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## European Resuscitation Council Guidelines 2021: Newborn resuscitation and support of transition of infants at birth

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### Abstract

The European Resuscitation Council has produced these newborn life support guidelines, which are based on the International Liaison Committee on Resuscitation (ILCOR) 2020 Consensus on Science and Treatment Recommendations (CoSTR) for Neonatal Life Support. The guidelines cover the management of the term and preterm infant. The topics covered include an algorithm to aid a logical approach to resuscitation of the newborn, factors before delivery, training and education, thermal control, management of the umbilical cord after birth, initial assessment and categorisation of the newborn infant, airway and breathing and circulation support, communication with parents, considerations when withholding and discontinuing support.

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## Introduction and scope

These guidelines are based on the International Liaison Committee on Resuscitation (ILCOR) 2020 Consensus on Science and Treatment Recommendations (CoSTR) for Neonatal Life Support.<sup>1</sup> For the purposes of the ERC Guidelines the ILCOR recommendations were supplemented by focused literature reviews undertaken by the ERC NLS guidelines Group for topics not reviewed by 2020 ILCOR CoSTR. When appropriate, the guidelines were informed by the expert consensus of the ERC guidelines group membership.

These guidelines were drafted and agreed by the Newborn Life Support Writing Group members. The methodology used for guideline development is presented in the Executive summary.<sup>2</sup> The guidelines were posted for public comment in October 2020. The feedback was reviewed by the writing group and the guidelines were updated where relevant (see supplemental material). The Guideline was presented to and approved by the ERC General Assembly on 10th December 2020.

Key messages from these guidelines are summarised in Fig. 2.

## COVID 19 context

The ERC has produced guidance on newborn life support in the context of coronavirus disease 2019 (SARS-CoV-2),<sup>3</sup> this is based on an ILCOR CoSTR and systematic review.<sup>4,5</sup> Our understanding of the risks to infants potentially exposed to SARS-CoV-2 and the risk of virus transmission and infection to those providing care is evolving. Please check ERC and national guidelines for the latest guidance and local policies for both treatment and rescuer precautions.

### Summary of changes since the 2015 guidelines

#### Management of the umbilical cord

Clamping after at least 60 s is recommended, ideally after the lungs are aerated. Where delayed cord clamping is not possible cord milking should be considered in infants >28 weeks gestation.

#### Infants born through meconium-stained liquor

In non-vigorous infants, recommendations are against immediate laryngoscopy with or without suction after delivery, because this may delay aeration and ventilation of the lungs.

#### Use of the laryngeal mask

If facemask ventilation is unsuccessful or if tracheal intubation is unsuccessful or not feasible a laryngeal mask may be considered as an alternative means of establishing an airway in infants of >34 weeks gestation (about 2000 g, although some devices have been used successfully in infants down to 1500 g).

#### Inflation pressure

If there is no response to initial inflations despite an open airway then a gradual increase in the inflation pressure is suggested.

A starting pressure of 25 cm H<sub>2</sub>O is suggested for preterm infants <32 weeks gestation.

#### Air/oxygen for preterm resuscitation

Recommendations are for starting in air at 32 weeks gestation or more, 21–30% inspired oxygen at 28–31 weeks gestation and 30% inspired oxygen at <28 weeks gestation.

The concentration should be titrated to achieve saturations of ≥80% at 5 min of age because there is evidence of poorer outcomes where this is not achieved.

#### Chest compressions

If chest compressions are required, the inspired oxygen concentration should be increased to 100% and consideration given towards securing the airway ideally with a tracheal tube.

### Vascular access

The umbilical vein is still favoured as the optimal route of access but, intraosseous access is an alternative method of emergency access for drugs/fluids.

### Adrenaline

Where the heart rate has not increased after optimising ventilation and chest compressions an intravenous dose of adrenaline of 10–30 micrograms kg<sup>-1</sup> is recommended, repeated every 3–5 min in the absence of a response.

### Glucose during resuscitation

An intravenous dose of 250 mg kg<sup>-1</sup> (2.5 mL kg<sup>-1</sup> of 10% glucose) is suggested in a prolonged resuscitation to reduce the likelihood of hypoglycaemia.

### Prognosis

Failure to respond despite 10–20 mins of intensive resuscitation is associated with high risk of poor outcome. It is appropriate to consider discussions with the team and family about withdrawal of treatment if there has been no response despite the provision of all recommended steps of resuscitation and having excluded reversible causes

## Concise guideline for clinical practice

### Factors before delivery

#### Transition and the need for assistance after birth

Most, but not all, infants adapt well to extra-uterine life but some require help with stabilisation, or resuscitation. Up to 85% breathe spontaneously without intervention; a further 10% respond after drying, stimulation and airway opening manoeuvres; approximately 5% receive positive pressure ventilation. Intubation rates vary between 0.4% and 2%. Fewer than 0.3% of infants receive chest compressions and only 0.05% receive adrenaline.

### Risk factors

A number of risk factors have been identified as increasing the likelihood of requiring help with stabilisation, or resuscitation (Fig. 1).

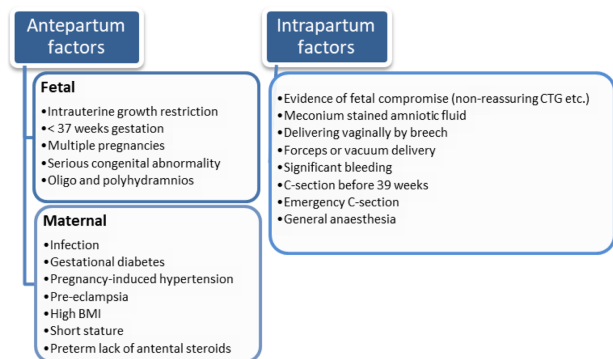
### Staff attending delivery

Any infant may develop problems during birth. Local guidelines indicating who should attend deliveries should be developed, based on current understanding of best practice and clinical audit, and taking into account identified risk factors (Fig. 1). As a guide,

- Personnel competent in newborn life support should be available for every delivery.
- If intervention is required, there should be personnel available whose sole responsibility is to care for the infant.
- A process should be in place for rapidly mobilising a team with sufficient resuscitation skills for any birth.

### Equipment and environment

- All equipment must be regularly checked and ready for use.
- Where possible, the environment and equipment should be prepared in advance of the delivery of the infant. Checklists facilitate these tasks.
- Resuscitation should take place in a warm, well-illuminated, draught-free area with a flat resuscitation surface and a radiant heater (if available).
- Equipment to monitor the condition of the infant and to support ventilation should be immediately available.



**Fig. 1 – Common factors associated with an increased risk of a need for stabilization, or resuscitation at birth.**

- Additional equipment, that might be required in case of more prolonged resuscitation should be easily accessible.

### Planned home deliveries

- Ideally, two trained professionals should be present at all home deliveries.
- At least one must be competent in providing mask ventilation and chest compressions to the newborn infant.
- Recommendations as to who should attend a planned home delivery vary from country to country, but the decision to undergo such a delivery, once agreed with medical and midwifery staff, should not compromise the standard of initial assessment, stabilisation or resuscitation at birth.
- There will inevitably be some limitations to the extent of the resuscitation of a newborn infant in the home, due to the distance from healthcare facilities and equipment available, and this must be made clear to the mother at the time plans for home delivery are made.
- When a birth takes place in a non-designated delivery area a minimum set of equipment of an appropriate size for the newborn infant should be available, including:
  - clean gloves for the attendant and assistants,
  - means of keeping the infant warm, such as heated dry towels and blankets,
  - a stethoscope to check the heart rate,
  - a device for safe assisted lung aeration and subsequent ventilation such as a self-inflating bag with appropriately sized facemask,
  - sterile instruments for clamping and then safely cutting the umbilical cord.
- Unexpected deliveries outside hospital are likely to involve emergency services who should be trained and prepared for such events and carry appropriate equipment.
- Caregivers undertaking home deliveries should have pre-defined plans for difficult situations.

### Briefing

- If there is sufficient time, brief the team to clarify responsibilities, check equipment and plan the stabilisation, or resuscitation.
- Roles and tasks should be assigned—checklists are helpful.
- Prepare the family if it is anticipated that resuscitation might be required.

### Training/education

#### Recommendations

- Newborn resuscitation providers must have relevant current knowledge, technical and non-technical skills.
- Institutions or clinical areas where deliveries may occur should have structured educational programmes, teaching the knowledge and skills required for newborn resuscitation.
- The content and organisation of such training programmes may vary according to the needs of the providers and the organisation of the institutions.
- Recommended programmes include:
  - regular practice and drills,
  - team and leadership training,
  - multi-modal approaches,
  - simulation-based training,
  - feedback on practice from different sources (including feedback devices),
  - objective, performance focused debriefings.
- Ideally, training should be repeated more frequently than once per year.
  - Updates may include specific tasks, simulation and/or behavioural skills and reflection.

### Thermal control

#### Recommendations

##### Standards

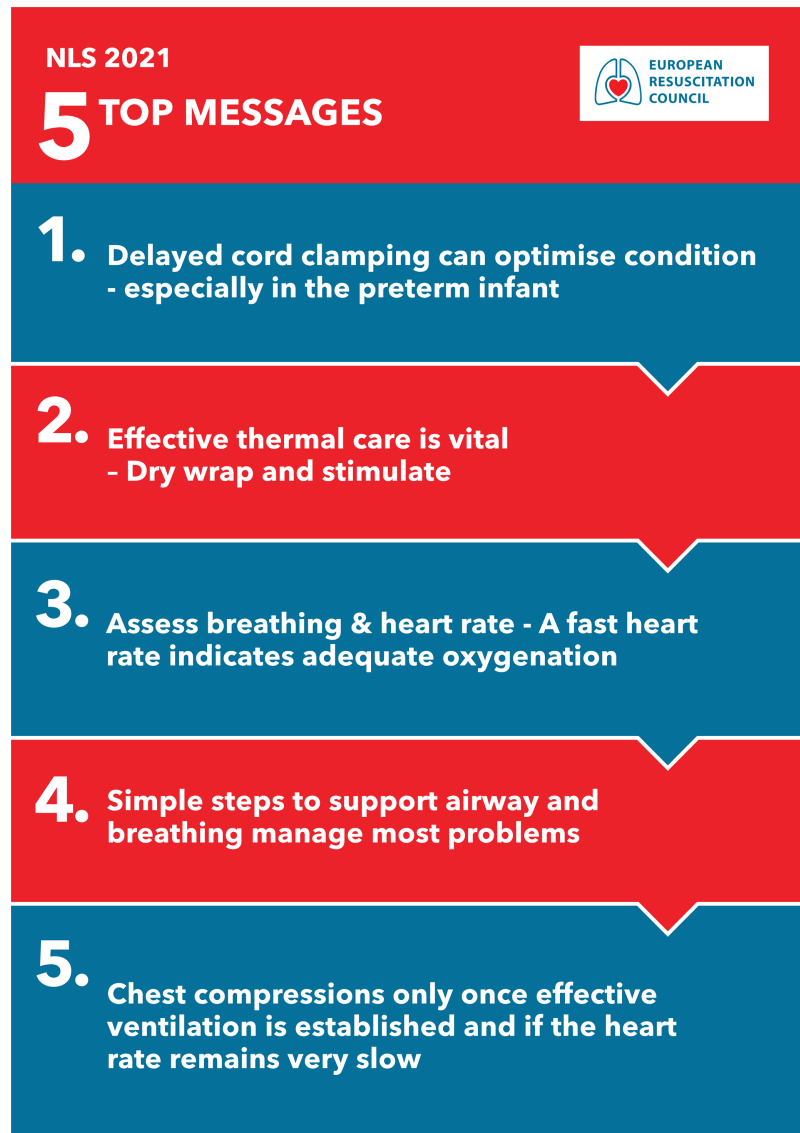
- The infant's temperature should be regularly monitored after birth and the admission temperature should be recorded as a prognostic and quality indicator.
- The temperature of newborn infants should be maintained between 36.5 °C and 37.5 °C.
- Hypothermia ( $\leq 36.0$  °C) and hyperthermia ( $> 38.0$  °C) should be avoided. In appropriate circumstances, therapeutic hypothermia may be considered after resuscitation (see post-resuscitation care)

### Environment

- Protect the infant from draughts. Ensure windows are closed and air-conditioning appropriately programmed.
- Keep the environment in which the infant is looked after (e.g. delivery room or theatre) warm at 23–25 °C.
- For infants  $\leq 28$  weeks gestation the delivery room or theatre temperature should be  $> 25$  °C.

### Term and near-term infants >32 weeks gestation

- Dry the infant immediately after delivery. Cover the head and body of the infant, apart from the face, with a warm and dry towel to prevent further heat loss.
- If no resuscitation is required place the infant skin-to-skin with mother and cover both with a towel. On-going careful observation of mother and infant will be required especially in more preterm and growth restricted infants to ensure they both remain normothermic.
- If the infant needs support with transition or when resuscitation is required, place the infant on a warm surface using a preheated radiant warmer.



**Fig. 2 – NLS infographic.**

#### **Preterm infants $\leq 32$ weeks gestation**

- Completely cover with polyethylene wrapping (apart from face) without drying and use a radiant warmer.
- If umbilical cord clamping is delayed and a radiant warmer is not accessible at this point, other measures (such as those listed below) will be needed to ensure thermal stability while still attached to the placenta.
- A combination of further interventions may be required in infants  $\leq 32$  weeks including increased room temperature, warm blankets, head cap and thermal mattress.
- Skin-to-skin care is feasible in less mature infants however caution is required in the more preterm or growth restricted infant in order to avoid hypothermia.
- For infants receiving respiratory support, use of warmed humidified respiratory gases should be considered.

- A quality improvement program including the use of checklists and continuous feedback to the team has been shown to significantly reduce hypothermia at admission in very preterm infants.

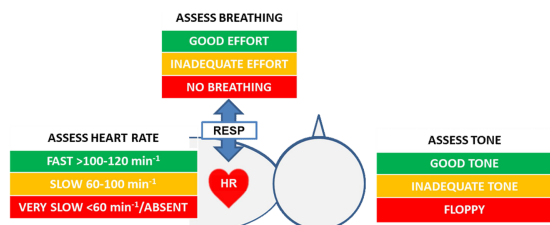
#### **Out of hospital management**

- Infants born unexpectedly outside a normal delivery environment are at higher risk of hypothermia and subsequent poorer outcomes.
- They may benefit from placement in a food grade plastic bag after drying and then swaddling. Alternatively, well newborns  $>30$  weeks gestation may be dried and nursed skin-to-skin to maintain their temperature whilst they are transferred as long as mothers are normothermic. Infants should be covered and protected from draughts and watched carefully to avoid hypothermia and ensure airway and breathing are not compromised.

## Management of the umbilical cord after birth

- The options for managing cord clamping and the rationale should be discussed with parents before birth.
- Where immediate resuscitation or stabilisation is not required, aim to delay clamping the cord for at least 60 s. A longer period may be more beneficial.
- Clamping should ideally take place after the lungs are aerated.
- Where adequate thermal care and initial resuscitation interventions can be safely undertaken with the cord intact it may be possible to delay clamping whilst performing these interventions.
- Where delayed cord clamping is not possible consider cord milking in infants >28 weeks gestation.

### Initial assessment (Fig. 3)



**Fig. 3 – Assessment of tone, breathing and heart rate help determine the need for intervention.**

May occur before the umbilical cord is clamped and cut (typically performed in this order):

- Observe Tone (& Colour)
- Assess adequacy of **Breathing**
- Assess the **Heart Rate**
- Take appropriate action to keep the baby warm during these initial steps.
- This rapid assessment serves to establish a baseline, identify the need for support and/or resuscitation and the appropriateness and duration of delaying umbilical cord clamping.
- Frequent re-assessment of heart rate and breathing indicates whether the infant is adequately transitioning or whether further interventions are needed.

### Tactile stimulation

Initial handling is an opportunity to stimulate the infant during assessment by

- Drying the infant.
- Gently stimulating as you dry them, for example by rubbing the soles of the feet or the back of the chest. Avoid more aggressive methods of stimulation.

### Tone and colour

- A very floppy infant is likely to need ventilatory support.
- Colour is a poor means of judging oxygenation. Cyanosis can be difficult to recognise. Pallor might indicate shock or rarely hypovolaemia – consider blood loss and plan appropriate intervention.

### Breathing

- Is the infant breathing? – Note the rate, depth and symmetry, work/effort of breathing as
  - Adequate
  - Inadequate/abnormal pattern – such as gasping or grunting
  - Absent

### Heart rate

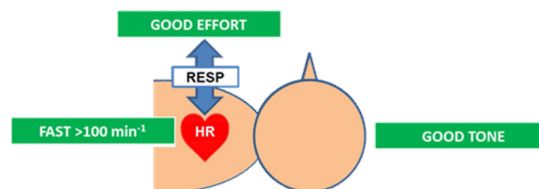
- Determine the heart rate with a stethoscope and a saturation monitor ± ECG (electrocardiogram) for later continuous assessment.
  - Fast ( $\geq 100 \text{ min}^{-1}$ ) – satisfactory
  - Slow ( $60\text{--}100 \text{ min}^{-1}$ ) – intermediate, possible hypoxia
  - Very slow/absent ( $< 60 \text{ min}^{-1}$ ) – critical, hypoxia likely

If the infant fails to establish spontaneous and effective breathing following assessment and stimulation, and/or the heart rate does not increase (and/or decreases) if initially fast, respiratory support should be started.

### Classification according to initial assessment

On the basis of the initial assessment, the infant can usually be placed into one of three groups as the following examples illustrate.

1.



**Fig. 4a – Satisfactory transition.**

Good tone  
Vigorous breathing or crying  
Heart rate – fast ( $\geq 100 \text{ min}^{-1}$ )

Assessment: *Satisfactory transition* – Breathing does not require support. Heart rate is acceptable (Fig. 4a).

Actions:

- Delay cord clamping.
- Dry, wrap in warm towel.
- Keep with mother or carer and ensure maintenance of temperature.
- Consider early skin-to-skin care if stable.

2.



**Fig. 4b – Incomplete transition.**

Reduced tone  
Breathing inadequately (or apnoeic)  
Heart rate – slow ( $< 100 \text{ min}^{-1}$ )

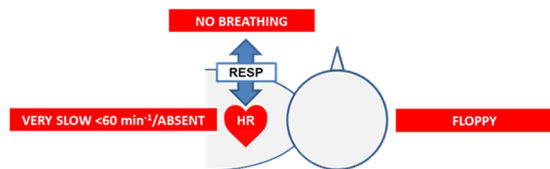
Assessment: *Incomplete transition* – Breathing requires support, slow heart rate may indicate hypoxia (Fig. 4b).

Actions:

- Delay cord clamping only if you are able to appropriately support the infant.

- Dry, stimulate, wrap in a warm towel.
- Maintain the airway, – lung inflation and ventilation.
- Continuously assess changes in heart rate and breathing
- If no improvement in heart rate, continue with ventilation.
- Help may be required.

3.



**Fig. 4c – Poor/failed transition.**

Floppy ± Pale  
Breathing inadequately or apnoeic  
Heart rate – very slow ( $<60 \text{ min}^{-1}$ ) or undetectable

Assessment: *Poor/Failed transition* – Breathing requires support, heart rate suggestive of significant hypoxia (Fig. 4c).

Actions:

- Clamp cord immediately and transfer to the resuscitation platform. Delay cord clamping only if you are able to appropriately support/resuscitate the infant.
- Dry, stimulate, wrap in warm towel.
- Maintain the airway – lung inflation and ventilation.
- Continuously assess heart rate, breathing, and effect of ventilation.

- Continue newborn life support according to response.
- Help is likely to be required.

### Preterm infants

- Same principles apply.
- Consider alternative/additional methods for thermal care e.g. polyethylene wrap.
- Gently support, initially with CPAP if breathing.
- Consider continuous rather than intermittent monitoring (pulse oximetry ± ECG)

### Newborn life support

Following initial assessment and intervention, continue respiratory support if:

- The infant has not established adequate, regular breathing, or
- The heart rate is  $<100 \text{ min}^{-1}$ .

**Ensuring an open airway, aerating and ventilating the lungs** is usually all that is necessary. Without these, other interventions will be unsuccessful.

### Airway

Commence life support if initial assessment shows that the infant has not established adequate regular normal breathing, or has a heart rate  $<100 \text{ min}^{-1}$  (Fig. 5).

Establishing and maintaining an open airway is essential to achieve postnatal transition and spontaneous breathing, or for further resuscitative actions to be effective.

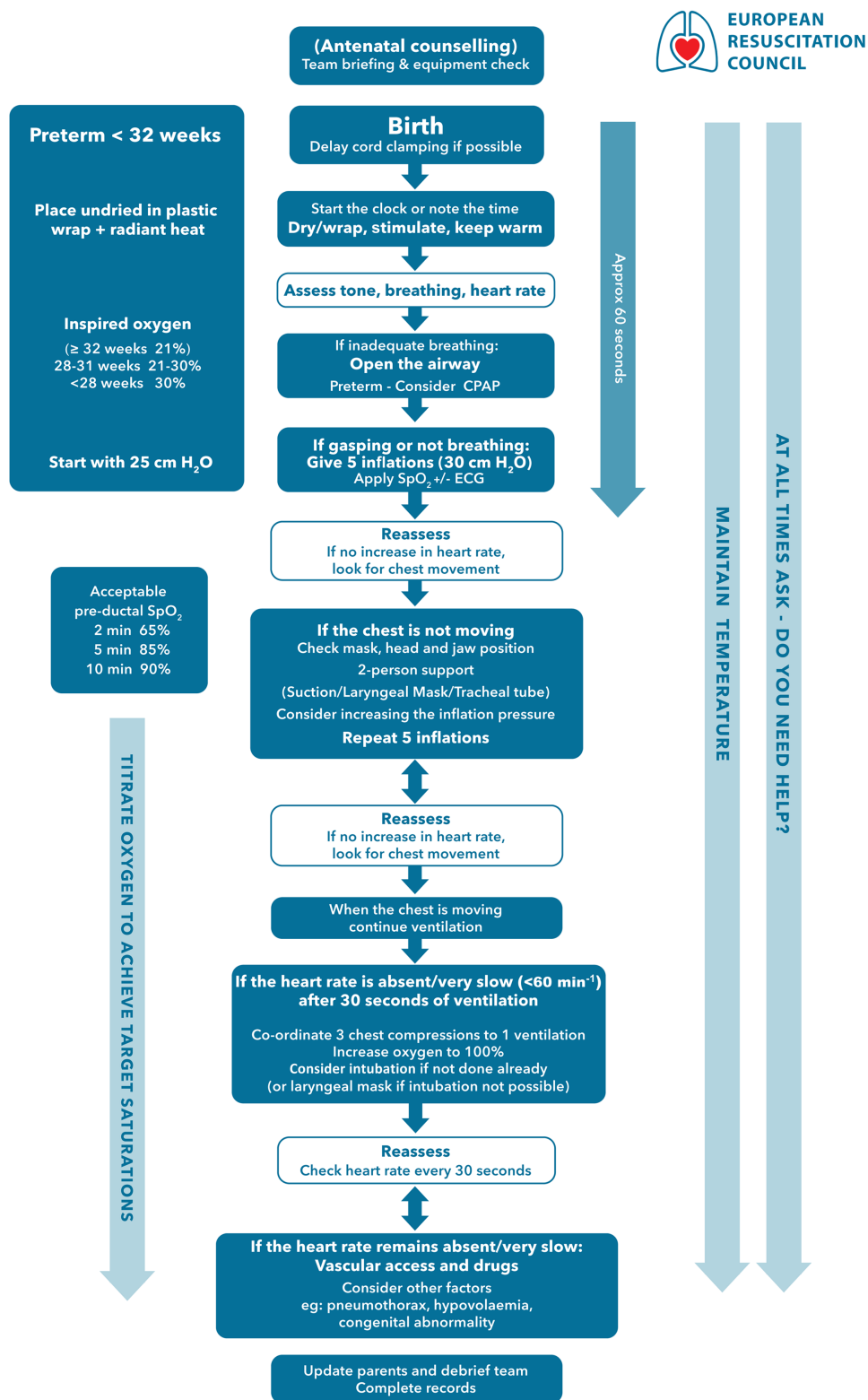
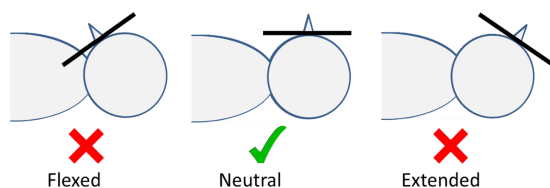


Fig. 5 – NLS algorithm.

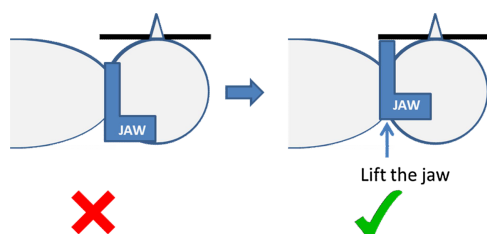
### Techniques to help open the airway

- Place the infant on their back with the head supported in a neutral position (Fig. 6a).



**Fig. 6a – Head in a neutral position. Face is horizontal (middle picture), neither flexed (left) or extended (right).**

- In floppy infants, pulling the jaw forwards (jaw lift) may be essential in opening and/or maintaining the airway and reducing mask leak (Fig. 6b). When using a facemask, two person methods of airway support are superior and permit true jaw thrust to be applied.



**Fig. 6b – Jaw lift – jaw lift enlarges the pharyngeal space.**

- An oropharyngeal airway may be useful in term infants when having difficulty providing both jaw lift and ventilation, or where the upper airway is obstructed, for instance in those with micrognathia. However, oropharyngeal airways should be used with caution in infants  $\leq 34$  weeks gestation as they may increase airway obstruction.
- A nasopharyngeal airway may also be considered where there is difficulty maintaining an airway and mask support fails to achieve adequate aeration.

### Airway obstruction

- Airway obstruction can be due to inappropriate positioning, decreased airway tone and/or laryngeal adduction, especially in preterm infants at birth.
- Suction is only required if airway obstruction due to mucus, vernix, meconium, blood clots, etc. is confirmed through inspection of the pharynx after failure to achieve aeration.
- Any suctioning should be undertaken under direct vision, ideally using a laryngoscope and a wide bore catheter.

### Meconium

- Non-vigorous newborn infants delivered through meconium-stained amniotic fluid are at significant risk for requiring advanced resuscitation and a neonatal team competent in advanced resuscitation may be required.
- Routine suctioning of the airway of non-vigorous infants is likely to delay initiating ventilation and is not recommended. In the absence of evidence of benefit for suctioning, the emphasis

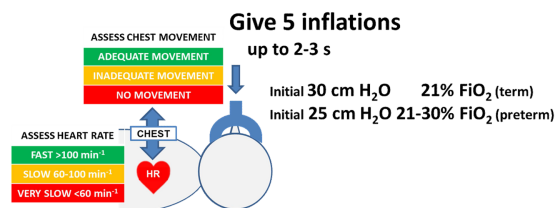
must be on initiating ventilation as soon as possible in apnoeic or ineffectively breathing infants born through meconium-stained amniotic fluid.

- Should initial attempts at aeration and ventilation be unsuccessful then physical obstruction may be the cause. In this case inspection and suction under direct vision be considered. Rarely, an infant may require tracheal intubation and tracheal suctioning to relieve airway obstruction.

### Initial inflations and assisted ventilation

#### Lung inflation (Fig. 7)

- If apnoeic, gasping or not breathing effectively, aim to start positive pressure ventilation as soon as possible – ideally within 60 s of birth.
- Apply an appropriately fitting facemask connected to a means of providing positive pressure ventilation, ensuring a good seal between mask and face.
- Give five “inflations” maintaining the inflation pressure for up to 2–3 s.
- Provide initial inflation pressures of 30 cm H<sub>2</sub>O for term infants commencing with air. Start with 25 cm H<sub>2</sub>O for preterm infants  $\leq 32$  weeks using 21–30% inspired oxygen (see ‘air/oxygen’).



**Fig. 7 – Five 2–3 s inflations are given via facemask. Assess heart rate response and chest movement.**

### Assessment

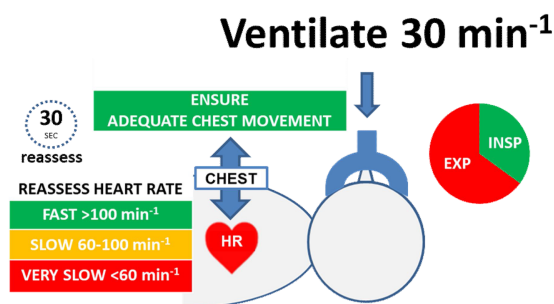
- Check the **heart rate**
  - An increase (within 30 s) in heart rate, or a stable heart rate if initially high, confirms adequate ventilation/oxygenation.
  - A slow or very slow heart rate usually suggests continued hypoxia and almost always indicates inadequate ventilation.
- Check for **chest movement**
  - Visible chest movement with inflations indicates a patent airway and delivered volume.
  - Failure of the chest to move may indicate obstruction of the airway, or insufficient inflation pressure and delivered volume to aerate the lungs.

### Ventilation (Fig. 8)

If there is a heart rate response

- Continue uninterrupted ventilation until the infant begins to breathe adequately and the heart rate is above 100 min<sup>-1</sup>.
- Aim for about 30 breaths min<sup>-1</sup> with an inflation time of under 1 s.
- Reduce the inflation pressure if the chest is moving well.
- Reassess heart rate and breathing at least every 30 s.
- Consider a more secure airway (laryngeal mask/tracheal tube) if apnoea continues or if mask ventilation is not effective.





**Fig. 8 – Once inflation breaths have been successfully delivered, ventilate at 30 breaths  $\text{min}^{-1}$ . Assess heart rate continuously.**

### Failure to respond

If there is *no* heart rate response *and* the chest is not moving with inflations

- Check if the equipment is working properly.
- Recheck the head-position and jaw lift/thrust
- Recheck mask size, position and seal.
- Consider other airway manoeuvres:
  - 2-person mask support if single handed initially.
  - Inspection of the pharynx and suction under direct vision to remove obstructing foreign matter if present.
  - Securing the airway via tracheal intubation or insertion of a laryngeal mask.
  - Insertion of an oropharyngeal/nasopharyngeal airway if unable to secure the airway with other means.
- Consider a gradual increase in inflation pressure.
- If being used, check on a respiratory function monitor that expired tidal volume is not too low or too high (target about 5–8 mL  $\text{kg}^{-1}$ ).

Then:

- Repeat inflations.
- Continuously assess heart rate and chest movement.

**If the insertion of a laryngeal mask or tracheal intubation is considered, it must be undertaken by personnel competent in the procedure with appropriate equipment. Otherwise continue with mask ventilation and call for help.**

Without adequate lung aeration, chest compressions will be ineffective; therefore, where the heart rate remains very slow, confirm effective ventilation through observed chest movement or other measures of respiratory function before progressing to chest compressions.

### CPAP and PEEP/airway adjuncts and assisted ventilation

#### Continuous positive airway pressure (CPAP) and positive end expiratory pressure (PEEP)

- In spontaneously breathing *preterm* infants consider CPAP as the initial method of breathing support after delivery – using either mask or nasal prongs.
- If equipment permits, apply PEEP at minimum of 5–6 cm  $\text{H}_2\text{O}$  when providing positive pressure ventilation (PPV) to these infants.

#### Assisted ventilation devices

- Ensure a facemask of appropriate size is used to provide a good seal between mask and face.

- Where possible use a T-piece resuscitator (TPR) capable of providing either CPAP or PPV with PEEP when providing ventilatory support, especially in the preterm infant.
- Nasal prongs of appropriate size may be a viable CPAP alternative to facemasks.
- If a self-inflating bag is used it should be of sufficient volume to deliver an adequate inflation. Care should be taken not to deliver an excessive volume. The self-inflating bag cannot deliver CPAP effectively.

#### Laryngeal mask

- Consider using a laryngeal mask
  - In infants of  $\geq 34$  weeks gestation (about 2000 g) – although some devices have been used successfully in infants down to 1500 g.
  - If there are problems with establishing effective ventilation with a facemask.
  - Where intubation is not possible or deemed unsafe because of congenital abnormality, a lack of equipment, or a lack of skill.
  - Or as an alternative to tracheal intubation as a secondary airway.

#### Tracheal tube

- Tracheal intubation may be considered at several points during neonatal resuscitation:
  - When ventilation is ineffective after correction of mask technique and/or the infant's head position, and/or increasing inspiratory pressure with TPR or bag-mask.
  - Where ventilation is prolonged, to enable a more secure airway to be established.
  - When suctioning the lower airways to remove a presumed tracheal blockage.
  - When chest compressions are performed.
  - In special circumstances (e.g., congenital diaphragmatic hernia or to give surfactant).
- Exhaled  $\text{CO}_2$  detection should be used when undertaking intubation to confirm tube placement in the airway.
- A range of differing sized tracheal tubes should be available to permit placement of the most appropriate size to ensure adequate ventilation with minimal leak and trauma to the airway [Table 1](#).
- Respiratory function monitoring may also help confirm tracheal tube position and adequate ventilation through demonstrating adequate expired tidal volume (about 5–8 mL  $\text{kg}^{-1}$ ) and minimal leak.
- The use of a video laryngoscope may aid tube placement.
- If retained, the position of the tracheal tube should be confirmed by radiography.

**Table 1 – Approximate oral tracheal tube size by gestation (for approximate nasotracheal tube length add 1 cm).**

Gestational age (weeks)	Length at lips (cm)	External diameter (mm)
23–24	5.5	2.5
25–26	6.0	2.5
27–29	6.5	2.5
30–32	7.0	3.0
33–34	7.5	3.0
35–37	8.0	3.5
38–40	8.5	3.5
41–43	9.0	4.0

## Air/oxygen

- Pulse-oximetry and oxygen blenders should be used during resuscitation in the delivery room.
- Aim to achieve target oxygen saturation above the 25<sup>th</sup> percentile for healthy term infants in the first 5 min after birth (Table 2).

**Table 2 – Approximate target SpO<sub>2</sub> in the first 10 min for healthy term infants (derived from Dawson et al.<sup>281</sup>).**

Time after birth (min)	Lower SpO <sub>2</sub> target (%)
2	65
5	85
10	90

- If, despite effective ventilation, there is no increase in heart rate, or saturations remain low, increase the oxygen concentration to achieve adequate productal oxygen saturations.
- Check the delivered inspired oxygen concentration and saturations frequently (e.g. every 30 s) and titrate to avoid both hypoxia and hyperoxia.
- wean the inspired oxygen if saturations >95% in preterms.

## Term and late preterm infants ≥35 weeks

- In infants receiving respiratory support at birth, begin with air (21%).

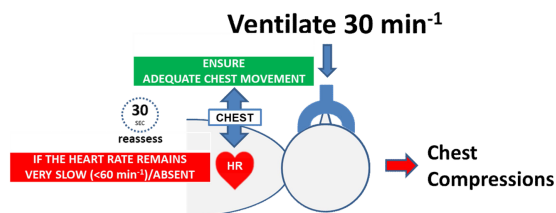
## Preterm infants <35 weeks

- Resuscitation should be initiated in air or a low inspired oxygen concentration based on gestational age:
  - ≥32 weeks 21%
  - 28–31 weeks 21–30%
  - <28 weeks 30%
- In infants <32 weeks gestation the target should be to avoid an oxygen saturation below 80% and/or bradycardia at 5 min of age. Both are associated with poor outcome.

## Chest compressions

### Assessment of the need for chest compressions (Fig. 9)

- If the heart rate remains very slow (<60 min<sup>-1</sup>) or absent after 30 s of good quality ventilation, start chest compressions.
- When starting compressions:
  - Increase the delivered inspired oxygen to 100%.
  - Call for experienced help if not already summoned.



**Fig. 9 – Deliver 30 s of good quality ventilation before reassessment of the heart rate.**

## Delivery of chest compressions

- Use a synchronous technique, providing three compressions to one ventilation at about 15 cycles every 30 s.
- Use a two-handed technique for compressions if possible.
- Re-evaluate the response every 30 s.
- If the heart rate remains very slow or absent, continue ventilation and chest compressions but ensure that the airway is secured (e.g. intubate the trachea if competent and not done already).
- Titrate the delivered inspired oxygen against oxygen saturation if a reliable value is achieved on the pulse oximeter.

Consider

- Vascular access and drugs.

## Vascular access

During the resuscitation of a compromised infant at birth peripheral venous access is likely to be difficult and suboptimal for vasopressor administration.

## Umbilical venous access

- The umbilical vein offers rapid vascular access in newborn infants and should be considered the primary method during resuscitation.
- Ensure a closed system to prevent air embolism during insertion should the infant gasp and generate sufficient negative pressure.
- Confirm position in a blood vessel through aspiration of blood prior to administering drugs/fluids.
- Clean, rather than sterile, access technique may be sufficient in an emergency.
- The umbilical route may still be achievable some days after birth and should be considered in cases of postnatal collapse.

## Intraosseous access

- Intraosseous (IO) access can be an alternative method of emergency access for drugs/fluids.

## Support of transition/post-resuscitation care

- If venous access is required following resuscitation, peripheral access may be adequate unless multiple infusions are required in which case central access may be preferred.
- IO access may be sufficient in the short term if no other site is available.

## Drugs

### During active resuscitation

Drugs are rarely required during newborn resuscitation and the evidence for the efficacy of any drug is limited. The following may be considered during resuscitation where, despite adequate control of the airway, effective ventilation and chest compressions for 30 s, there is an inadequate response and the HR remains below 60 min<sup>-1</sup>.

#### • Adrenaline

- When effective ventilation and chest compressions have failed to increase the heart rate above 60 min<sup>-1</sup>
- Intravenous or intraosseous is the preferred route:
  - At a dose of 10–30 micrograms kg<sup>-1</sup> (0.1–0.3 mL kg<sup>-1</sup> of 1:10,000 adrenaline [1000 micrograms in 10 mL]).

- Intra-tracheally if intubated and no other access available.
  - At a dose of 50–100 micrograms  $\text{kg}^{-1}$ .
- Subsequent doses every 3–5 min if heart rate remains  $< 60 \text{ min}^{-1}$ .
- **Glucose**
  - In a prolonged resuscitation to reduce likelihood of hypoglycaemia.
  - Intravenous or intraosseous:
    - 250  $\text{mg kg}^{-1}$  bolus (2.5  $\text{mL kg}^{-1}$  of 10% glucose solution).
- **Volume replacement**
  - With suspected blood loss or shock unresponsive to other resuscitative measures.
  - Intravenous or intraosseous:
    - 10  $\text{mL kg}^{-1}$  of group O Rh-negative blood or isotonic crystalloid.
- **Sodium bicarbonate**
  - May be considered in a prolonged unresponsive resuscitation with adequate ventilation to reverse intracardiac acidosis.
  - Intravenous or intraosseous:
    - 1–2  $\text{mmol kg}^{-1}$  sodium bicarbonate (2–4  $\text{mL kg}^{-1}$  of 4.2% solution) by slow intravenous injection.

### In situations of persistent apnoea

- **Naloxone**
  - Intramuscular
    - An initial 200 microgram dose may help in the few infants who, despite resuscitation, remain apnoeic with good cardiac output when the mother is known to have received opioids in labour. Effects may be transient so continued monitoring of respiration is important.

### In the absence of an adequate response

Consider other factors which may be impacting on the response to resuscitation and which require addressing such as the presence of pneumothorax, hypovolaemia, congenital abnormalities, equipment failure etc.

### Post-resuscitation care

Infants who have required resuscitation may later deteriorate. Once adequate ventilation and circulation are established, the infant should be cared for in, or transferred to, an environment in which close monitoring and anticipatory care can be provided.

### Glucose

- Monitor glucose levels carefully after resuscitation.
- Have protocols/guidance on the management of unstable glucose levels.
- Avoid hyper- and hypoglycaemia.
- Avoid large swings in glucose concentration.
- Consider the use of a glucose infusion to avoid hypoglycaemia.

### Thermal care

- Aim to keep the temperature between  $36.5^{\circ}\text{C}$  and  $37.5^{\circ}\text{C}$ .
- Rewarm if the temperature falls below this level and there are no indications to consider therapeutic hypothermia (see below).

### Therapeutic hypothermia

- Once resuscitated, consider inducing hypothermia to  $33\text{--}34^{\circ}\text{C}$  in situations where there is clinical and/or biochemical evidence of significant risk of moderate or severe HIE (hypoxic-ischaemic encephalopathy).
- Ensure the evidence to justify treatment is clearly documented; include cord blood gases, and neurological examination.
- Arrange safe transfer to a facility where monitoring and treatment can be continued.
- Inappropriate application of therapeutic hypothermia, without concern about a diagnosis of HIE, is likely to be harmful (see temperature maintenance).

### Prognosis (documentation).

- Ensure clinical records allow accurate retrospective time-based evaluation of the clinical state of the infant at birth, any interventions and the response during the resuscitation to facilitate any review and the subsequent application of any prognostic tool.

### Communication with the parents

#### Where intervention is anticipated

- Whenever possible, the decision to attempt resuscitation of an extremely preterm or clinically complex infant should be taken in close consultation with the parents and senior paediatric, midwifery and obstetric staff.
- Discuss the options including the potential need and magnitude of resuscitation and the prognosis before delivery in order to develop an agreed plan for the birth.
- Record carefully all discussions and decisions in the mother's notes prior to delivery and in the infant's records after birth.

#### For every birth

- Where intervention is required it is reasonable for mothers/fathers/partners to be present during the resuscitation where circumstances, facilities and parental inclination allow.
- The views of both the team leading the resuscitation and the parents must be taken into account in decisions on parental attendance.
- Irrespective of whether the parents are present at the resuscitation, ensure wherever possible, that they are informed of the progress of the care provided to their infant.
- Witnessing the resuscitation of their infant may be distressing for parents. If possible, identify a member of healthcare staff to support them to keep them informed as much as possible during the resuscitation.
- Allow parents to hold or even better to have skin-to-skin contact with their infant as soon as possible after delivery or resuscitation, even if unsuccessful.
- Provide an explanation of any procedures and why they were required as soon as possible after the delivery.
- Ensure a record is kept of events and any subsequent conversations with parents.
- Allow for further discussions later to enable parents to reflect and to aid parental understanding of events.
- Consider what additional support is required for parents following delivery and any resuscitation.

## Withholding and discontinuing resuscitation

- Any recommendations must be interpreted in the light of current national/regional outcomes.
- When discontinuing, withdrawing or withholding resuscitation, care should be focused on the comfort and dignity of the infant and family.
- Such decisions should ideally involve senior paediatric staff.

### Discontinuing resuscitation

- National committees may provide locally appropriate recommendations for stopping resuscitation.
- When the heart rate has been undetectable for longer than 10 min after delivery review clinical factors (for example gestation of the infant, or presence/absence of dysmorphic features), effectiveness of resuscitation, and the views of other members of the clinical team about continuing resuscitation.
- If the heart rate of a newborn term infant remains undetectable for more than 20 min after birth despite the provision of all recommended steps of resuscitation and exclusion of reversible causes, consider stopping resuscitation.
- Where there is partial or incomplete heart rate improvement despite apparently adequate resuscitative efforts, the choice is much less clear. It may be appropriate to take the infant to the intensive care unit and consider withdrawing life-sustaining treatment if they do not improve.
- Where life-sustaining treatment is withheld or withdrawn, infants should be provided with appropriate palliative (comfort focused) care.

### Withholding resuscitation

- Decisions about withholding life-sustaining treatment should usually be made only after discussion with parents in the light of regional or national evidence on outcome if resuscitation and active (survival focused) treatment is attempted.
- In situations where there is extremely high (>90%) predicted neonatal mortality and unacceptably high morbidity in surviving infants, attempted resuscitation and active (survival focused) management is usually not appropriate.
- Resuscitation is nearly always indicated in conditions associated with a high (>50%) survival rate and what is deemed to be acceptable morbidity. This will include most infants with gestational age of 24 weeks or above (unless there is evidence of fetal compromise such as intrauterine infection or hypoxia-ischaemia) and most infants with congenital malformations. Resuscitation should also usually be commenced in situations where there is uncertainty about outcome and there has been no chance to have prior discussions with parents.
- In conditions where there is low survival (<50%) and a high rate of morbidity, and where the anticipated burden of medical treatment for the child is high, parental wishes regarding resuscitation should be sought and usually supported.

## Evidence informing the guidelines

### Factors before delivery

#### Transition

Survival at birth involves major physiological changes during transition from fetal to newborn life. First, lung liquid-clearance and aeration need

to occur after which pulmonary gas exchange can be established.<sup>6</sup> This critical event initiates a sequence of inter-dependent cardiopulmonary adaptations which enable transition to independent life.<sup>7</sup> Spontaneous breathing effort (negative pressure) or less effective, artificial ventilation (positive pressure) are essential to generate the transpulmonary pressures required to aerate the liquid-filled lung to form and then maintain a functional residual capacity.<sup>8,9</sup> Most, but not all, infants transition smoothly. Some infants have problems with transition, and without timely and adequate support, might subsequently need resuscitation. Recent, large-scale observational studies confirm that approximately 85% of infants born at term initiate respiration spontaneously; 10% will respond to drying, stimulation, opening the airway and/or applying CPAP or PEEP, approximately 5% will breathe following positive pressure ventilation. Estimates of intubation rates vary between 0.4% and 2%; <0.3% receive chest compressions and approximately 0.05% adrenaline.<sup>10–16</sup>

### Risk factors

Several maternal and fetal pre- and intrapartum factors increase the risk for compromised birth or transition and the need for resuscitation. In a recent ILCOR evidence update most recent studies confirm previously identified risk factors for needing assistance after birth.<sup>1,17–26</sup> There is no universally applicable model to predict risk for resuscitation or need of support during transition, and the list of risk factors in the guidelines is not exhaustive.

Elective caesarean delivery at term, in the absence of other risk factors, does not increase the risk of needing newborn resuscitation.<sup>18,27,28</sup> Following the review of evidence, ILCOR recommendations are unchanged: When an infant is delivered at term by caesarean delivery under regional anaesthesia a provider capable of performing assisted ventilation should be present at the delivery. It is not necessary for a provider skilled in neonatal intubation to be present at that delivery.<sup>1</sup>

### Staff attending delivery

It is not always possible to predict the need for stabilisation or resuscitation before an infant is born. Interventions may not be necessary but those in attendance at a delivery need to be able to undertake initial resuscitation steps effectively. It is essential that teams can respond rapidly if not present and needed to provide additional support. The experience of the team and their ability to respond in a timely manner can influence outcome.<sup>29</sup> Units have different guidelines for when teams attend in advance, potentially leading to widely different outcomes.<sup>30</sup> A prospective audit of 56 Canadian neonatal units found that, with the guidelines in force at that time, the need for resuscitation was unanticipated in 76% of cases.<sup>31</sup> In a series of video recorded resuscitations in 2 Norwegian tertiary level units, the need for resuscitation was not anticipated in 32%.<sup>32</sup> Approximately 65% of all deliveries in a single Canadian unit were attended by the resuscitation team – only 22% of these infants required IPPV, as did another 4.6% where resuscitation was not anticipated.<sup>17</sup>

### Equipment and environment

The detailed specification of the equipment required to support stabilisation and resuscitation of the newborn may vary and those using the equipment need to be aware of any limitations. Suggestions have been made on standardising an optimal layout of a resuscitation area,<sup>33</sup> but no published evidence has demonstrated improvement in outcome as a result of specific arrangements. The guidelines are based on international expert opinion.<sup>1,34</sup>

## Planned home deliveries

A systematic review of 8 studies involving 14 637 low risk planned home deliveries compared to 30 177 low risk planned hospital births concluded that the risks of neonatal morbidity and mortality were similar.<sup>35</sup> Those attending deliveries at home need to recognise that despite risk stratification and measures to avoid the event, infants born at home may still require resuscitation and they must be prepared for this possibility.<sup>34</sup>

## Briefing and checklists

Briefing with role allocation to improve team functioning and dynamics is recommended<sup>36</sup> although there is a lack of evidence of improved clinical outcomes.<sup>37</sup> Likewise, use of checklists during briefings (and debriefings) may help improve team communication and process, but again, there is little evidence of effect on clinical outcome.<sup>38,39</sup> A recent ILCOR scoping review on the effect of briefing/debriefing on the outcome of neonatal resuscitation concluded that briefing or debriefing may improve short-term clinical and performance outcomes for infants and staff but the effects on long-term clinical and performance outcomes were uncertain.<sup>1</sup>

The opportunity to brief the family before delivery can significantly influence their expectation and understanding of events, decision-making and interactions with health providers. Therefore, anticipatory liaison often forms part of national recommendations on practice (see section – parents and family).<sup>33</sup>

## Training/education

Meta-analysis of adult resuscitations showed that attendance by one or more personnel on an advanced life support course improves outcome.<sup>40</sup> Research on educational methods in neonatal resuscitation is evolving, but due to study heterogeneity with non-standardised outcome measures, there is still little evidence on the effect of different training modalities on clinical outcome.<sup>41–43</sup>

For those taking resuscitation courses training or retraining distributed over time (spaced learning) may be an alternative to training provided at one single time point (massed learning) (weak recommendation, very low certainty of evidence).<sup>44</sup> Intermittent, infrequent training without interval refreshment leads to skills decay in neonatal resuscitation.<sup>45</sup> whereas frequent and brief, on-site simulation-based training has been shown to improve patient 24 h survival in a low-resource setting.<sup>46</sup> Two observational studies analysing video recordings of real-time resuscitations against checklists of expected actions indicated frequent errors in the application of structured guidelines in newborn resuscitation.<sup>15,47</sup> This suggests that training should be repeated more frequently than once per year, however, the optimal interval remains to be established.<sup>48,49</sup>

A structured educational programme in neonatal resuscitation was recommended in the 2015 ERC guidelines and supported by two systematic reviews and meta-analyses.<sup>34</sup> A Cochrane review of 14 studies (187 080 deliveries) concluded that there was moderate quality evidence that such training decreased early neonatal mortality (typical RR 0.88 95% CI 0.78–1.00).<sup>50</sup> Findings of a meta-analysis of 20 trials comparing periods before and after neonatal resuscitation training and including 1 653 805 births showed an 18% reduction in perinatal mortality (RR 0.82 95% CI 0.74–0.91) but these findings had to be downgraded for risk of bias and indirectness.<sup>43</sup> The optimal content or organisation of such training programmes will vary according to the needs of the providers and the organisation of the institutions.

A recent ILCOR systematic review included several studies on team training in neonatal resuscitation.<sup>51–55</sup> Team performance and patient safety appeared to be enhanced by regular practice and drills that enabled those likely to be involved to rehearse and improve their abilities at an individual level and in teams. This suggested that specific team and leadership training be included as part of Advanced Life Support training for healthcare providers (weak recommendation, very low certainty of evidence).<sup>37</sup>

Multi-modal approaches to teaching neonatal resuscitation are thought to be the most beneficial for learning, especially when simulation-based training with emphasis on feedback on practice is incorporated as a teaching method.<sup>42,50,56–60</sup> Feedback may come from different sources such as the facilitator, the manikin itself or digital recordings (video, audio, respiratory function monitor etc.).<sup>37,60–62</sup> The role of modalities such as virtual reality, tele-education and board game simulation in resuscitation training remain to be established. A review of 12 such neonatal resuscitation-based games concluded that they had a potential to improve knowledge, skills and adherence to the resuscitation algorithm.<sup>63</sup>

Feedback devices providing information on the quality of intervention may also be used in real-life settings to improve performance and compliance with guidelines.<sup>37,64,65</sup> Debriefing on individual and team performance at resuscitations supported by objective data are recommended after cardiac arrest for both adult and children (weak recommendation, very low certainty of evidence).<sup>37,66–69</sup> This approach to debrief also applies to neonatal resuscitation.<sup>53,70,71</sup>

## Thermal control

Exposed, wet, newborn infants cannot maintain their body temperature in a room that feels comfortably warm for adults. The mechanisms and effects of cold stress and how to avoid these have been reviewed.<sup>72,73</sup> Heat loss can occur through convection, conduction, radiation and evaporation meaning unprotected infants will drop their body temperature quickly. Cold stress lowers the arterial oxygen tension and increases the risk of metabolic acidosis. Compromised infants are particularly vulnerable to cold stress. The admission temperature of newborn non-asphyxiated infants is a strong predictor of mortality and morbidity at all gestations and in all settings.<sup>74,75</sup> ILCOR recommendations are that it should be recorded as a predictor of outcomes as well as a quality indicator (strong recommendation, moderate-quality evidence).<sup>49</sup> Immediate drying and wrapping infants in a warm towel to avoid exposure to a cold environment will help them maintain their temperature.

Preterm infants are especially vulnerable and hypothermia is also associated with serious morbidities such as intraventricular haemorrhage, need for respiratory support, hypoglycaemia, and in some studies late onset sepsis.<sup>49</sup> In a European cohort study of 5697 infants <32 weeks gestation admitted for neonatal care, an admission temperature <35.5 °C was associated with increased mortality in the first 28 days.<sup>76</sup> For each 1 °C decrease in admission temperature below the recommended range, an increase in the baseline mortality by 28% has been reported.<sup>77</sup>

A Cochrane review involving 46 trials and 3850 dyads of infants >32 weeks gestation where resuscitation was not required concluded that skin-to-skin care may be effective in maintaining thermal stability (low quality evidence) and also improves maternal bonding and breast feeding rates (low to moderate quality evidence).<sup>78</sup> However, most trials were small and unblinded with heterogeneity between groups. Skin-to-skin care is feasible in less

mature infants however caution is required in the more preterm or growth restricted infant in order to avoid hypothermia. In one single centre observational study of 55 infants between 28<sup>+0</sup> and 32<sup>+6</sup> weeks gestation randomised to either skin-to-skin or conventional thermal care the mean body temperature of the skin-to-skin group was 0.3 °C lower 1 h after birth (36.3 °C ± 0.52,  $p=0.03$ );<sup>79</sup> further studies are ongoing.<sup>80</sup>

Following a recent ILCOR evidence update including a Cochrane systematic review of 25 studies including 2433 preterm and low birth weight infants, treatment recommendations are unchanged from 2015.<sup>75</sup> It is recommended that newborn temperatures be kept between 36.5 °C and 37.5 °C in order to reduce the metabolic stress on the infant (strong recommendation, very low quality of evidence).<sup>1,49</sup> For newborn preterm infants of ≤32 weeks gestation under radiant warmers in the hospital delivery room, a combination of interventions is suggested which may include raising the environmental temperature to 23 °C–25 °C, use of warmed blankets, plastic wrapping without drying, cap and thermal mattress to reduce hypothermia on admission to the neonatal intensive care unit (NICU) (weak recommendation, very-low quality of evidence).<sup>1</sup> For infants <28 weeks gestation the room temperature should ideally be above 25 °C.<sup>72,73,81</sup> In the absence of exothermic devices, food grade plastic wrap and swaddling can be effective in preterm infants.<sup>72,73,82</sup>

It is suggested that hyperthermia (greater than 38.0 °C) should be avoided because it introduces potential associated risks (weak recommendation, very-low quality of evidence).<sup>1,49</sup> Infants born to febrile mothers have a higher incidence of perinatal respiratory compromise, neonatal seizures, early mortality and cerebral palsy.<sup>83–85</sup> Animal studies indicate that hyperthermia during or following ischaemia is associated with a progression of cerebral injury.<sup>85</sup>

Temperature monitoring is key to avoiding cold stress. However, there is very little evidence to guide the optimal placement of temperature monitoring probes on the infant in the delivery room. In an observational study of 122 preterm infants between 28 and 36 weeks gestation randomised to different sites for temperature monitoring, dorsal, thoracic and axillary sited probes measured comparable temperatures.<sup>29</sup> There are, to date, no published studies comparing the use of rectal temperature probes.

Heated humidified gases reduced the incidence of moderate hypothermia in preterm infants.<sup>86</sup> A meta-analysis of two RCTs involving 476 infants <32 weeks gestation indicated that heated, humidified inspired gases immediately following delivery reduced the likelihood of admission hypothermia in preterm infants by 36% (95% CI 17–50%) (high level of evidence).<sup>87,88</sup> There was no significant increase in the risk of hyperthermia or a difference in mortality between humidified and non-humidified groups. It is unclear if other outcomes are improved.

Quality improvement programs including the use of checklists and continuous feed-back to the team have been shown to significantly reduce hypothermia at admission in very preterm infants.<sup>81,89</sup>

### Clamping the umbilical cord

There is no universally accepted definition of ‘delayed’ or ‘deferred’ cord clamping’ (DCC), only that it does not occur immediately after the infant is born. In recent systematic reviews and meta-analyses early or immediate cord clamping (ICC) has been defined as application of the clamp within 30 s of birth, later or delayed cord clamping as application of a clamp to the cord greater than 30 s after birth or based on

physiological parameters (such as when cord pulsation has ceased or breathing has been initiated), without cord milking.<sup>90,91</sup>

### Physiology of cord clamping

Observational data, physiological studies, animal models and some clinical studies suggest that ICC, currently widely practiced and introduced primarily to prevent maternal postpartum haemorrhage, is not as innocuous as was once thought.<sup>92,93</sup> ICC significantly reduces ventricular preload whilst simultaneously adding to left ventricular afterload.<sup>7,94</sup> Effects of this are seen in observational studies, with a decrease in cardiac size for 3–4 cardiac cycles<sup>95</sup> and bradycardia,<sup>96</sup> and in experimental animal models.<sup>97</sup>

### Differences with gestation

In term infants, DCC results in the transfer of approximately 30 mL kg<sup>-1</sup> of blood from the placenta.<sup>98</sup> This improves iron status and haematological indices over the next 3–6 months in all infants and reduces need for transfusion in preterm infants.<sup>99,100</sup> Concerns about polycythaemia and jaundice requiring intervention do not seem to be borne out in randomised trials. Concerns about the position of the infant in relation to the introitus also seem unfounded as the effects of uterine contraction and lung expansion seem to exert a greater impact on umbilical blood flow than gravity.<sup>101,102</sup>

In an ILCOR meta-analysis of 23 studies of 3514 eligible infants comparing ICC versus a delay of at least 30 s in preterm infants <34 weeks gestation the conclusion was that compared to ICC DCC may marginally improve survival (RR 1.02, 95% CI 0.993–1.04) (certainty of evidence moderate).<sup>90</sup> Early cardiovascular stability was improved with less inotropic support (RR 0.36, 95% CI 0.17–0.75) and higher lowest mean blood pressure (MD 1.79 mmHg, 95% CI 0.53–3.05) in the first 12–24 h. Infants had better haematological indices: The peak haematocrit appeared higher at 24 hrs (MD 2.63, 95% CI 1.85–3.42) and at 7 days (MD 2.70, 95% CI 1.88–3.52). Infants required fewer blood transfusions (MD –0.63, 95% CI –1.08 to –0.17). No effects were seen on any of the complications of prematurity such as severe IVH, NEC or chronic lung disease, nor was there any obvious adverse impact on other neonatal or maternal outcomes (moderate to high quality evidence). In sub-group analyses of DCC vs. ICC, there seemed to be an almost linear relationship between survival to discharge and duration of DCC; DCC for ≤1 min, RR 1.00 (95% CI 0.97–1.04); DCC for 1–2 min, RR 1.03 (95% CI 1.00–1.05); DCC for >2 min, RR 1.07 (95% CI 0.99–1.15). None of these results were statistically significant due to the relatively small numbers involved.

In term and late preterm infants an ILCOR meta-analysis of 33 trials (5236 infants) of DCC vs ICC updated the findings of a previous 2013 Cochrane study.<sup>91,103</sup> Analysis demonstrated no significant effect on mortality (RR 2.54, 95% CI 0.50–12.74; 4 trials, 537 infants) or need for resuscitation (RR 5.08, 95% CI 0.25–103.58; 3 trials, 329 infants) There were improved early haematological and circulatory parameters (haemoglobin ≤24 h after birth (MD 1.17 g dL<sup>-1</sup> 95% CI 0.48–1.86, 9 trials, 1352 infants) and 7 days after birth (MD 1.11 g dL<sup>-1</sup> 95% CI 0.40–1.82, 3 trials, 695 infants) but no impact on longer term anaemia. This updated review does not suggest clear differences in receipt of phototherapy (RR 1.28, 95% CI 0.90–1.82) (all findings low or very low certainty evidence). The analysis did not provide clear evidence on longer term neurodevelopmental outcomes.

Further study is warranted; most studies used a temporal definition for the timing of cord clamping, there are insufficient data to

recommend 'physiological' cord clamping (i.e. after the onset of respirations),<sup>104</sup> although this may confer benefit.<sup>105</sup> Physiological studies suggest that the hypoxic and bradycardic response observed after immediate clamping is not seen when clamping occurs after the first breaths.<sup>96,97,106</sup>

The question of resuscitating infants with the intact cord warrants further study; in most studies of delayed cord clamping infants who required resuscitation at birth were excluded, as resuscitation could only be undertaken away from the mother. Equipment now exists that allows mother-side resuscitation and initial studies show that delayed cord clamping is feasible in such infants.<sup>107–109</sup> However, it remains unclear which is the optimum strategy in these infants.

### Cord milking

Delayed umbilical cord clamping is contra-indicated when placental blood flow is compromised by placental abruption, cord prolapse, vasa praevia, cord avulsion or maternal haemorrhage. Umbilical cord milking with intact or cut cords has been considered an alternative in these situations. In 'intact cord milking' the cord is milked 3–5 times, resulting in a faster blood flow towards the baby than occurs with passive return due to uterine contraction. A term infant can receive up to 50 mL of 'placental' blood through this action. After milking the cord is clamped and cut, and the infant can be taken to the resuscitation area.<sup>110</sup>

'Cut cord milking' involves milking from a length of cord (~25 cm) after clamping and cutting. The volume of blood is less than from an intact cord, but still gives the term infant about 25 mL. The infant is taken to the resuscitation area immediately and milking occurs during resuscitation or stabilisation.<sup>111</sup>

In preterm infants born before 34 weeks gestation, intact cord milking shows only transient benefits over ICC including less use of inotropic support, fewer infants needing blood transfusion, and higher haemoglobin and haematocrit on day 1 but not at 7 days. There were no differences in major neonatal morbidities (low to moderate quality evidence). There was no demonstrable benefit over DCC.<sup>90</sup> In the meta-analyses, there was no effect on mortality (RR 0.99; 95% CI 0.95–1.02), but of particular concern is that one large study of intact cord milking versus delayed cord clamping was terminated early when analysis demonstrated an excess of severe intraventricular haemorrhage (RD 16% 95% CI 6% to 26%;  $p=0.002$ ) in those infants born before 28 weeks allocated to the intact cord milking arm.<sup>112</sup>

In term and late preterm infants there are insufficient data to allow meta-analysis of umbilical cord milking.<sup>91</sup>

## Initial assessment

### Initial assessment

The Apgar score was not designed to identify infants in need of resuscitation.<sup>113</sup> However, individual components of the score, namely respiratory rate, heart rate (HR) and tone, if assessed rapidly, may help identify infants likely to need resuscitation.

### Tactile stimulation

Methods of tactile stimulation vary widely but the optimal method remains unknown.<sup>114,115</sup> In preterm infants, tactile stimulation is often omitted,<sup>115–118</sup> but in a single centre RCT of repetitive stimulation against standard stimulation only if deemed necessary in 51 infants between 28 and 32 weeks gestation, repetitive stimulation was shown to improve breathing effort and oxygen saturation ( $\text{SpO}_2$   $87.6 \pm 3.3\%$  vs  $81.7 \pm 8.7\%$ ,  $p=0.007$ ).<sup>119</sup> Stimulation of more infants at birth (after

introduction of a basic resuscitation training program) was associated with an increased 24-h survival in a multi-centre observational study in Tanzania, including 86,624 mainly term/near-term infants.<sup>120</sup>

### Tone and colour

Healthy infants are cyanosed at birth but start to become pink within approximately 30 s of the onset of effective breathing.<sup>121</sup> Peripheral cyanosis is common and does not, by itself, indicate hypoxia. Persistent pallor despite ventilation may indicate significant acidosis, or, more rarely, hypovolaemia with intense cutaneous vascular vasoconstriction. A pink upper-part of the body and a blue lower part can be a sign of right-left shunting over an open duct.

Colour is an unreliable marker of oxygenation which is better assessed using pulse oximetry. There are few studies in the newborn. In an observational study involving 27 clinicians making a subjective assessment of oxygenation status using videos of preterm infants where saturations were known there was a lack of concordance with both under and over estimation of values.<sup>122</sup>

### Breathing

Not crying may be due to apnoea but can also function as a marker of inadequate breathing needing support. In an observational study of 19 977 infants just after birth in a rural hospital setting 11% were not crying, around half of whom were assessed as apnoeic. About 10% of those assessed as breathing at birth became apnoeic. Not crying but breathing was associated with a 12-fold increase in morbidity.<sup>123</sup>

The presence or adequacy of breathing effort in preterm infants can be difficult to assess as breathing can be very subtle and is often missed.<sup>121,124</sup> Breathing perceived as inadequate will prompt an intervention. In a retrospective video based observational study of 62 preterm infants delivered at <28 weeks or with birth weight <1000 g 80% were assessed as showing signs of breathing but all received respiratory support with CPAP or intubation.<sup>125</sup>

### Heart rate

Immediately after birth, the heart rate is assessed to evaluate the condition of the infant and subsequently, heart rate is the most sensitive indicator of a successful response to interventions.<sup>126–128</sup> There is no published evidence unambiguously defining the thresholds for intervention during newborn resuscitation. The rates of  $100 \text{ min}^{-1}$  and  $60 \text{ min}^{-1}$  around which interventions are prompted are essentially pragmatic in nature.<sup>129</sup>

In uncompromised breathing term infants, where umbilical cord clamping was delayed, the heart rate is usually above  $100 \text{ min}^{-1}$ .<sup>128</sup> In an observational study of 1237 term/near-term infants resuscitated in a rural setting the initial heart rates at birth were distributed in a bimodal peak around 60 and  $165 \text{ min}^{-1}$ . Ventilation increased heart rate in most bradycardic newborns to a final median of  $161 \text{ min}^{-1}$ . Lower initial and subsequent heart rates were associated with poorer outcomes.<sup>130</sup> In preterm infants <30 weeks gestation the heart rate does not stabilise until it reaches approximately  $120 \text{ min}^{-1}$  and, in some, stability was only achieved once the heart rate was  $>150 \text{ min}^{-1}$ .<sup>131</sup>

Auscultation by stethoscope is inexpensive, simple, and permits a reasonably accurate rapid assessment of heart rate. In delivery room studies of low risk infants heart rate determination was possible within 14(10–18) seconds (median(IQR)) and was found to underestimate ECG or pulse oximetry (PO) values by between  $-9(\pm 7)$  and  $-14(\pm 21) \text{ min}^{-1}$  (mean difference (95% CI)).<sup>132,133</sup>

Palpation for a pulse at the base of the umbilical cord or (less reliably) the brachial or femoral arteries is also simple and rapid. Values may be considered valid if the heart rate is determined to be fast ( $>100 \text{ min}^{-1}$ ), however they are often inaccurate, intermittent and affected by movements with a tendency to significantly underestimate, potentially prompting inappropriate interventions.<sup>133,134</sup>

Continuous monitoring provides a more dynamic indication of heart rate change during resuscitation and is preferable to intermittent counting. A pulse oximeter (ideally connected to the right hand) can give an accurate heart rate as well as information on oxygenation. Initial values may underestimate the ECG a little: In a study of 53 infants pulse oximeter values were significantly lower than ECG over the first 2 min (81 (60–109) vs 148 (83–170)  $\text{min}^{-1}$  at 90 seconds ( $p < 0.001$ )).<sup>135</sup> Later differences of  $-2(26) \text{ min}^{-1}$  (mean(SD)) were observed when compared with ECG,<sup>136</sup> but the time to obtain reliable values may take longer than auscultation.<sup>137</sup> Findings differ as to whether advantage is gained from connecting the sensor to infant<sup>138</sup> or oximeter<sup>139</sup> first, however, signal acquisition can be achieved within about 15 s once connected. Peripheral hypoperfusion, signal dropout, movement, arrhythmias, and ambient lighting can interfere with PO measurements. Pulse oximetry may significantly underestimate values when signal quality is poor.<sup>140 141,142</sup>

ECG has been demonstrated to be a practical and rapid means of accurately determining the heart rate which may be a few seconds faster than pulse oximetry and more reliable, especially in the first 2 min after birth.<sup>141,142</sup> Two RCTs reported faster times to HR assessment using ECG compared to PO with a mean(SD) 66(20) vs 114(39) seconds and a median(IQR) 24(19–39) vs 48(36–69) seconds both  $p = 0.001$ .<sup>132,143</sup>

A recent ILCOR evidence update concluded that the 7 new studies identified since 2015 (2 systematic reviews, 2 RCTs and 3 observational studies) supported the previous recommendations that in infants requiring resuscitation,<sup>1</sup> ECG can be used to provide a rapid and accurate estimation of heart rate (weak recommendation, low quality of evidence).<sup>49,144</sup>

It is important to be aware of the limitations of the methods. ECG does not replace oximetry as whilst ECG may indicate a heart rate in the absence of output (PEA),<sup>145</sup> pulse oximetry has advantages over ECG in providing a measure of perfusion and oxygenation. Newer technologies such as dry electrodes may improve signal; and methods such as plethysmography and Doppler may permit rapid reliable output-based determination of heart rate, but clinical validation is still needed before they can be recommended.<sup>141,142</sup>

## Airway

### Airway

With flexion and extension, the airway can become occluded.<sup>146</sup> The evidence on the mechanisms of airway occlusion in the newborn is limited. A retrospective analysis of images of the airway of 53 sedated infants between 0 and 4 months undergoing cranial MRI indicates how, in extension, obstruction might occur through anterior displacement of the posterior airway at the level of the tongue.<sup>147</sup> Therefore, a neutral position is favoured to ensure optimal airway patency.

### Jaw lift

There are no studies of jaw thrust/lift in the newborn. Studies in children demonstrate that anterior displacement of the mandible enlarges the pharyngeal space through lifting the epiglottis away from the posterior pharyngeal wall, reversing the narrowing of the laryngeal

inlet.<sup>148</sup> Two-person manual ventilation techniques are superior to single handed airway support.<sup>146</sup>

### Oropharyngeal/nasopharyngeal airway

Although the oropharyngeal airway (OPA) has been shown to be effective in children,<sup>149</sup> there is no published evidence demonstrating effectiveness in helping maintain the patency of the airway at birth. In a randomised study of 137 preterm infants where gas flow through a mask was measured, obstructed inflations were more common in the OPA group (complete 81% vs. 64%;  $p = 0.03$ , partial 70% vs. 54%;  $p = 0.04$ ).<sup>150</sup> However, by helping lift the tongue and preventing it occluding the laryngeal opening, an OPA may facilitate airway support where difficulty is experienced and manoeuvres, like jaw lift, fail to improve ventilation. A nasopharyngeal airway (NPA) may help establish an airway where there is congenital upper airway abnormality<sup>151</sup> and has been used successfully in preterm infants at birth.<sup>152</sup>

### Airway obstruction

The cause of airway obstruction is usually unknown. It may be due to inappropriate positioning of the head, laryngeal adduction, or pushing a facemask onto the mouth and nose too hard, especially in preterm infants at birth. In an animal model of premature birth Crawshaw used phase contrast X-ray to demonstrate that the larynx and epiglottis were predominantly closed (adducted) in those with unaerated lungs and unstable breathing patterns, making intermittent positive pressure ventilation (IPPV) ineffective unless there was an inspiratory breath, and only opening once the lungs were aerated.<sup>153</sup> In an observational study of 56 preterm infants  $<32$  weeks gestation significant mask leak ( $>75\%$ ) and/or obstruction to inspiratory flow (75%) were identified using respiratory function monitoring in 73% of interventions during the first 2 min of PPV.<sup>154</sup> There is no evidence that normal lung fluid and secretions cause obstruction, and thus no need to aspirate fluid from the oropharynx routinely.

### Oropharyngeal and nasopharyngeal suction

Oropharyngeal and nasopharyngeal suction has in newborn infants not been shown to improve respiratory function and may delay other necessary manoeuvres and the onset of spontaneous breathing. Consequences may include irritation to mucous membranes, laryngospasm, apnoea, vagal bradycardia, hypoxaemia, desaturation and impaired cerebral blood flow regulation.<sup>155–159</sup> A recent ILCOR scoping review of 10 studies (8 RCTs, 1 observational study and 1 case study) into the suctioning of clear fluid involving  $>1500$  mainly term/near-term infants found no evidence to challenge the current recommendations: Routine intrapartum oropharyngeal and nasopharyngeal suction for newborn infants with clear or meconium-stained amniotic fluid is not recommended (very low certainty evidence – downgraded for risk of bias, indirectness and imprecision).<sup>1</sup> If suctioning is attempted it should be undertaken under direct vision, ideally using a laryngoscope and a wide bore catheter.

There have been few studies investigating the effectiveness of suction devices for clearing the newborn airway. An in vitro study using simulated meconium demonstrated the superiority of the Yankauer sucker in clearing particulate matter when compared to large bore (12–14F) flexible catheters and bulb devices. Most devices could clear non-particulate matter but the only devices that cleared simulated particulate meconium were a Yankauer sucker or a bulb syringe device. Bulb suction devices are less effective but do not require a separate vacuum source. Smaller diameter suction catheters were much less effective.<sup>160</sup> The paediatric Yankauer sucker has the advantage of



single-handed use and effectiveness at lower vacuum pressures which may be less likely to damage mucosa. A meconium aspirator, attached to a tracheal tube functions in a similar manner and can be used to remove tenacious material from the trachea. These devices should be connected to a suction source not exceeding 150 mmHg (20 kPa).<sup>161</sup>

### Meconium

Lightly meconium-stained liquor is common and does not, in general, give rise to much difficulty with transition. The less common finding of very thick meconium-stained liquor is an indicator of perinatal distress and should alert to the potential need for resuscitation.

There is no evidence to support intrapartum suctioning nor routine intubation and suctioning of vigorous infants born through meconium-stained liquor.<sup>162,163</sup> Retrospective registry based studies do not demonstrate an increase in morbidity following a reduction in delivery room intubation for meconium.<sup>164,165</sup> An ILCOR systematic review of three RCTs involving 449 infants and one observational study of 231 infants demonstrated no benefit from the use of immediate laryngoscopy with or without tracheal suctioning compared with immediate resuscitation without laryngoscopy (RR 0.99; 95% CI 0.93–1.06;  $p=0.87$ ).<sup>1</sup> Parallel meta-analyses including a further RCT with 132 infants derived similar conclusions.<sup>166–168</sup> A post policy change impact analysis of the resuscitation of 1138 non-vigorous neonates born through meconium-stained amniotic fluid, found reduced NICU admissions and no increase in the incidence of Meconium Aspiration Syndrome (MAS) where suctioning was omitted in favour of immediate ventilation.<sup>169</sup>

Routine suctioning of non-vigorous infants may result in delays in initiating ventilation although some newborn infants may still require laryngoscopy with or without tracheal intubation in order to clear a blocked airway or for subsequent ventilation. Therefore, in apnoeic or ineffectively breathing infants born through meconium-stained amniotic fluid ILCOR treatment recommendations suggest against routine immediate direct laryngoscopy and/or suctioning after delivery with the emphasis on initiating ventilation in the first minute of life (weak recommendation, low certainty evidence).<sup>1</sup>

In infants with respiratory compromise due to meconium aspiration, the routine administration of surfactant or bronchial lavage with either saline or surfactant is not recommended.<sup>170,171</sup>

### Initial inflations and assisted ventilation

After initial assessment at birth, if breathing efforts are absent or inadequate, lung aeration is the priority and must not be delayed. An observational study in low resource settings suggested those resuscitating took around  $80 \pm 55$  s to commence ventilation with a 16% ( $p=0.045$ ) increase in morbidity/mortality in apnoeic infants for every 30 s delay in starting ventilation after birth.<sup>10</sup> In term infants, respiratory support should start with air.<sup>172</sup>

### Inflation pressure and duration

In newborn infants, spontaneous breathing or assisted initial inflations create the functional residual capacity (FRC).<sup>9,173</sup> When assisting ventilation, the optimum inflation pressure, inflation time and flow required to establish an effective FRC are subject to technical and biological variation and have not yet been conclusively determined. Debate continues about the validity of longer inflation breaths with recent discussion on the merits of sustained inflation (see below).<sup>1</sup> Current ERC NLS recommendations on inflation breaths are for a

longer duration although there is a lack of evidence demonstrating advantage or disadvantage over other recommended approaches. Once an airway is established, five initial breaths with inflation pressures maintained for up to 2–3 s are suggested and may help lung expansion.<sup>49,173–175</sup>

The evidence for the optimal initial pressure for lung aeration is limited. The consensus is that inflation pressures of 30 cm H<sub>2</sub>O are usually sufficient to inflate the liquid filled lungs of apnoeic term infants. This value was originally derived from historical studies of limited numbers of infants.<sup>173,176,177</sup> A more recent prospective study of 1237 term and near-term infants resuscitated in a rural setting using a bag-mask without PEEP suggests that higher initial pressures may sometimes be required, with median peak pressures of 37 cm H<sub>2</sub>O required for successful stabilisation.<sup>178</sup> In preterm infants, critical review of the available evidence suggests that previously advocated initial inflation pressures of 20 cm H<sub>2</sub>O are probably to be too low to recruit the lungs effectively.<sup>175,179–181</sup> Therefore, it is suggested that a starting pressure of 25 cm H<sub>2</sub>O would be reasonable. Acknowledging that smaller airways have greater resistance than larger airways, some preterm infants may need higher pressures than 25 cm H<sub>2</sub>O for lung inflation.

The time to initiation of spontaneous breathing is reported to be inversely correlated with the peak inflation pressure and the inflation time.<sup>174</sup> If the infant has any respiratory effort, ventilation is most effective when inflation coincides with the inspiratory efforts.<sup>181</sup> However, the tidal volume of positive pressure ventilations may then exceed that of spontaneous breaths.<sup>124,182</sup> It is acknowledged that such synchronisation is difficult to achieve.<sup>183</sup>

A recent observational study in preterm infants under 32 weeks suggested that the application of a mask to support breathing might induce apnoea in spontaneously breathing infants.<sup>184</sup> However, the significance of this effect on outcome is currently unclear.<sup>185</sup>

### Ventilation

There is limited evidence on the optimal rate of ventilation for newborn resuscitation. In an observational study of 434 mask ventilated late preterm and term infants, ventilation at a rate of about 30 min<sup>-1</sup> achieved adequate tidal volumes without hypocarbia and the frequency of 30 min<sup>-1</sup> with V<sub>TE</sub> of 10–14 mL kg<sup>-1</sup> was associated with the highest CO<sub>2</sub> clearance.<sup>186</sup> In an observational study of 215 near-term/term infants there was a non-linear relationship between delivered tidal volume and heart rate. The minimum volume necessary to produce an increase in heart rate was 6.0 (3.6–8.0) mL kg<sup>-1</sup>. A tidal volume of 9.3 mL kg<sup>-1</sup> produced the most rapid and largest increase in heart rate.<sup>127</sup>

The delivered tidal volume required to form the FRC may exceed that of the exhaled TV: Foglia et al. describe this as being over 12 mL kg<sup>-1</sup> for a term infant.<sup>183</sup> Exhaled tidal volumes increase during the first positive pressure ventilations as aeration takes place, compliance increases and the FRC is established.<sup>178</sup> In most instances, it should be possible to reduce peak pressures once the lungs are aerated to prevent excessive tidal volumes.<sup>183</sup>

There are no published studies clearly determining the optimal inflation time when providing positive pressure ventilation. Longer inspiratory times may permit lower pressures.<sup>183</sup> Observational studies on spontaneously breathing newborn infants suggest that once lung inflation has been achieved they breathe at a rate between 30 and 40 breaths min<sup>-1</sup>, and regardless of which breathing pattern, an inspiratory time of 0.3–0.4 s is used.<sup>187</sup>

## Assessment

The primary response to adequate initial lung inflation is a prompt improvement in heart rate.<sup>126,127</sup> Most newborn infants needing respiratory support will respond with a rapid increase in heart rate within 30 s of lung inflation.<sup>188</sup> Chest wall movement usually indicates aeration/inflation. This may not be so obvious in preterm infants.<sup>189</sup> Large chest excursions during positive pressure ventilation may be a marker of excessive tidal volumes, which should be avoided. Continued ventilation is required if the heart rate increases but the infant is not breathing adequately.

Failure of the heart rate to respond is most likely secondary to inadequate airway control or inadequate ventilation. Mask position or seal may be suboptimal.<sup>182,190,191</sup> Head/Airway position may be in need of adjustment.<sup>146</sup> Inflation pressures may need to be higher to achieve adequate inflation/ tidal volumes.<sup>178</sup> In preterm infants excessive mask pressure and glottal closure have been demonstrated to be factors.<sup>8,153,154,192</sup>

Using a two-person approach to mask ventilation reduces mask leak in term and preterm infants and is superior to the single handed approach.<sup>191,193</sup> Published evidence on the incidence of physical matter as a cause of obstruction is lacking but it is recognised that meconium or other matter (e.g. blood, mucus, vernix) may cause airway obstruction.<sup>194</sup> The use of adjuncts to support the airway is discussed elsewhere (see airway and adjuncts).

## Sustained inflations (SI) > 5 s

Animal studies have suggested that a longer SI may be beneficial for establishing functional residual capacity at birth during transition from a liquid filled to air-filled lung.<sup>195,196</sup> A Cochrane systematic review of initial inflation >1 s vs. standard inflations ≤1 s was updated in 2020. Eight RCTs enrolling 941 infants met inclusion criteria for the primary comparison of the use of SI without chest compressions. SIs were of 15–20 s at 20–30 cm H<sub>2</sub>O. No trial used SIs of ≤5 s. SI was not better than intermittent ventilation for reducing mortality in the delivery room (low quality evidence—limitations in study design and imprecision) and during hospitalisation (moderate quality evidence—limitations in study design). There was no benefit for SI vs. intermittent ventilation for the secondary outcomes of intubation, need for respiratory support or BPD (moderate quality evidence).<sup>197</sup>

A large multicentre RCT which was not included in this analysis investigating effects of SI vs. IPPV among extremely preterm infants (23–26 weeks gestational age) concluded that a ventilation strategy involving 2 SIs of 15 s did not reduce the risk of BPD or death at 36 weeks postmenstrual age. The study enrolled 460 infants out of a planned 600 but was stopped early due to excess early mortality in the SI group possibly attributable to resuscitation. Death at less than 48 h of age occurred in 16 infants (7.4%) in the SI group vs 3 infants (1.4%) in the standard resuscitation group (adjusted risk difference (aRD), 5.6% [95% CI, 2.1% to 9.1%];  $p=0.002$ ). but this finding could not be attributed to the SI directly.<sup>198</sup>

A recent ILCOR systematic review identified 10 eligible RCTs including those above with 1509 newborn infants.<sup>1</sup> For the primary outcome of death before discharge no significant benefit or harm was noted from the use of SI >1 s (actually >5 s) compared to PPV with inflations of ≤1 s (low certainty evidence downgraded for risk of bias and inconsistency). No studies were identified reporting on the secondary critical outcomes of long-term neurodevelopmental outcome or death at follow up.

Subgroup analysis of different lengths of SI (6–15 s 9 RCTs 1300 infants, >15 s 2 RCTs 222 infants) and of different inspiratory pressures (>20 mmHg 6 RCTs 803 infants, ≤20 mmHg 699 infants) demonstrated no significant benefit or harm from SI compared to IPPV of ≤1 s (downgraded for risk of bias and variously for imprecision and inconsistency).

In subgroup analyses comparing SI >1 s to inflations of ≤1 s in infants at <28<sup>+0</sup> weeks there was low certainty evidence (downgraded for risk of bias and imprecision) from 5 RCTs enrolling 862 infants of potential harm (RR 1.38 95% CI 1.00–1.91). In infants 28<sup>+1</sup>–31<sup>+6</sup> weeks there was very low certainty evidence (downgraded for risk of bias and very serious imprecision) from 4 RCTs enrolling 175 preterm infants demonstrating no significant benefit or harm (RR 1.33 95% CI 0.22–8.20). No SIs were <5 s. There was no published data available for more mature infants.

Further sub-analyses excluding studies with a high risk of bias (9 RCTs 1390 infants RR 1.24 95%CI 0.92–1.68), studies with only a single breath (9 RCTs 1402 infants RR 1.17 95%CI 0.88–1.55) and those with sustained inflation with mask only (9 RCTs 1441 infants (RR 1.06 95%CI 0.61–1.39) demonstrated no difference in outcome between SI and normal inflations (low certainty evidence, downgraded for risk of bias and imprecision).

ILCOR treatment recommendations suggest that the routine use of initial SI ≥5 s cannot be recommended for preterm newborn infants who receive positive pressure ventilation prompted by bradycardia or ineffective respirations at birth (weak recommendation, low-certainty evidence) but that a sustained inflation might be considered in research settings. There was insufficient evidence to make any specific recommendation on the duration of inflations in late preterm or term infants. It was recognised that the total number of infants studied were insufficient to have confidence in the estimate of effect; larger trials being needed to determine if there are benefits or harms from sustained inflation.<sup>1</sup>

There are no randomised trials comparing the use of initial breaths of ≤1 s with breaths of 2–3 s. A recent RCT in 60 preterm infants <34 weeks gestation of 2–3 s inflation breaths vs. a single 15 s SI demonstrated no difference in minute volume or end tidal CO<sub>2</sub>.<sup>199</sup> Infants receiving the SI made a respiratory effort sooner (median 3.5 (range 0.2–59) versus median 12.8 (range 0.4–119) seconds,  $p=0.001$ ). SI was associated with a shorter duration of ventilation in the first 48 h (median 17 (range 0–48) versus median 32.5 (range 0–48) h,  $p=0.025$ )

## PEEP and CPAP/airway adjuncts and assisted ventilation devices

### PEEP

Animal studies have shown that immature lungs are easily damaged by large tidal volume inflations immediately after birth<sup>200,201</sup> and suggest that maintaining a PEEP immediately after birth may help reduce lung damage<sup>202,203</sup> although one study suggests no benefit.<sup>204</sup> PEEP applied immediately after birth improves lung aeration, functional residual capacity, compliance and gas exchange, particularly oxygenation.<sup>205,206</sup>

PEEP is more reliably delivered by pressure limiting devices which use continuous gas flow, like TPR devices. A recent review of the evidence undertaken by ILCOR identified two randomized trials and one quasi-randomized trial (very low quality evidence) comparing ventilation with TPR vs. SIB and reported similar rates

of death and chronic lung disease.<sup>1</sup> There was no difference in SpO<sub>2</sub> at 5 min after birth in 80 infants <29 weeks gestation (61% [13–72%] versus 55% [42–67%];  $p=0.27$ ).<sup>207</sup> No difference was identified in achieving HR >100 min<sup>-1</sup> in 1027 infants ≥26 weeks (1 (0.5–1.6) vs 1 (0.5–1.8)  $p=0.068$  (min(IQR)).<sup>208</sup> There were reductions in the magnitude of some interventions with TPR. 86 (17%) vs. 134(26%) were intubated in the delivery room (OR 0.58 (0.4–0.8) 95% CI  $p=0.002$ ). The maximum positive inspiratory pressure was 26(2) cm H<sub>2</sub>O TPR vs 28(5) cm H<sub>2</sub>O SIB ( $p<0.001$ ) mean (SD).

In a quasi-randomised study of 90 infants of 34 (3.7) (mean (SD)) weeks gestation the duration of PPV in delivery room was significantly less with TPR (median (IQR) 30 s (30–60) vs. 60 s (30–90) ( $p<0.001$ )).<sup>209</sup> A higher proportion were intubated in the SIB group (34 vs 15%  $p=0.04$ ). In one large multicentre observational study of 1962 infants between 23 and 33 weeks gestation improved survival and less BPD was seen when PEEP was used at birth (OR = 1.38; 95% CI 1.06–1.80).<sup>210</sup>

All term and preterm infants who remain apnoeic despite adequate initial steps must receive positive pressure ventilation. ILCOR treatment recommendations are unchanged from 2015, suggesting PEEP should be used for the initial ventilation for premature newborn infants during delivery room resuscitation (weak recommendations, low-quality evidence).<sup>1</sup> It is suggested that positive end expiratory pressure (PEEP) of approximately 5–6 cm H<sub>2</sub>O to begin with should be administered to preterm newborn infants receiving PPV. No clear recommendations on the level of PEEP can be made for term infants because of a lack of evidence.<sup>49,144</sup>

## CPAP

A Cochrane systematic review of CPAP applied within the first 15 min of life in preterm infants <32 weeks identified 7 RCTs involving 3123 infants and concluded that CPAP reduced the need for additional breathing assistance but with insufficient evidence to evaluate prophylactic CPAP compared to oxygen therapy and other supportive care.<sup>211</sup> Evidence was downgraded to low quality because of considerable heterogeneity, imprecision and lack of blinding. In 3 of the studies involving 2354 infants comparing CPAP with assisted ventilation, prophylactic nasal CPAP in very preterm infants reduced the need for mechanical ventilation and surfactant and also reduced the incidence of BPD and death or BPD (evidence downgraded due to imprecision).

Another systematic review included 4 RCTs 3 of which were included in the Cochrane analysis and one additional study.<sup>212</sup> Pooled analysis showed a significant benefit for the combined outcome of death or bronchopulmonary dysplasia, or both, at 36 weeks corrected gestation for infants treated with nasal CPAP (RR 0.91, 95% CI 0.84–0.99, RD 0.04, 95% CI –0.07 to 0.00) NNT 25. Following a review of the evidence ILCOR recommendations are unchanged from 2015, that for spontaneously breathing preterm newborn infants with respiratory distress requiring respiratory support in the delivery room, it is suggested that CPAP should be used initially rather than intubation and IPPV (weak recommendation, moderate certainty of evidence).<sup>1,49,144</sup> There are few data to guide the appropriate use of CPAP in term infants at birth.<sup>213,214</sup> Caution is prompted by retrospective cohort studies which suggest that delivery-room CPAP may be associated with an increased incidence of pneumothorax in term/near term infants.<sup>215–217</sup>

## Assisted ventilation devices

Effective ventilation in the newborn can be achieved with a flow-inflating bag (FIB), a self-inflating bag (SIB) or with a pressure limited TPR.<sup>207,208,218–220</sup> An attribute of a TPR device is its ability to deliver a consistent measure of PEEP or CPAP when compared to standard SIB's and this may be a factor contributing to any observed difference in outcomes between the devices (see section on PEEP).

Whilst the TPR appears to confer benefit it cannot be used in all circumstances. Unlike the TPR, the self-inflating bag can be used in the absence of a positive pressure gas supply. However, the blow-off valves of SIB are flow-dependent and pressures generated may exceed the value specified by the manufacturer, usually 30–40 cm H<sub>2</sub>O, if the bag is compressed vigorously.<sup>221,222</sup> More training is required to provide an appropriate peak and end pressure using FIBs compared with self-inflating bags. In an observational manikin-based study of 50 clinicians, technical difficulties with the FIB impaired performance when compared to an SIB.<sup>223</sup>

A qualitative review identified 30 studies comparing TPR against other neonatal manual ventilation devices and noted that the majority of studies were manikin based with 2 infant based studies.<sup>154,207</sup> Users of the TPR could provide PIPs closest to the target PIP, with least variation when compared to SIB and FIB.<sup>224–228</sup> Similarly TPR users provided a PEEP closer to the predetermined PEEP value with potentially less volutrauma with the TPR as tidal volumes are smaller and less variable in comparison to the SIB.<sup>225–228</sup> TPR provided a more consistent inspiratory time than SIB independent of experience. Prolonged inflation could be more reliably provided by the TPR.<sup>229</sup> Limitations of the TPR device were identified. Resuscitation is a dynamic process where the resuscitator needs to adapt to the response or non-response of the newborn. TPR users were not as good at detecting changes in compliance as users of the SIB and FIB.<sup>230</sup> PEEP valves could be inadvertently screwed down leading to excess PEEP.<sup>231</sup> TPR users needed more time to change the inflating pressures during resuscitation compared to users of the SIB or FIB. Mask leak can be greater with the TPR than with SIB<sup>227,228</sup> and changes to TPR gas flow rate had significant effects on PIP, PEEP<sup>232–235</sup> and mask leak.<sup>232</sup> The TPR can require more training to set up properly but once in use provided more consistent ventilation than the SIB even with inexperienced operators.<sup>236</sup> The SIB cannot deliver CPAP and may not be able to achieve a consistent end expiratory pressure even with a PEEP valve.<sup>224–226,237–240</sup> The performance of various TPRs and self-inflating bags may differ considerably.<sup>241</sup> A newer upright design of SIB and revised mask confers advantages in use including improved delivery of PEEP.<sup>188,242–244</sup>

In addition to the 1107 infants in the two RCTs included in the 2015 analysis,<sup>207,208</sup> a recent ILCOR scoping review of TPR vs. SIB for ventilation<sup>1,245</sup> reported a substantial number of additional patients in one further RCT ( $n=90$ )<sup>209</sup> and one large observational study ( $n=1962$ ).<sup>210</sup> Studies differed regarding the investigated populations (two studies included term and preterm infants,<sup>208,209</sup> two studies were in preterm infants only).<sup>207,210</sup> The findings of these studies are outlined in the section on PEEP and suggest improved survival and less need for intubation and BPD with TPR use compared to SIB, particularly in preterm infants.

The ILCOR task force concluded that whilst the direction of evidence is shifting towards support for the use of TPR devices, until a further systematic review is conducted recommendations would remain unchanged.<sup>1</sup> The 2015 consensus on science stated that the use of the TPR showed marginally but not statistically significant

benefits for the clinical outcome of achieving spontaneous breathing.<sup>49</sup>

### Facemask versus nasal prong

A problem when using a facemask for newborn ventilation is a potentially large and variable leak and loss of inflating gas volume arising from suboptimal selection of mask size and poor technique. In manikin studies using a T-piece and different masks, 50 volunteer operators had variable mask leak up to 80% with improvement after written instruction and demonstration of alternative mask hold techniques.<sup>190,191</sup> Using flow monitoring recordings of the airway management of 56 newborn preterm infants Schmölzer demonstrated variable degrees of either obstruction ( $\geq 75\%$ ) and/or leak ( $> 75\%$ ) during first 2 min of support in 73% of cases.<sup>154</sup>

Nasopharyngeal tubes have been suggested as an alternative. An observational study investigating respiratory function found that when using a single nasopharyngeal tube it took longer before PPV was given, leak was increased and obstruction occurred more frequently, inadequate tidal volumes were delivered more often and SpO<sub>2</sub> was lower in the first minutes during PPV.<sup>246</sup> However, two randomised trials in preterm infants of <31 weeks gestation involving 507 infants did not find any difference in intubation rates in the delivery room between facemask and single nasal prong.<sup>152,247</sup>

### Laryngeal mask

The laryngeal mask (LM) may be used in ventilation of the newborn, particularly if facemask ventilation or tracheal intubation is unsuccessful or not feasible.<sup>49</sup> A recent systematic review of seven trials (794 infants) showed that the laryngeal mask was more effective than bag-mask in terms of shorter resuscitation and ventilation times, and less need for tracheal intubation (low- to moderate-quality evidence).<sup>248</sup> Of note, bag-mask was effective in more than 80% of enrolled infants. Efficacy of the laryngeal mask was comparable to that offered by tracheal intubation (very low to low quality evidence), suggesting that it is a valid alternative airway device when attempts at tracheal intubation are unsuccessful during resuscitation or where those involved lack the skills or equipment to intubate safely.

As available studies included infants with birth weight >1500 g or 34 or more weeks gestation, evidence supporting laryngeal mask use in more premature infants is lacking.<sup>248,249</sup> The laryngeal mask has not been evaluated in the setting of meconium-stained fluid, during chest compressions, or for the administration of emergency intra-tracheal medications.

### Tracheal tube placement

The use and timing of tracheal intubation will depend on the skill and experience of the available resuscitators. Formulae may be unreliable in determining tracheal tube lengths.<sup>250,251</sup> Appropriate tube lengths for oral intubation derived from observational data based on gestation are shown in Table 1.<sup>252</sup> Nasotracheal tube length was found to be approximately 1 cm more than the oral length.<sup>253</sup> Uncuffed tubes are typically used. There is no published evidence to support the routine use of cuffed tubes during neonatal resuscitation. Efficacy has been demonstrated in infants <3 kg during perioperative respiratory support.<sup>254</sup>

The diameter of the narrowest part of the airway and varies with gestational age and size of the infant whereas the external diameter of the tube (of the same internal diameter) may vary depending on

manufacturer.<sup>255</sup> A range of differing sized tubes should be available to permit placement of that most appropriate to ensure adequate ventilation with only a small leak of gas around the tracheal tube and without trauma to the airway. A narrow diameter tube in a large airway may be confirmed in the correct position but fail to provide adequate ventilation because of low lung compliance and excessive leak. The tube diameter may be estimated as  $\leq 1/10$  of the gestational age.<sup>256</sup>

Tracheal tube placement should be confirmed by exhaled CO<sub>2</sub> detection (see below), the length inserted assessed visually during intubation and the tip position confirmed clinically and ideally radiographically. Markings on the tips of tracheal tubes to aid tube placement distal to the vocal cords vary considerably between manufacturers.<sup>257</sup> Within institutions users will likely gain familiarity with specific types. Tube position may alter during the securing process.<sup>252</sup> A systematic review of published literature on methods of confirming correct tube placement concluded that objective assessments of tube position were better validated than subjective ones such as visual assessment of chest movement.<sup>258</sup> Following tracheal intubation and IPPV, a prompt increase in heart rate and observation of expired CO<sub>2</sub> are good indications that the tube is in the trachea.<sup>258</sup>

### End tidal CO<sub>2</sub> and respiratory function monitoring

Detection of exhaled CO<sub>2</sub> in addition to clinical assessment is recommended to confirm correct placement of a tracheal tube in neonates with spontaneous circulation.<sup>49</sup> Even in VLBW infants,<sup>259,260</sup> detecting evidence of exhaled CO<sub>2</sub> confirms tracheal intubation in neonates with a cardiac output more rapidly and more accurately than clinical assessment alone.<sup>260,261</sup> However, studies have excluded infants in need of extensive resuscitation. Failure to detect exhaled CO<sub>2</sub> strongly suggests tube misplacement, most likely oesophageal intubation or tube dislodgement.<sup>259,261</sup> False negative end tidal carbon dioxide (ETCO<sub>2</sub>) readings have been reported during cardiac arrest.<sup>259</sup> and in VLBW infants despite models suggesting effectiveness with low tidal volumes.<sup>262</sup> Poor or absent pulmonary blood flow or tracheal obstruction may prevent detection of exhaled CO<sub>2</sub> despite correct tracheal tube placement. There is a lack of evidence in the neonate as to the effect of drugs on exhaled CO<sub>2</sub> monitoring, however studies in adults suggest drugs such as adrenaline and bicarbonate may affect end-tidal CO<sub>2</sub> determination.<sup>263</sup> Insufficient inflating pressure to recruit an adequate FRC and generate sufficient expiratory flow might also be a factor. The inability to detect exhaled CO<sub>2</sub> despite correct placement may lead to a decision to extubate. Where CO<sub>2</sub> detection is unreliable tube position should be confirmed by direct laryngoscopy.

Both qualitative (colorimetric) and quantitative (waveform) methods have been successfully used after delivery.<sup>264</sup> Studies in adults suggest that waveform capnography may be more sensitive than colorimetry in detecting exhaled CO<sub>2</sub>, however, due to lack of data on the validity of waveform capnography in neonates, caution must be exercised when considering its use.<sup>263,265,266</sup>

Flow monitoring is useful for confirming tracheal tube position. In a randomised controlled trial a flow sensor confirmed appropriate tube placement faster and more reliably than capnography.<sup>267</sup>

Respiratory flow/volume monitoring<sup>268</sup> and end tidal CO<sub>2</sub><sup>269,270</sup> may be used in non-intubated patients. The effectiveness of quantitative capnography in confirming mask ventilation has been demonstrated but may not provide reliable ETCO<sub>2</sub> values.<sup>270</sup> The use of exhaled CO<sub>2</sub> detectors to assess ventilation with other interfaces (e.g., nasal airways, laryngeal masks) during positive pressure ventilation in the delivery room has not been reported.

## Video-laryngoscopy

A systematic review of studies of video-laryngoscopy in newborn infants concluded by suggesting that video-laryngoscopy increases the success of intubation in the first attempt but does not decrease the time to intubation or the number of attempts for intubation (moderate to very low-certainty evidence). However, included studies were conducted with trainees performing the intubations and highlight the potential usefulness of video-laryngoscopy as a teaching tool. Well-designed, adequately powered RCTs are necessary to confirm efficacy and address safety and cost-effectiveness of video-laryngoscopy for neonatal endotracheal intubation by trainees and those proficient in direct laryngoscopy.<sup>271</sup> The effectiveness in the context of resuscitation at birth has not been fully evaluated.

## Air/oxygen

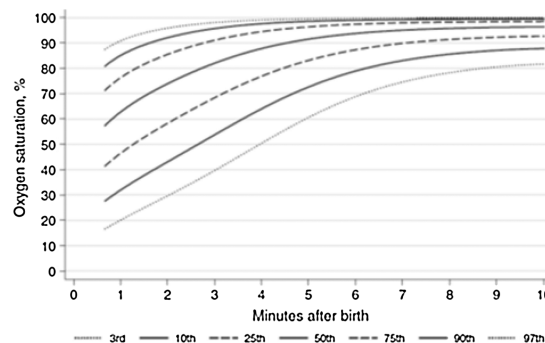
### Term infants and late preterm infants $\geq 35$ weeks

A recent ILCOR CoSTR suggests that for term and late preterm newborns ( $\geq 35$  weeks gestation) receiving respiratory support at birth, support should start with 21% oxygen (weak recommendation, low certainty evidence).<sup>1</sup> It recommends against starting with 100% inspired oxygen (strong recommendation, low certainty evidence). A systematic review and meta-analysis of 5 RCTs and 5 quasi RCTs included 2164 patients demonstrated a 27% relative reduction in short-term mortality when initial room air was used compared with 100% oxygen for neonates  $\geq 35$  weeks gestation receiving respiratory support at birth (RR = 0.73; 95% CI 0.57–0.94).<sup>172</sup> No differences were noted in neurodevelopmental impairment or hypoxic-ischaemic encephalopathy (low to very low certainty evidence). Use of low concentrations of inspired oxygen may result in suboptimal oxygenation where there is significant lung disease<sup>272</sup> and in term infants a high inspired oxygen may be associated with a delay in onset of spontaneous breathing.<sup>273</sup> Therefore oxygen should be titrated to achieve adequate productal saturations. If increased oxygen concentrations are used, they should be weaned as soon as possible.<sup>274–276</sup>

### Preterm infants $< 35$ weeks

In an ILCOR systematic review and meta-analysis of 10 RCTs and 4 cohort studies including 5697 infants comparing initial low with high inspired oxygen for preterm infants  $< 35$  weeks gestation who received respiratory support at birth, there were no statistically significant benefits or harms from starting with lower compared to higher inspired oxygen in short or long term mortality ( $n=968$ ; RR=0.83 (95% CI 0.50–1.37)), neurodevelopmental impairment or other key preterm morbidities.<sup>277</sup> It is suggested that low (21–30%) rather than a higher initial concentration (60–100%) be used (weak recommendation, very low certainty evidence). The range selected reflects the low oxygen range used in clinical trials. Oxygen concentration should be titrated using pulse oximetry (weak recommendation, low certainty evidence).<sup>1</sup>

In contrast to term infants, in preterm infants the use of supplemental oxygen to reach adequate oxygenation increases breathing efforts. In an animal experimental study<sup>278</sup> and one RCT in 52 preterm infants  $< 30$  weeks gestation,<sup>279</sup> initiating stabilisation with higher oxygen concentrations (100% vs. 30%) led to increased breathing effort, improved oxygenation, and a shorter duration of mask ventilation. Minute volumes were significantly higher at 100% ( $146.34 \pm 112.68 \text{ mL kg}^{-1} \text{ min}^{-1}$ ) compared to 30% ( $74.43 \pm 52.19 \text{ mL kg}^{-1} \text{ min}^{-1}$ ),  $p=0.014$ .



**Fig. 10 – Oxygen saturations in healthy infants at birth without medical intervention (3rd, 10th, 25th, 50th, 75th, 90th, 97th centiles). Reproduced with permission – from Dawson 2010.**

A recent European consensus statement recommended the use of an initial inspired oxygen concentration of 30% for newborns  $< 28$  weeks gestation, of 21–30% for 28–31 weeks gestation, and of 21% for  $> 32$  weeks gestation.<sup>280</sup>

### Target oxygen saturation

The target range recommended for both term and preterm infants are similar and based upon time based values for productal saturations in normal term infants in air.<sup>281</sup> Consensus recommendations suggest aiming for values approximating to the interquartile range,<sup>282</sup> or using the 25th centile as the lower threshold value<sup>49</sup> (Fig. 10).

A systematic review of 8 RCTs with 768 preterm infants  $< 32$  weeks involving low ( $\leq 30\%$ ) vs higher ( $\geq 60\%$ ) initial oxygen concentrations, concluded that failure to reach a minimum SpO<sub>2</sub> of 80% at 5 min was associated with a two-fold risk of death (OR 4.57, 95% CI 1.62–13.98,  $p < 0.05$ ), and had an association with lower heart rate (mean difference  $-8.37$ , 95% CI  $-15.73$  to  $-1.01$ ,  $p < 0.05$ ) and a higher risk of severe intraventricular haemorrhage (OR 2.04, 95% CI 1.01–4.11,  $p < 0.05$ ).<sup>283</sup> It remained unclear whether this was because of the severity of illness, or the amount of oxygen administered during stabilisation.

Available data suggest nearly all preterm newborns  $< 32$  weeks gestation will receive oxygen supplementation in the first 5 min after delivery in order to achieve commonly recommended oxygen saturation targets.<sup>276,281,283</sup> However, it may be difficult to titrate the oxygen concentration in the first minutes and preterm infants  $< 32$  weeks gestation may spend a significant time outside the intended target range.<sup>284,285</sup> In an individual patient analysis of the 706 preterm infants enrolled in the RCTs only 12% reached the threshold SpO<sub>2</sub> of 80% at 5 min after birth.<sup>283</sup>

### Titration of oxygen

It is important to select the appropriate initial oxygen concentration, with careful and timely titration of inspired oxygen against time sensitive threshold saturation levels in order to avoid extremes of hypoxia and hyperoxia and avoid bradycardia. A recent review suggested that oxygen delivery should be reviewed and titrated as necessary every 30 s to achieve this.<sup>286</sup>

An important technical aspect of the titration of supplemental oxygen when using a TPR device is that it takes a median 19 s (IQR 0–57) to achieve the desired oxygen concentration at the distal end of

the TPR.<sup>287</sup> Although the cause of this delay is unclear, mask leak contributes significantly. A good mask seal can lead to a longer delay with a resulting lag between adjustment and response.

### Circulatory support

Circulatory support with chest compressions is effective only if the lungs have been successfully inflated and oxygen can be delivered to the heart. Ventilation may be compromised by compressions so it is vital to ensure that satisfactory ventilation is occurring before commencing chest compressions.<sup>288</sup>

The most effective traditional technique for providing chest compressions is with two thumbs over the lower third of the sternum with the fingers encircling the chest and supporting the back.<sup>289–292</sup> This technique generates higher blood pressures and coronary artery perfusion with less fatigue than the alternative two-finger technique.<sup>293,294</sup> In a manikin study, overlapping the thumbs on the sternum was more effective than adjacent positioning but more likely to cause fatigue.<sup>295</sup> The sternum is compressed to a depth of approximately one-third of the anterior-posterior diameter of the chest allowing the chest wall to return to its relaxed position between compressions.<sup>296–300</sup> Delivering compressions from 'over the head' appears as effective as the lateral position.<sup>301</sup>

A recent ILCOR review of the evidence identified 19 studies published since 2015 including one systematic review and 18 RCTs all of which were manikin studies.<sup>302</sup> No evidence was found to alter treatment recommendations from 2015 in suggesting that chest compressions in the newborn should be delivered by the two thumb, hand encircling the chest method as the preferred option (weak recommendation, very low certainty evidence).<sup>1</sup> However newer techniques, one using two thumbs at an angle of 90° to the chest and the other a 'knocking finger' technique, have been reported in manikins. Further studies are required to determine if they have any clear advantage over the standard two thumb technique.<sup>1,303</sup>

A recent evidence update was undertaken by ILCOR to identify the most effective compression to ventilation ratio for neonatal resuscitation.<sup>1</sup> 13 trials published since 2015 were found to be relevant. Four neonatal manikin studies comparing alternative compression to ventilation ratios or asynchronous ventilation strategies found no advantage over traditional synchronised 3:1 techniques. A number of animal trials compared the delivery of cardiac compressions during a sustained inflation with traditional 3:1 compression to ventilation. No consistently clear advantages were identified. Some trials are ongoing.

ILCOR found no evidence to change the 2015 recommendations for a 3:1 compression to ventilation ratio (weak recommendation, very low quality evidence), aiming to achieve a total of approximately 90 compressions and 30 ventilations per minute.<sup>1,49,144</sup> Compressions and ventilations should be coordinated to avoid simultaneous delivery.<sup>304</sup> There are theoretical advantages to allowing a relaxation phase that is slightly longer than the compression phase, however, the quality of the compressions and breaths are probably more important than the rate.<sup>305</sup>

A 3:1 compression to ventilation ratio is used at all times for resuscitation at birth where compromise of gas exchange is nearly always the primary cause of cardiovascular collapse. Rescuers may consider using higher ratios (e.g. 15:2) if the arrest is believed to be of cardiac origin, more likely in a witnessed postnatal collapse than at birth. When chest compressions are indicated by a persistent very slow/absent heart rate, it would appear reasonable to increase the supplementary inspired oxygen to 100%. However, there are no

human studies to support this and animal studies demonstrate no advantage to 100% inspired oxygen during CPR.<sup>306–312</sup>

Unless using continuous monitoring such as pulse oximetry or ECG, check the heart rate after no longer than 30 s and periodically thereafter. Whilst chest compressions may be discontinued when the spontaneous heart rate is faster than 60 min<sup>-1</sup>, a continued increase in rate is necessary to truly demonstrate improvement. It is not until the heart rate exceeds 120 min<sup>-1</sup> that it becomes stable.<sup>130,131</sup>

Exhaled carbon dioxide monitoring and pulse oximetry have been reported to be useful in determining the return of spontaneous circulation<sup>313–316</sup>; however, current evidence does not support the use of any single feedback device in a clinical setting and extrapolation of their use from adult and paediatric settings have, for a variety of reasons, been proven error prone in neonates.<sup>49,144,265</sup>

### Vascular access

#### Umbilical vein catheterisation (UVC) and intraosseous (IO) access

In a systematic review no evidence was identified comparing the umbilical venous route or use of intravenous (IV) cannulas against the IO route in the newborn for drug administration in any setting.<sup>1</sup> No case series or case reports on IO administration in the delivery room setting were identified. Consensus suggests UVC as the primary method of vascular access. If umbilical venous access is not feasible, or delivery occurs in another setting, the IO route is suggested as a reasonable alternative (weak recommendation, very low certainty of evidence).

A systematic review on the use of IO in neonates in any situation identified one case series and 12 case reports of IO device insertion into 41 neonates delivering several drugs including adrenaline and volume.<sup>317</sup> However, whilst the IO route has been demonstrated to be a practical alternative to the UVC significant adverse events include tibial fractures, osteomyelitis, and extravasation of fluid and medications resulting in compartment syndrome and amputation.<sup>1</sup>

The actual route and method used may depend on local availability of equipment, training and experience.<sup>1</sup> There is limited evidence on the effective use of IO devices immediately after birth, or the optimal site or type of device<sup>318</sup> although simulation studies undertaken in a delivery room setting suggest that the IO route can be faster to insert and use than UVC.<sup>319</sup>

#### Peripheral access

No studies were identified reviewing the use of peripheral IV cannulation in infants requiring resuscitation at birth. A retrospective analysis of 61/70 newborn preterm infants requiring i/v access in a single centre showed that peripheral i/v cannulation is feasible and successful in most cases at first attempt.<sup>320</sup>

### Drugs

Drugs are rarely indicated in resuscitation of the newborn infant.<sup>11,12</sup> Bradycardia is usually caused by profound hypoxia and the key to resuscitation is aerating the fluid filled lungs and establishing adequate ventilation. However, if the heart rate remains less than 60 min<sup>-1</sup> despite apparently effective ventilation and chest compressions, it is reasonable to consider the use of drugs.

Knowledge of the use of drugs in newborn resuscitation is largely limited to retrospective studies, as well as extrapolation from animals and adult humans.<sup>321</sup>

## Adrenaline

A recent systematic review identified 2 observational studies involving 97 newborn infants comparing doses and routes of administration of adrenaline.<sup>322</sup> There were no differences between IV and endotracheal adrenaline for the primary outcome of death at hospital discharge (RR = 1.03 [95% CI 0.62–1.71]) or for failure to achieve return of spontaneous circulation, time to return of spontaneous circulation (1 study; 50 infants), or proportion receiving additional adrenaline (2 studies; 97 infants). There were no differences in outcomes between 2 endotracheal doses (1 study). No human infant studies were found addressing IV dose or dosing interval (very low certainty evidence). Despite the lack of newborn human data it is reasonable to use adrenaline when effective ventilation and chest compressions have failed to increase the heart rate above 60 min<sup>-1</sup>. ILCOR treatment recommendations suggest that if adrenaline is used, an initial dose of 10–30 micrograms kg<sup>-1</sup> (0.1–0.3 mL kg<sup>-1</sup> of 1:10,000 adrenaline [1 mg in 10 mL]) should be administered intravenously (weak recommendation, very low certainty evidence). If intravascular access is not yet available, endotracheal adrenaline at a larger dose of 50–100 micrograms kg<sup>-1</sup> (0.5–1.0 mL kg<sup>-1</sup> of 1:10,000 adrenaline [1 mg in 10 mL]) is suggested (weak recommendation, very low certainty evidence) but should not delay attempts at establishing venous access (weak recommendation, very low certainty evidence). If the heart rate remains less than 60 min<sup>-1</sup> further doses – preferably intravascularly – every 3–5 min are suggested (weak recommendation, very low certainty evidence). If the response to tracheal adrenaline is inadequate it is suggested an intravenous dose is given as soon as venous access is established regardless of the interval between doses (weak recommendation, very low certainty evidence).<sup>1</sup>

## Glucose

Hypoglycaemia is an important additional risk factor for perinatal brain injury.<sup>323</sup> Endogenous glycogen stores are rapidly depleted during prolonged hypoxia. In one study infants with birth asphyxia had, prior to administration of glucose in the delivery room, significantly lower blood glucose (1.9 ± 0.6 mmol/L vs. 3.2 ± 0.3 mmol/L),<sup>324</sup> therefore in protracted resuscitation it is reasonable to use glucose by giving a 250 mg kg<sup>-1</sup> bolus (2.5 mL kg<sup>-1</sup> of 10% glucose). After successful resuscitation formal steps to prevent both hypoglycaemia and hyperglycaemia should be instituted (see post-resuscitation care).

## Volume replacement

A recent ILCOR evidence update<sup>1</sup> identified no further human studies and a single animal RCT which supported the 2010 CoSTR recommendations.<sup>34,274</sup> Early volume replacement is indicated for newborn infants with blood loss who are not responding to resuscitation. Therefore, if there has been suspected blood loss or the infant appears to be in shock (pale, poor perfusion, weak pulse) and has not responded adequately to other resuscitative measures then consider giving volume replacement with crystalloid or red cells. Blood loss causing acute hypovolaemia in the newborn infant is a rare event. There is little to support the use of volume replacement in the absence of blood loss when the infant is unresponsive to ventilation, chest compressions and adrenaline. However, because blood loss may be occult and distinguishing normovolaemic infants with shock due to asphyxia from those who are hypovolaemic can be problematic, a trial of volume administration may be considered.<sup>1</sup>

In the absence of suitable blood (i.e. group O Rh-negative blood), isotonic crystalloid rather than albumin is the solution of choice for restoring intravascular volume. Give a bolus of 10 mL kg<sup>-1</sup> initially. If successful it may need to be repeated to maintain an improvement. When resuscitating preterm infants, volume is rarely needed and has been associated with intraventricular and pulmonary haemorrhages when large volumes are infused rapidly.<sup>325</sup>

## Sodium bicarbonate

If effective spontaneous cardiac output is not restored despite adequate ventilation and adequate chest compressions, reversing intracardiac acidosis may improve myocardial function and achieve a spontaneous circulation. There are insufficient data to recommend routine use of bicarbonate in resuscitation of the newborn. The hyperosmolarity and carbon dioxide-generating properties of sodium bicarbonate may impair myocardial and cerebral function.<sup>326</sup>

A recent review of the evidence<sup>1</sup> concluded that there were no reasons to change the 2010 recommendations.<sup>34,274</sup> Use of sodium bicarbonate is not recommended during brief cardiopulmonary resuscitation. Use, however, may be considered during prolonged cardiac arrest unresponsive to other therapy, when it should be given only after adequate ventilation is established and chest compressions are being delivered. A dose of 1–2 mmol kg<sup>-1</sup> sodium bicarbonate (2–4 mL kg<sup>-1</sup> of 4.2% solution) may be given by slow intravenous injection.

## Naloxone

There is no strong evidence that naloxone confers any clinically important benefits to newborn infants with respiratory depression due to hypoxia.<sup>327,328</sup> Current recommendations do not support use of naloxone during resuscitation with the preference being to concentrate on providing effective respiratory support.

Use is best reserved for those infants whose cardiac output has been restored but who remain apnoeic despite resuscitation and where the mother has received opioid analgesia in labour. An initial intramuscular 200 microgram dose, irrespective of weight, provides a pragmatic delivery room approach suitable for most infants. An IM dose provides steady plasma concentrations for about 24 h.<sup>329</sup> Infants whose breathing is suppressed by opioids may show a rebound tachypnoea after naloxone is given.<sup>330</sup>

## Post-resuscitation care

### Hypo and hyperglycaemia

Perinatal hypoxia interferes with metabolic adaptation and maintenance of cerebral energy supply in several ways. Significantly lower blood glucose levels in the delivery room promote ketogenesis.<sup>324</sup> Hypoglycaemia is common; a quarter of infants with moderate to severe HIE reported to a national cooling registry had a blood glucose less than 2.6 mmol/L.<sup>331</sup>

Animal studies suggest hypoxic cerebral injury is worsened by both hypoglycaemia and hyperglycaemia.<sup>332–334</sup> In human infants with hypoxic ischaemic encephalopathy an abnormal early postnatal glycaemic profile (i.e. hypoglycaemia, hyperglycaemia or labile blood glucose) is associated with distinct patterns of brain injury on MRI compared to normoglycaemia.<sup>324</sup> Hyperglycaemia and a labile blood glucose were also associated with amplitude-integrated electroencephalography evidence of worse global brain function and seizures.<sup>335</sup>

Both hypoglycaemia and hyperglycaemia were associated with poorer neurological outcomes in the CoolCap study<sup>336</sup> and there is a

clear association between initial hypoglycaemia and poorer neurological outcome in infants with perinatal hypoxia.<sup>337,338</sup>

A recent ILCOR review of the evidence on the post resuscitation management of glucose identified no systematic reviews or RCTs specifically addressing the management of blood glucose in the first few hours after birth.<sup>1</sup> 13 non randomised trials or observational studies were identified published since 2015 investigating whether the maintenance of normoglycaemia during or immediately after resuscitation improved outcome.

The update suggests that infants who require significant resuscitation should be monitored and treated to maintain glucose in the normal range. Protocols for blood glucose management should be used that avoid both hypo and hyperglycaemia and also avoid large swings in blood glucose level. The evidence update suggests that research to determine the optimal protocols for glycaemic management for preterm and term infants in the aftermath of resuscitation, and the optimal target range should be a high priority. Overall no change has been made to the previous recommendation that intravenous glucose infusion should be considered soon after resuscitation with the goal of avoiding hypoglycaemia (low certainty evidence).<sup>339</sup>

### Rewarming

If therapeutic hypothermia is not indicated, hypothermia after birth should be corrected because of evidence of poor outcomes.<sup>76,77</sup> Infants should be maintained within the normal range of temperature.

A recent ILCOR evidence review identified no systematic reviews or RCTs published since the previous guidelines.<sup>1</sup> Two retrospective observational studies involving 182<sup>340</sup> and 98<sup>341</sup> patients were identified which investigated whether in hypothermic infants ( $\leq 36^\circ\text{C}$  on admission) rapid or slow rewarming changed outcome. The findings of both studies were that the rate of rewarming (after adjustment for confounders) did not affect the critical and important outcomes. However, one study suggested that rapid rewarming reduces risk for respiratory distress syndrome.<sup>340</sup> The conclusion was that there was no new evidence to alter the 2015 ILCOR consensus that a recommendation for either rapid ( $0.5^\circ\text{C/h}$  or greater) or slow rewarming ( $0.5^\circ\text{C/h}$  or less) of unintentionally hypothermic newborn infants (temperature less than  $36^\circ\text{C}$ ) at hospital admission would be speculative.<sup>274,339,342</sup>

### Induced hypothermia

This topic has not been reviewed as part of the most recent ILCOR process. A Cochrane review including 11 randomised controlled trials comprising 1505 term and late preterm infants calculated that therapeutic hypothermia resulted in a statistically significant and clinically important reduction in the combined outcome of mortality or major neurodevelopmental disability to 18 months of age (typical RR 0.75 (95% CI 0.68–0.83); typical RD  $-0.15$  (95% CI  $-0.20 - 0.10$ )) and concluded that newborn infants at term or near-term with evolving moderate to severe hypoxic-ischaemic encephalopathy should be offered therapeutic hypothermia.<sup>343</sup> Cooling should be initiated and conducted under clearly defined evidence-based protocols with treatment in neonatal intensive care facilities and with the capabilities for multidisciplinary care. Treatment should commence within 6 h of birth, target a temperature between  $33.5^\circ\text{C}$  and  $34.5^\circ\text{C}$ , continue for 72 h after birth and re-warm over at least 4 h. A four way clinical trial of 364 infants randomised to receive longer (120 h) or deeper ( $32^\circ\text{C}$ ) cooling found no evidence of benefit of longer cooling or lower temperatures.<sup>344</sup> Animal data strongly suggests that the effectiveness of cooling is related to early intervention. Hypothermia initiated at 6–24 h after birth may have benefit but there is uncertainty in its

effectiveness.<sup>345</sup> Such therapy is at the discretion of the treating team on an individualised basis. Current evidence is insufficient to recommend routine therapeutic hypothermia for infants with mild encephalopathy.<sup>346</sup>

### Prognostic tools

This subject was not reviewed through the ILCOR process. No systematic or scoping reviews have been identified.

The APGAR score was proposed as a “*simple, common, clear classification or grading of newborn infants*” to be used “*as a basis for discussion and comparison of the results of obstetric practices, types of maternal pain relief and the effects of resuscitation*” (our emphasis).<sup>113</sup> Although widely used in clinical practice and for research purposes, the applicability has been questioned due to large inter- and intra-observer variations. In a retrospective study involving 42 infants between 23 and 40 weeks gestation O'Donnell found a significant discrepancy (average 2.4 points) between observers retrospectively scoring the APGAR from videos of the deliveries compared to the scores applied by those attending the delivery.<sup>347</sup>

A lack of correlation with outcome is partly explained by a lack of agreement on how to score infants receiving medical interventions or being born preterm. Variations in the APGAR score have been proposed attempting to correct for maturity and the interventions undertaken, such as the Specified, Expanded and Combined versions (which incorporates elements of both). These might have greater precision in predicting outcome in preterm and term infants when compared to the conventional score, but are not used widely.<sup>348,349</sup>

### Communication with the parents

The principles governing the need for good communication with parents are derived from clinical consensus and enshrined in published European and UK guidance.<sup>350,351</sup>

Mortality and morbidity for newborns varies according to region, ethnicity and to availability of resources.<sup>352–354</sup> Social science studies indicate that parents wish to be involved in decisions to resuscitate or to discontinue life support in severely compromised infants.<sup>355,356</sup> Local survival and outcome data are important in appropriate counselling of parents. The institutional approach to management (for example at the border of viability) affects the subsequent results in surviving infants.<sup>357</sup>

European guidelines are supportive of family presence during cardiopulmonary resuscitation.<sup>358</sup> Healthcare professionals are increasingly offering family members the opportunity to remain present during resuscitation and this is more likely if this takes place within the delivery room. Parents' wishes to be present during resuscitation should be supported where possible.<sup>1,359,360</sup>

There is insufficient evidence to indicate an interventional effect on patient or family outcome. Being present during the resuscitation of their baby seems to be a positive experience for some parents but concerns about an effect upon performance exist in professionals and family members (weak recommendation very low certainty of evidence).<sup>1,360</sup>

In a single centre review of management of birth at the bedside, parents who were interviewed were supportive but some found witnessing resuscitation difficult.<sup>361</sup> Clinicians involved felt the close proximity improved communication but interviews suggested support and training in dealing with such situations might be required for staff.<sup>362</sup> In a retrospective questionnaire based survey of clinicians' workload during resuscitation the presence of parents appeared to be beneficial in reducing perceived workload.<sup>363</sup>



Qualitative evidence emphasizes the need for support during and after any resuscitation, without which the birth may be a negative experience with post traumatic consequences.<sup>364,365</sup> There should be an opportunity for the parents to reflect, ask questions about details of the resuscitation and be informed about the support services available.<sup>359</sup> It may be helpful to offer any parental witness of a resuscitation the opportunity to discuss what they have seen at a later date.<sup>364,365</sup>

Decisions to discontinue or withhold resuscitation should ideally involve senior paediatric staff.

## Discontinuing or withholding treatment

### Discontinuing resuscitation

Failure to achieve return of spontaneous circulation in newborn infants after 10–20 min of intensive resuscitation is associated with a high risk of mortality and a high risk of severe neurodevelopmental impairment among survivors. There is no evidence that any specific duration of resuscitation universally predicts mortality or severe neurodevelopmental impairment.

When the heart rate has been undetectable for longer than 10 min outcomes are not universally poor.<sup>366–368</sup> For the composite outcome of survival without neurodevelopmental impairment a recent ILCOR systematic review identified low certainty evidence (downgraded for risk of bias and inconsistency) from 13 studies involving 277 infants reporting neurodevelopmental outcomes. Among all 277 infants 69% died before last follow up, 18% survived with moderate to severe neurodevelopmental impairment and 11% were judged to have survived without moderate or severe neurodevelopmental impairment (2% lost to follow up).<sup>1</sup> It can be helpful to consider clinical factors, effectiveness of resuscitation and the views of other members of the clinical team about continuing resuscitation.<sup>369</sup>

If despite provision of all the recommended steps of resuscitation, and excluding reversible causes a newborn infant requires ongoing cardiopulmonary resuscitation for a prolonged period, it would be appropriate to discontinue resuscitative efforts. A reasonable time frame to consider this is around 20 min after birth (weak recommendation, very low certainty evidence).<sup>1</sup>

The decision to cease resuscitation is a clinical decision, but it is important, where possible, to give the family updates during the resuscitation and advance warning that there is a high chance the baby will not survive. In extremely preterm infants, prolonged resuscitation is associated with lower survival rates and higher morbidity, the decision should be individualised.<sup>370,371</sup>

### Withholding resuscitation

In situations where there is extremely high predicted mortality and severe morbidity in surviving infants, withholding resuscitation may be reasonable, particularly when there has been the opportunity for prior discussion with parents.<sup>372–379</sup> Examples from the published literature include: extreme prematurity (gestational age less than 22 weeks and/or birth weight less than 350 g),<sup>380</sup> and anomalies such as anencephaly and bilateral renal agenesis.

Withholding resuscitation and discontinuation of life-sustaining treatment during or following resuscitation are considered by many to be ethically equivalent and clinicians should not be hesitant to withdraw treatment when it would not be in the best interests of the infant.<sup>381</sup>

A consistent and coordinated approach to individual cases by the obstetric and neonatal teams and the parents is an important goal. In conditions where there is low survival (<50%) and a relatively high rate

of morbidity, and where the anticipated burden to the child is high, parental wishes regarding resuscitation should be sought and supported.<sup>351</sup>

## Conflict of interest

CR declares speaker honorarium from Chiesi and funding from the National Institute for Health Research. JM declares occasional advice to Laerdal Medical and Brayden on Newborn Resuscitation Equipment. HE declares research funding for Safer Births project from Laerdal foundation, Governmental, World Bank, Global Financing Facility and Laerdal Global Health. CM declares honorarium from Dräger and Chiesi, and his role of consultant for Fisher and Paykel and Laerdal. TS declares educational funding from GE and Chiesi. CS Research declares funding from Government and ZOLL foundation. ATP is science advisor for CONCORD neonatal; he is patent holder of the Concord resuscitation table. MR declares his role of consultant for surfactant study Chiesi. JW declares NIH grant as co-applicant for “Baby-OSCAR” project.

## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.resuscitation.2021.02.014>.

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