT) and term infants with respiratory distress syndrome (RDS).

Mechanisms of injury

Ventilation-induced lung injury:

	Cause	Effects
Barotrauma	Excessive inspiratory pressure delivery	Alveolar damage, pulmonary oedema, pulmonary air leak
Volutrauma	Excessive inspiratory tidal volume delivery	Disruption of alveolar cells and epithelial and endothelial layers
Atelectrauma	Repeated recruitment and derecruitment of lung units due to inadequate PEEP and positive pressure ventilation	'Shearing' effect on alveoli during reopening of lung units Over-expansion of some lung units due to inability to deliver the inspiratory volume to other closed lung units
Biotrauma	Inflammation or infection	Ongoing lung inflammation
Rheotrauma	Inappropriate airway flow	Excessive flow: turbulence, excessive PEEP, lung over-inflation Insufficient flow: air hunger, increased work of breathing



Respiratory distress syndrome:

Surfactant deficiency
Premature anti-oxidant system
Premature lung structure
Compliant chest wall

- Loss of FRC, collapse of the alveoli, atelectasis
- Hypoventilation, hypoperfusion, hypoxemia, hypercarbia, acidosis
- endothelial and epithelial damage
- leakage of plasma proteins

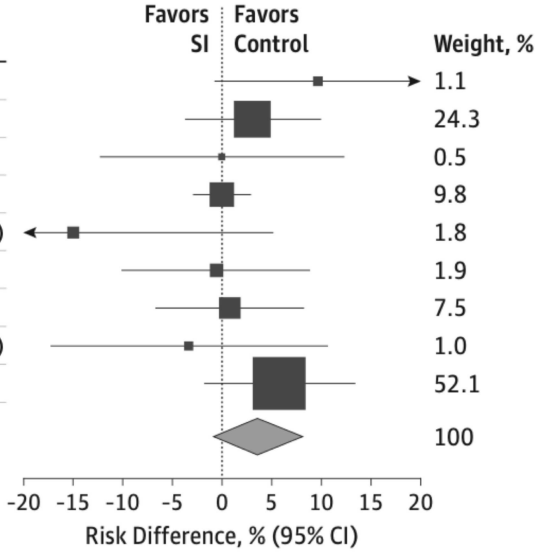
Chitty H et al. Infant 2015; 11(1): 8-12.

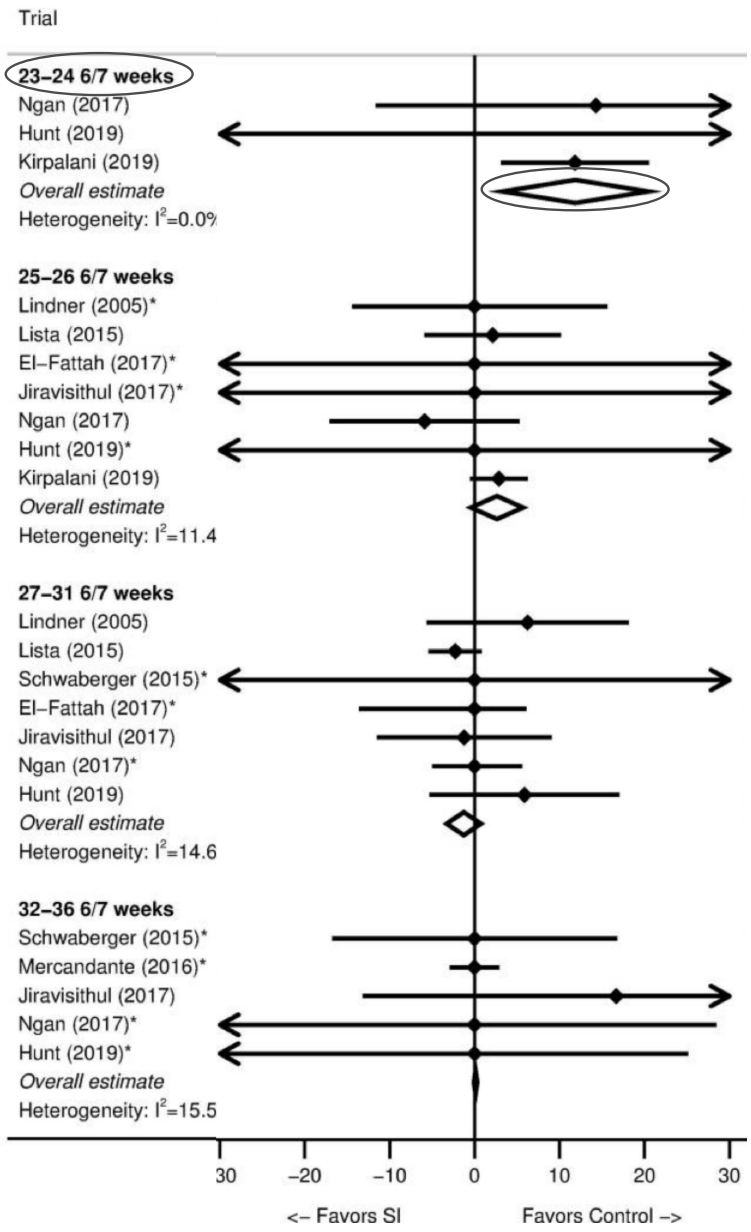
JAMA Pediatrics | Original Investigation

Sustained Inflation vs Standard Resuscitation for Preterm Infants
A Systematic Review and Meta-analysis

Figure 1. Fixed-Effects Meta-analysis of Risk Difference of Primary Outcome, Death During Hospitalization

Source	SI, No./ Total No.	Control, No./ Total No.	Risk Difference, % (95% CI)	Weight, %
Lindner et al,[22] 2005	3/31	0/30	9.7 (-0.7 to 20.1)	1.1
Lista et al,[23] 2015	17/148	12/143	3.1 (-3.8 to 10.0)	24.3
Schwaberger et al,[25] 2015[a]	0/20	0/20	0.0 (-12.3 to 12.3)	0.5
Mercadante et al,[26] 2016[a]	0/93	0/92	0.0 (-2.9 to 2.9)	9.8
Abd El-Fattah et al,[27] 2017	8/80	5/20	-15.0 (-35.1 to 5.1)	1.8
Jiravisitkul et al,[24] 2017	2/43	2/38	-0.6 (-10.1 to 8.9)	1.9
Ngan et al,[28] 2017	5/76	5/86	0.8 (-6.7 to 8.2)	7.5
Hunt et al,[29] 2019	2/30	3/30	-3.3 (-17.3 to 10.6)	1.0
Kirpalani et al,[9] 2019	48/215	35/211	5.7 (-1.8 to 13.2)	52.1
Overall estimate Heterogeneity: I^2 = 16.5%	85/736	62/670	3.6 (-0.7 to 7.9)	100





Foglia EE et al. *JAMA Pediatr*. 2020;174(4):e195897.