European Consensus Guidelines

on the

RDS Management

2019 update

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European Consensus

The “European Consensus Guidelines for the Management of RDS” were first published in 2007 and have been updated

in 2010, 2013 and 2016 .

Grades of recommendation and levels of evidence

- Quality of evidence

High quality	**A**
Moderate quality	B
Low quality	C
Very low quality	D

- Strength of recommendation

Strong recommendation for using intervention	1
Weak recommendation for using intervention	2

Quality of Evidence: Definitions

- **High Quality** - further research is very unlikely to change our confidence in the estimate of effect
- **Moderate Quality –** further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
- **Low Quality –** further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate

Very Low Quality – any estimate of effect is very uncertain

Introduction:

- How many babaies have genuine RDS ?

  Definitions 0f RDS ?

EUROPEAN CONSENSUS STATEMENT ON RDS MANAGEMENT (2019)

- Aim of management of RDS:
  - Maximise survival
  - Minimising adverse effects including BPD

- Summary of Recommendations are under the following heads:
  - A. Prenatal Care
  - B. Delivery Room Stabilization
  - C. Respiratory support and Surfactant
  - D. Supportive Care

A) Prenatal Care

Prenatal care

- **Treatment for RDS should begin before birth.**

1. identify high-risk pregnancies early and aim for effective prevention of preterm birth.

2. Tocolytic drugs

3. One Course of Steroids

4. Second Course of steroids ?

5. Mgso4

6. Antibiotics

- **A. PRENATAL CARE:**

- 1. Mothers at high risk of preterm birth < 28–30 weeks' gestation should be transferred to perinatal centres with experience in management of RDS. **(C1)**

- 2. In women with symptoms of preterm labour, cervical length and fibronectin measurements should be considered to prevent unnecessary use of tocolytic drugs and/or antenatal steroids. **(B2)**

- **A. PRENATAL CARE:**

- 3. Clinicians should consider short-term use of tocolytic drugs in very preterm pregnancies **(B1)**
  - To allow completion of a course of corticosteroids and/or
  - In-utero transfer to a perinatal centre

- 4. Clinicians should offer a single course of prenatal corticosteroids to all women at risk of preterm delivery from when pregnancy is considered potentially viable until 34 weeks' gestation ideally at least 24 h before birth **(A1)**

- **A. PRENATAL CARE:**

- 5. A single repeat course of steroids may be given in threatened preterm birth before 32 weeks' gestation if the first course was administered at least 1–2 weeks earlier. **(A2)**

- 6. $MgSO_4$ should be administered to women in imminent labour before 32 weeks' gestation. **(A2)**

Prenatal care

- A **single course of prenatal corticosteroids** given to mothers with anticipated preterm delivery **improves survival, reduces RDS, NEC and IVH** and does not appear to be associated with any significant maternal or short-term fetal adverse effects .
- In pregnancies **between 34 and 36 weeks**' gestation, prenatal steroids also reduce risk of short-term **respiratory morbidity but not mortality**, and there is increased risk of neonatal **hypoglycaemia**
- The optimal treatment to **delivery interval is more than 24 h and less than 7 days after the start of steroid** treatment; beyond 14 days, benefits are diminished.

Prenatal care

- **Magnesium sulphate** (MgSO4) given to women with **imminent preterm delivery,before 32,** reduces cerebral palsy at 2 years of age by about 30%.
- **A repeat course steroids reduces the risk of respiratory support. However, it** decreases fetal growth, and **repeat doses do not reduce mortality or other serious health outcomes.**
- **WHO recommends** that a single repeat course of steroids may be considered if preterm birth does not occur within 7 days after the initial course and there is a high risk of preterm birth in the next 7 days .**It is unlikely that repeat courses given after 32 weeks' gestation improve outcome**

B. Delivery Room Stabilization

Delivery Room/ Stabilization Oxygen

- **Supporting transition**
- Timing of umbilical cord clamping
- polythene bag , body temperature
- FIO2
- CPAP, PPV, Intubation
- Pulse oximetry/ Blender.

Delivery Room

"**Supporting transition**" rather than "**resuscitation**" is therefore in most cases **the preferred term in RDS management,** and infants should be allowed to gently transition whilst being exposed to a minimum number of interventions that may cause harm

- **B. DELIVERY ROOM STABILIZATION:**

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

- 2. Plastic bags or occlusive wrapping under radiant warmers should be used during stabilisation in the delivery suite for babies < 28 weeks' gestation to reduce the risk of hypothermia. **(A1)**

- **B. DELIVERY ROOM STABILIZATION:**

- 3. In spontaneously breathing babies, stabilise with CPAP of at least 6 cm H2O via mask or nasal prongs **(B1).**

- 4. Do not use Sustained Inflation as there is no long-term benefit **(B1).**

- 5. Gentle positive pressure lung inflations with 20–25 cm H2O peak inspiratory pressure (PIP) should be used for persistently apnoeic or bradycardic infants.

- **B. DELIVERY ROOM STABILIZATION:**

- 6. Oxygen for resuscitation should be controlled using a blender.

- Use an initial FiO2 of
  - 0.30 for babies < 28 weeks' gestation
  - 0.21–0.30 for those 28–31 weeks,
  - 0.21 for 32 weeks' gestation and above.

- FiO2 adjustments up or down should be guided by pulse oximetry (**B2).**

- **B. DELIVERY ROOM STABILIZATION:**

- 7. For infants < 32 weeks' gestation, SpO2 of 80% or more (and heart rate > 100/min) should be achieved within 5 min. **(C2)**

- 8. Intubation should be reserved for babies not responding to positive pressure ventilation via face mask or nasal prongs. **(A1)**

- 9. Babies who require intubation for stabilisation should be given surfactant. **(B1)**

C. Respiratory support & Surfactant

a) Surfactant Therapy
b) Oxygen Supplementation beyond Stabilisation
c) Non-Invasive Respiratory Support
d) MV Strategies
e) Monitoring and Supportive Care

Surfactant Therapy

- Surfactant Administration Methods:

1. IN-SUR-E , 2. LISA , 3. Nebulisation (more mature infants of 32–33 w),

4.laryngeal mask , 5.pharyngeal deposition

- When to Treat with Surfactant?

- Surfactant Preparations

Surfactant Therapy

- **the main purpose of**

avoiding surfactant prophylaxis is

to avoid intubation.

- surfactant given **earlier in the course of disease**

  works **better than later in terms of**

reducing :

1. air leaks,

and

2. avoiding MV…

When to Treat with Surfactant?

……earlier in the course

of RDS……???

…. as early as possible

A Dilemma for neonatologists.?

When to Treat with Surfactant?

- At present, **severity of RDS** can only be determined

1.**clinically using a combination of FiO2** to maintain normal saturations, coupled with

2. **judgement of work of breathing** and

degree of aeration of **the lungs on**

3. chest X-ray,

all of which can be influenced by CPAP.

- **Lung ultrasound** may be a useful adjunct to clinical decision making in experienced hands

When to Treat with Surfactant?

- **If intubation** is required as part of stabilisation, then surfactant should be **given immediately**
- Many preterm infants will **transition successfully on CPAP**.

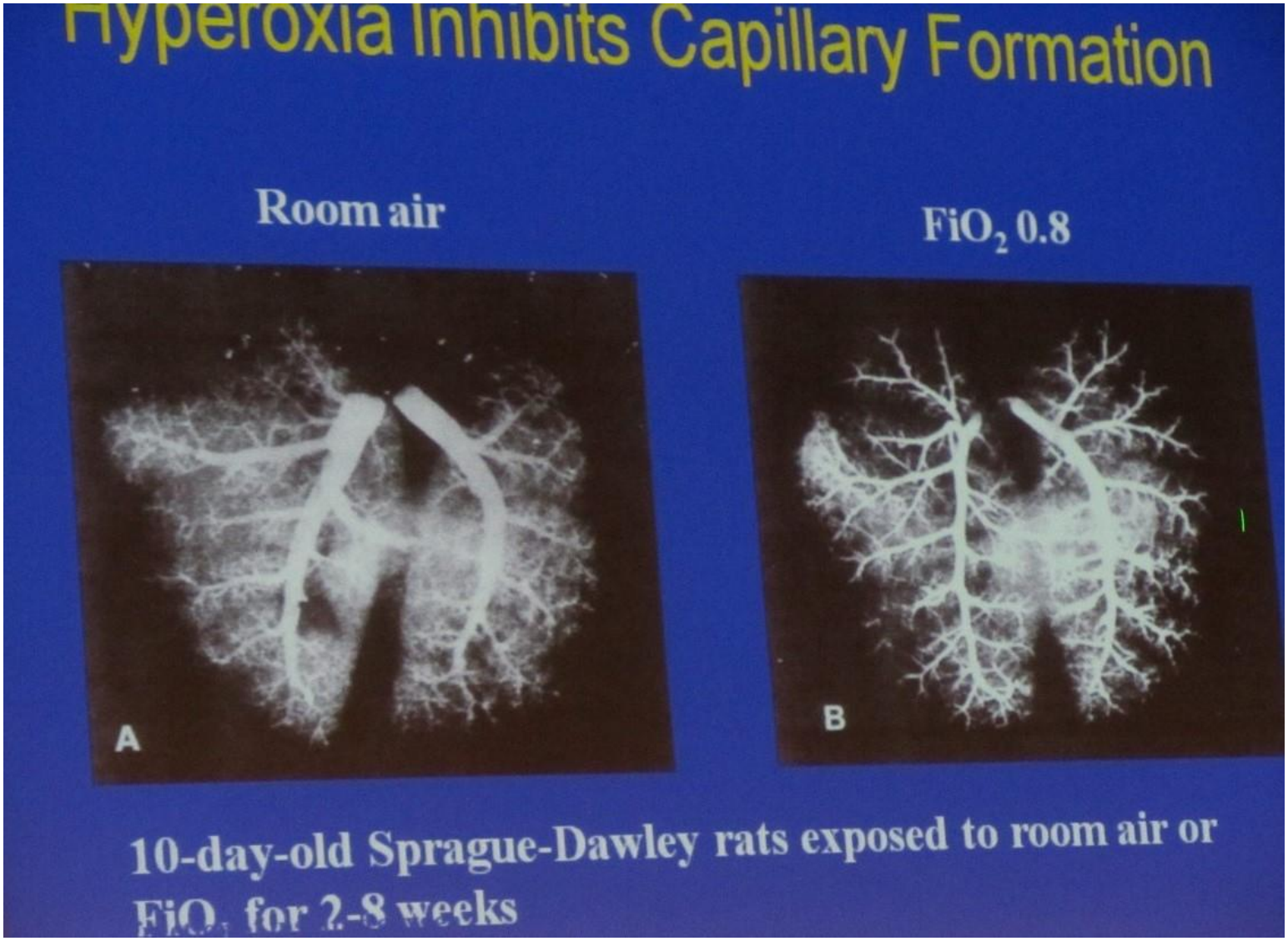
- **Those with RDS will develop progressively worsening** lung disease, **clinically presenting** as:
  - increased work of breathing,
  - sternal recession and
  - **increasing oxygen requirements**

to maintain normal saturations.

FIO2?

- The **2013 Guideline** suggested that **surfactant should be administered** when **FiO2 >0.30 for very immature** babies and **>0.40 for more mature** infants based on thresholds used in the early clinical trials.
- Observational studies have confirmed that **FiO2 exceeding 0.30 in the first hours after birth in babies on CPAP is a reasonably good test for predicting subsequent CPAP failure .**
- **Therefore it is recommended that the threshold of FiO2 >0.30 is used for all babies with a clinical diagnosis of RDS, especially in the early phase of worsening disease.**

FIO2?


Hyperoxia Inhibits Capillary Formation
Room air
FiO_2 0.8
A
B
10-day-old Sprague-Dawley rats exposed to room air or
FiO_2 for 2-8 weeks

- C. RESPIRATORY SUPPORT AND SURFACTANT:

- The overall aim is:
  - To avoid invasive MV if possible,
  - To give surfactant as early as possible in the course of RDS once it is deemed necessary.

- C. RESPIRATORY SUPPORT AND SURFACTANT:
- a) Surfactant Therapy

- 1. Babies with RDS should be given an animal-derived surfactant preparation. **(A1)**

- 2. Policy of early rescue surfactant should be standard. **(A1).**

- 3. Surfactant should be given in the delivery suite,when intubation is needed for stabilisation. **(A1).**

- C. RESPIRATORY SUPPORT AND SURFACTANT:
- a) Surfactant Therapy

- 4. 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)**

- 5. 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).**

- C. RESPIRATORY SUPPORT AND SURFACTANT:
- a) Surfactant Therapy

- 6. LISA is the preferred mode of surfactant administration for spontaneously breathing babies on CPAP, provided that clinicians are experienced with this technique. **(B2)**

- 7. 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)**

Surfactant Preparations

- Most of trials show that **surfactants have similar efficacy when used in similar doses;** however, **there is a survival advantage when 200 mg/kg** of poractant alfa is compared with 100 mg/kg of beractant or 100 mg/kg poractant alfa to treat RDS .
- **Surfactant combined with budesonide significantly reduces BPD**

multiple doses of surfactant

- Clinical trials comparing **multiple doses** to a single dose showed **fewer air leaks**, although these were conducted in an era when babies were maintained on MV. **Today many infants are maintained on non-invasive ventilation even when surfactant is required.**
- **Need for re-dosing can be minimised by using the :**

1- larger dose of 200 mg/kg of poractant alfa .

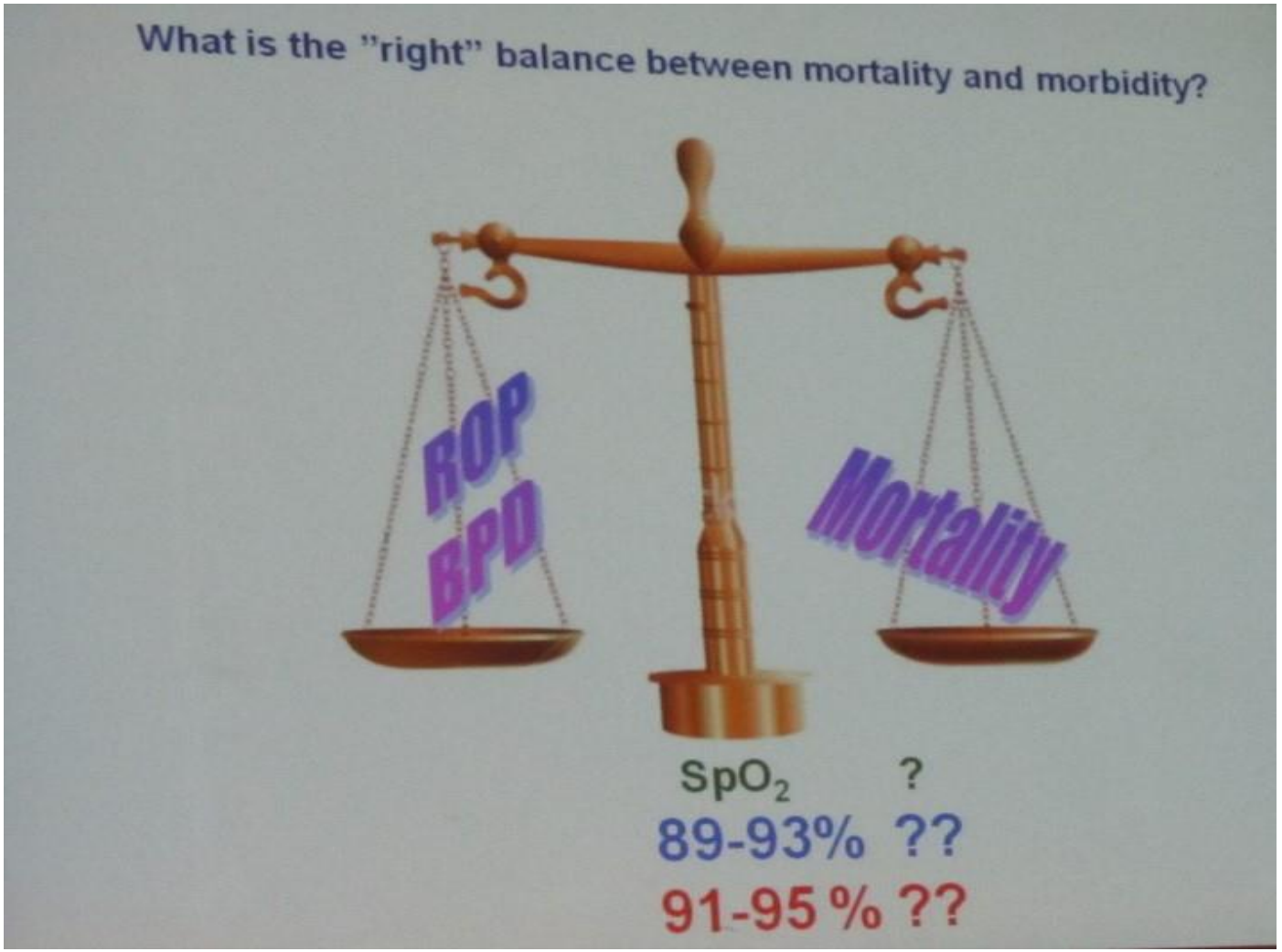
2- Prediction of IN-SUR-E failure using **clinical criteria** and **blood gases** could define a population that would be reasonable to maintain on MV for a while after surfactant has been given

- C. RESPIRATORY SUPPORT AND SURFACTANT:
- **b) Oxygen Supplementation beyond Stabilisation**

- 1. In preterm babies receiving oxygen, the saturation target should be between 90 and 94%. **(B2)**

- 2. Alarm limits should be set to 89 and 95%. **(D2)**

Episodes of intermittent hypoxa emia and bradycardia are associated with increased risk of late death or disability at 18 months,



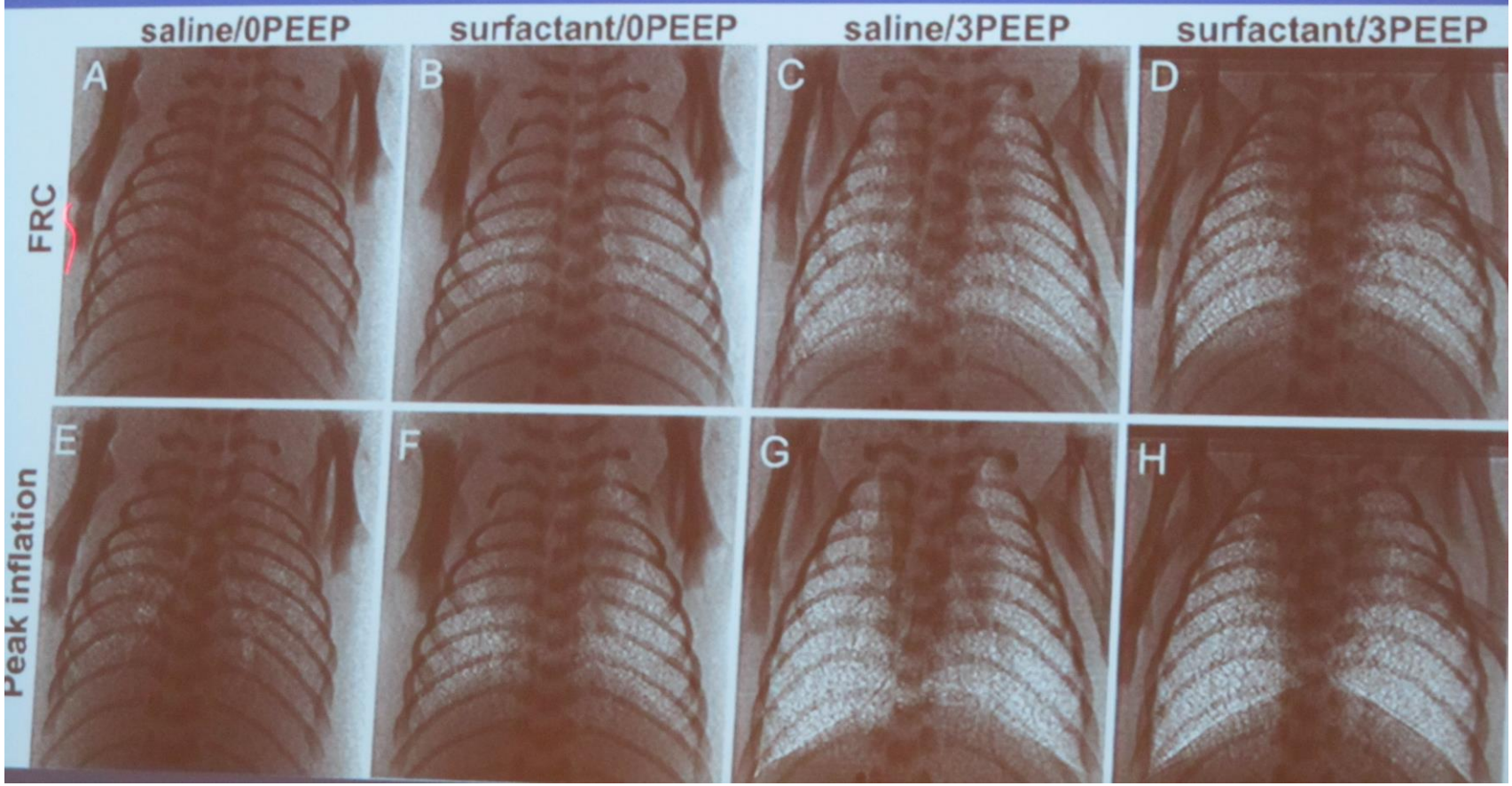
- C. RESPIRATORY SUPPORT AND SURFACTANT:
- **c) Non-Invasive Respiratory Support**

- 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 H2O**. **(A2)**
- 3. PEEP can then be individualised depending on clinical condition, oxygenation and perfusion. **(D2)**

Preterm newborn rabbits (gestational age 28 d) treated with either saline or surfactant with or without PEEP

Lung gas volumes

2.5 ml/kg 0.9 ml/kg 7.5 ml/kg 8.5 ml/kg



- C. RESPIRATORY SUPPORT AND SURFACTANT:
- c) Non-Invasive Respiratory Support

- 4. CPAP with early rescue surfactant is considered optimal management for babies with RDS. **(A1)**
- 5. 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)**
- 6. During weaning, HFNC can be used as an alternative to CPAP for some babies with the advantage of less nasal trauma. **(B2)**

- C. RESPIRATORY SUPPORT AND SURFACTANT:
- d) Mechanical Ventilation Strategies

- 1. After stabilisation, MV should be used in babies with RDS when other methods of respiratory support have failed. **(A1).**
- 2. **Duration of MV should be minimised. (B2)**
- 3. 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)**

Several strategies have been used specifically to shorten duration of MV

1. Extubating to a relatively higher **CPAP** pressure of 7–9 cm H2O or NIPPV will improve chance of success .

2. permissive hypercarbia,

3. caffeine therapy,

4. postnatal steroid treatment and

5. avoiding over-use of sedation.

- C. RESPIRATORY SUPPORT AND SURFACTANT:
- d) Mechanical Ventilation Strategies

- 4. When weaning from MV, it is reasonable to tolerate a modest degree of hypercarbia provided the pH remains above 7.22. **(B2)**

- 5. Caffeine should be used to facilitate weaning from MV. **(A1)**

- 6. Early caffeine should be considered for babies at high risk of needing MV such as those on non-invasive respiratory support. **(C1)**

- C. RESPIRATORY SUPPORT AND SURFACTANT:
- **d) Mechanical Ventilation Strategies**
- 7. A short tapering course of low dose or very low dexamethasone should be considered to facilitate extubation in babies who remain on MV after 1–2 weeks. **(A2)**
- 8. Inhaled budesonide can be considered for infants at very high risk of BPD. **(A2)**
- 9. Opioids should be used selectively when indicated by clinical judgment and evaluation of pain indicators (**D1).**
- 10. The routine use of morphine or midazolam infusions in ventilated preterm infants is not recommended (**A1).**

D. Supportive Care

supportive care:

1. **monitoring physiological variables**
2. **Temperature** Control:

   Servo-controlled incubators with skin temperature set at 36.5 °C decrease neonatal mortality

3. Antibiotics:
4. **Fluids** and Nutritional Support
5. Managing **Blood Pressure** and Perfusion
6. PDA
7. **H**aemoglobin (Hb) concentration

supportive care:

- **optimal supportive care with monitoring physiological variables** is important.

1.**Oxygen blenders** **2. Pulse oximetry** **3. ECG** monitoring and

4. monitoring of **PaCO2 levels**.

5**. Detection of exhaled CO2** and continuous **measurement of end-tidal CO2**

6. Umbilical arterial cannulation ..

7. micro-sampling techniques : Close monitoring of serum electrolytes and haematological values is necessary.

8. Blood pressure should be recorded

9. radiology services and portable ultrasound

Antibiotics:

- Antibiotics are often started in babies with RDS until sepsis has been ruled out.
- Routine antibiotic prophylaxis may do more harm than good.
- If screening is necessary, then antibiotics are started empirically **whilst waiting for test results**

Fluid:

- adjustments individualised according to fluid balance, **weight change** and **serum electrolyte levels**.
- A modest early postnatal weight loss is normal.
- Regimens with more restricted fluids have better outcomes with **reductions in PDA, NEC and BPD .**
- Delaying introduction of sodium supplementation until beyond the **third day or 5% weight loss will also improve outcome**

- **D. SUPPORTIVE CARE**

- 1. Core temperature should be maintained between 36.5 and 37.5 °C at all times. **(C1)**

- 2. Most babies should be started on intravenous fluids of 70–80 mL/kg/day in a humidified incubator, although some very immature babies may need more. **(C2)**

- 3. Fluids must be tailored individually according to serum sodium levels, urine output and weight loss. **(D1)**

- **D. SUPPORTIVE CARE**

- 4. Parenteral nutrition should be started from birth. Amino acids 1–2 g/kg/day should be started from day one and quickly built up to 2.5–3.5 g/kg/day. **(C2)**

- 5. Lipids should be started from day one and built up to a maximum of 4.0 g/kg/day if tolerated. **(C2)**

- 6. Enteral feeding with mother's milk should be started from the first day if the baby is haemodynamically stable. **(B2)**

- **D. SUPPORTIVE CARE**

- 7. Treatment of hypotension is recommended when it is confirmed by evidence of poor tissue perfusion such as oliguria, acidosis and poor capillary return rather than purely on numerical values. **(C2)**

- 8. If a decision is made to attempt therapeutic closure of the PDA then indomethacin, ibuprofen or paracetamol can be used. **(A2)**

Managing Blood Pressure and Perfusion

1. Antenatal steroids, 2. delayed cord clamping and

3. avoidance of MV

are associated with higher mean blood pressure after birth.

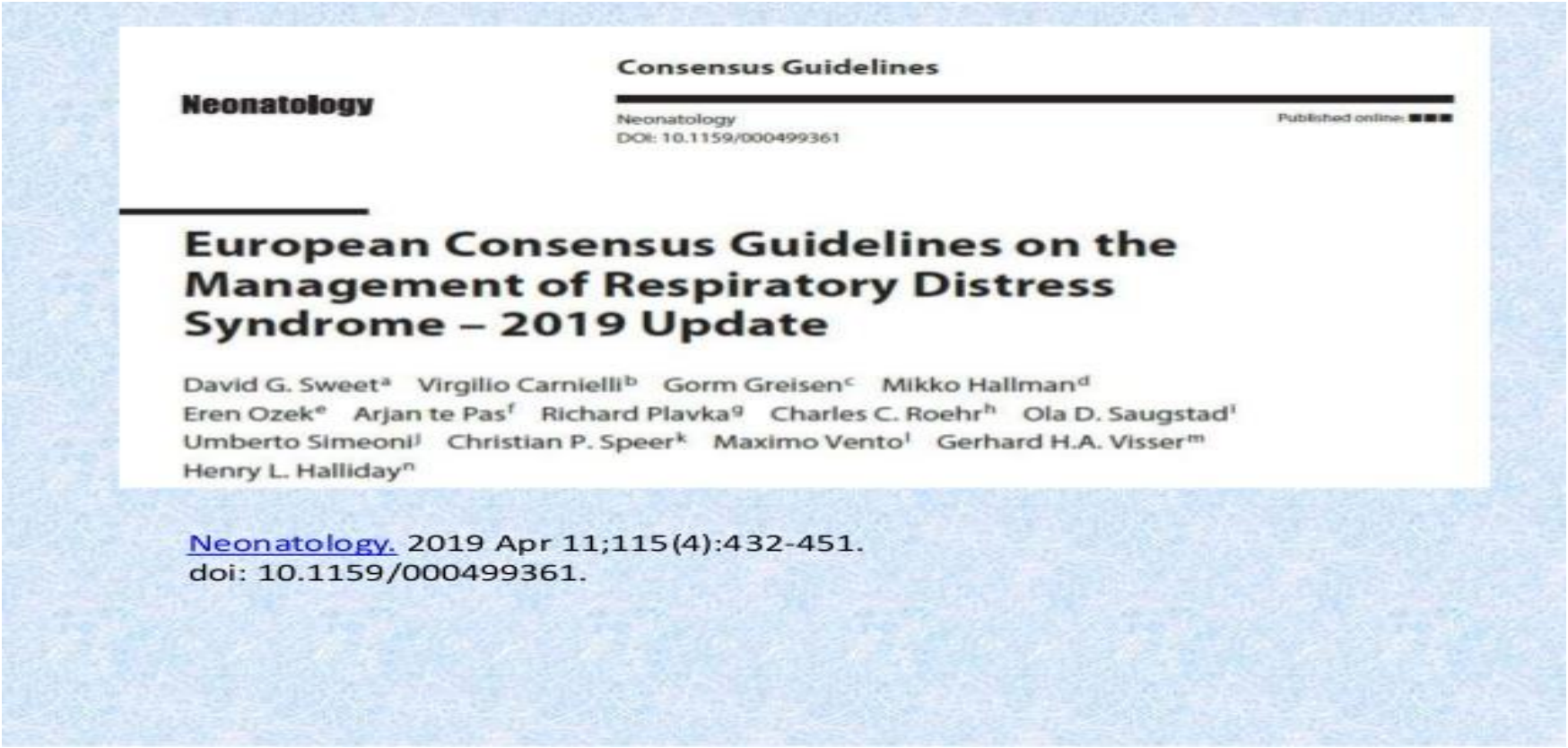
- **Hypotension and low systemic blood flow are associated with adverse long-term outcome**,
- although thresholds for intervention and optimal treatment are unclear

Managing Blood Pressure and Perfusion

- **Hypovolaemia** is probably over-diagnosed, and administration of **saline boluses** is associated with **poorer outcomes .**
- **Dopamine** is more effective than dobutamine at increasing blood pressure in hypotensive infants, although
- **dobutamine or epinephrine** may be a more rational choice in the setting of **reduced ventricular function**

- **D. SUPPORTIVE CARE**

- 9. Haemoglobin (Hb) concentration should be maintained within acceptable limits.
- Hb thresholds are
  - 12 g/dL (HCT 36%) for infants with severe cardiopulmonary disease ,
  - 11 g/dL (HCT 30%) for those who are oxygen dependent and
  - 7 g/dL (HCT 25%) for stable infants beyond 2 weeks of age. **(C2)**



Consensus Guidelines

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

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- **Henry Halliday and Christian Speer** are or have been **consultants to Chiesi Farmaceutici**, Parma, the manufacturer of a leading animal-derived surfactant preparation used to treat RDS and a caffeine product for treatment of apno ea of prematurity.
- **Virgilio Carnielli** is a member of **the Chiesi Farmaceutici Advisory Board**.
- **Henry Halliday and Christian Speer are joint Chief Editors of Neonatology.**


ما زنده به آنیم که آرام نگیریم
موجیم که آسودگی ما عدم ماست