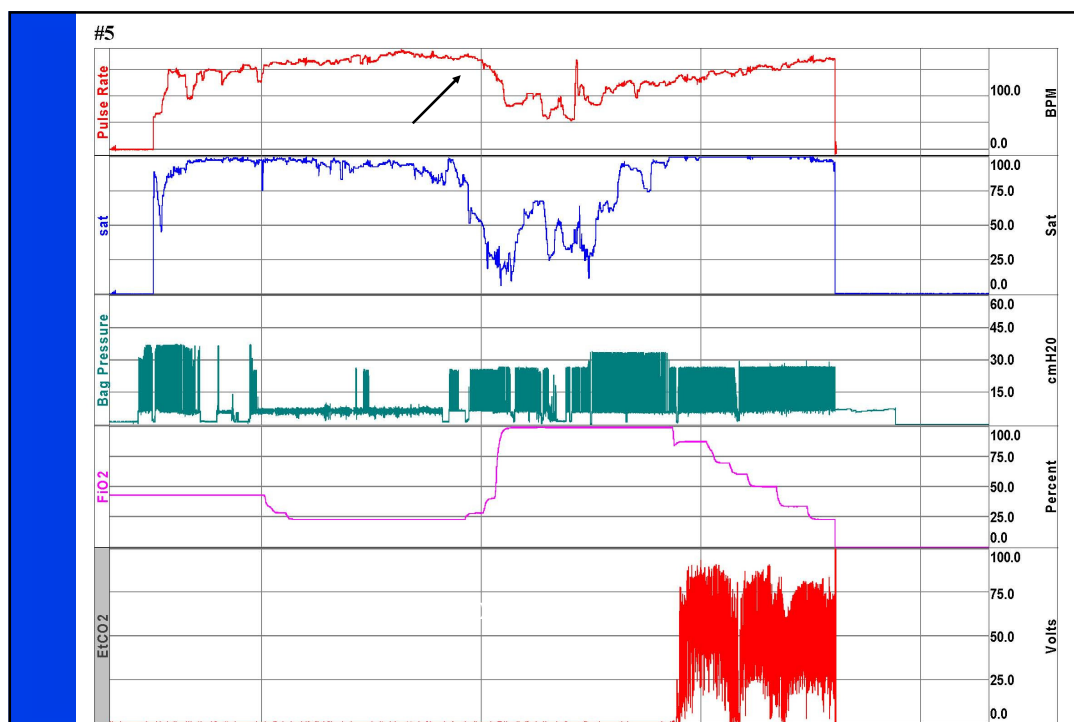


Neonatal Intubation When and How?

**Neil Finer
Professor Emeritus
Division of Neonatology
UCSD School of Medicine**

Invasiveness = Intubation What do we know??

- **Intubation required for mechanical ventilation**
- **Current trend is to use non-invasive ventilation and this is growing**
- **However, many very preterm infants cannot be managed by Non-invasive support alone**
- **Surfactant introduction was associated with a reduction in death and respiratory morbidity (but NOT BPD or NDI)**
- **Currently surfactant requires intubation**



Adverse Events during Bolus Surfactant Administration

- ✗ Oxygen desaturations of 25-50%
- ✗ Reflux of drug up the endotracheal tube
- ✗ Bradycardia (associated with desaturations) or vagal with airway obstruction
- ✗ Fluctuations in cerebral blood flow (decreased)
- ✗ Fall in blood pressure
- ✗ Rise in pCO₂
- ✗ Reduction in cortical EEG voltage – also seen with intubation!!
- ✗ Extubation during manipulation of infant
- ✗ Increased IVH (Gleissner et al J Perinat Med. 2000; 28(2):104-10.)



Intubation and Surfactant Administration (SA) - Effects on EEG

Shangle et al J Peds, 2012 Aug;161(2):252-7

- 18 of 29 (62%) infants had brainwave suppression following SA on EEG (p=0.008).
- EEG suppression seen in 9 infants during endotracheal intubation, all of who received premedication prior to intubation.
- Five infants had EEG suppression during endotracheal suctioning.
- *Is this benign???*

Less Invasive Support What is the Evidence?

- Does avoiding intubation decrease morbidity/mortality?
- Does decreasing exposure to invasive support decrease Morbidity/Mortality?
- Is surfactant given by less/non-invasive routes as effective as that given intratracheally?
- What else can we do to decrease the need for invasive support?

Early DR CPAP and Outcomes

Aly et al Pediatrics. 2005 Jun; 115(6):1660-5.

- **None of the Early CPAP only infants developed intraventricular hemorrhage of grade III or IV or retinopathy of prematurity of stage 3 or 4.**
- **Infants with early CPAP failure had a higher incidence of necrotizing enterocolitis compared with infants intubated in DR (15.6% vs 7.3%; $b = 2.5 \pm 1.2$).**
- **Need to consider CPAP failure criteria carefully**

Intubation in DR

- **Was frequently performed to give prophylactic surfactant**
- **Now this indication is decreasing with use of early CPAP**
- **Especially a problem for the ELBW infant**
- **They are more difficult to intubate and require usually 2-3 attempts**
- **No premedication used in DR**

Intubation and IVH

- We reviewed 100 ELBW infants < 750 gm
- Found that > 3 intubations was associated with severe IVH – almost all in Delivery Room!!
- Need to avoid such frequent attempts and perhaps avoid intubation in the delivery room



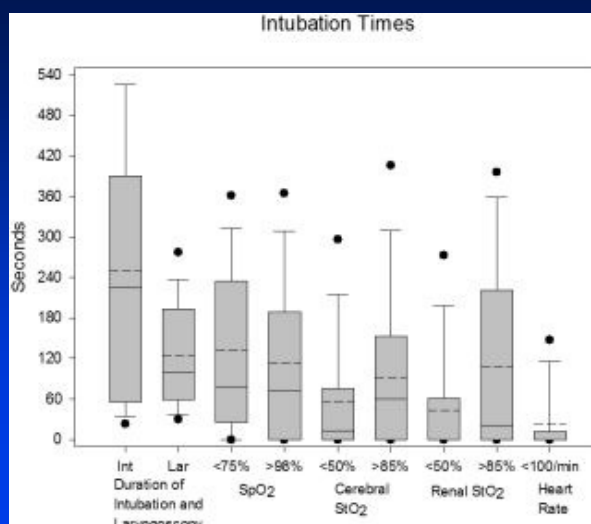
Neonatal Intubation: Physiologic Responses

- All attempts are associated with fall in SaO₂, HR, increase followed by decrease in BP, except in ELBW where BP falls very quickly
- Laryngoscope in mouth triggers responses
- Longer the attempt – worse are effects!!
- All of these can be prevented or reduced with premedication with atropine, a muscle relaxant and a narcotic or anesthetic agent
- Intubation following premedication was faster!!

Kelly, M. A. and Finer, N. J Pediatr. 1984 Aug; 105:303-9.

Physiology of Intubation Schmid et al E-PAS2014:3843.563

Studies 24 infants of 24.6 weeks, 630 gm



Surfactant – Other Routes Avoiding Intubation

- ✓ Pharyngeal route has been tried intrapartum (Kattwinkel et al J Perinatol. 2004 Jun; 24(6):360-5.)
- ✓ Nebulized Surfactant may be an option to avoid intubation (Finer N et al. J Aerosol Med Pulm Deliv. 2010 Oct; 23(5):303-9.)
- ✓ Given via LMA
- ✓ Given via a fine tracheal catheter passed via the larynx
- ✓ One report of giving to fetus via catheter using endoscope!

Surfactant by LMA

Abdel-Latif & Osborne. Cochrane Database Syst Rev. 2011; (7):CD008309.

- ✓ Evidence from a single small trial that LMA surfactant in infants ≥ 1200 g with established RDS may reduce short term oxygen requirements – Not powered for important clinical effects.
- ✓ One current multicenter study and one single center study currently recruiting

(<http://clinicaltrials.gov/ct2/show/NCT01116921?term=LMA+and+surfactant&rank=2> ,
<http://clinicaltrials.gov/ct2/show?term=LMA+and+surfactant&rank=3>)

Surfactant by Fine Catheter

Gopel et al, Lancet. 2011 Nov 5; 378(9803):1627

- ✓ A thin catheter was inserted into the trachea by laryngoscopy if randomized infants needed a fraction of inspired oxygen more than 0.30.
- ✓ First described by Kribs from Cologne in 2007 (Ped Anesth, 2007;17:364)
- ✓ 108 infants were assigned to the intervention group and 112 infants to the standard treatment group
- ✓ Primary was number of infants ventilated at 72 hrs

***Gopel et al, Lancet. 2011 Nov 5;
378(9803):1627***

- ✓ **36 (33%) infants in the Catheter group were mechanically ventilated compared with 82 (73%) in the standard treatment group (number needed to treat 3, 95% CI 2-4, $p < 0.0001$).**
- ✓ **The Catheter group had significantly fewer median days on mechanical ventilation, (0 days. IQR 0-3 vs 2 days, 0-5) and a lower need for oxygen therapy at 28 days (30 infants [30%] vs 49 infants [45%], $p = 0.032$) compared with the standard treatment group.**
- ✓ **No increase in other morbidities or Death**

***Also known as LISA Technique
Klebermass-Schrehof et al Neonatology
2013;103(4):252-8***

- **LISA technique – similar also reported better outcomes compared to historical controls**
- **Caffeine is administered before MIST technique – usually within 15-30 min of birth – Not mentioned in manuscripts!!**
- **Operators are experienced, gentle, infants are swaddled, and was initially used with very high CPAP levels – Benivista valve used in Europe**

MIST Approach

***Dargaville et al., Arch Dis Child Fetal Neonatal
Ed. 2013 Mar; 98(2):F122-6.***

Dargaville et al Neonatology 2012; 101: 326

- ✓ For infants at 25-28 weeks gestation, need for intubation <72 h was diminished after MIST compared with controls (32% vs 68%; OR 0.21, 95% CI 0.083 to 0.55), with a similar trend at 29-32 weeks
- ✓ Infants receiving MIST had a shorter duration of oxygen therapy.
- ✓ Planning Trial to compare MIST to INSURE using angiocatheter #16 - OPTIMIST Trial

Surfactant by Aerosol

Minocchieri et al- E-PAS2013:3500.7

- Compared CPAP to CPAP and 200 mg/kg nebulized surfactant (Curosurf, Chiesi Farmaceuti) using a customized vibrating membrane nebulizer (*eFlow Neonatal Nebulizer System, Pari Pharma GmbH*) in 64 infants. Surfactant (100 mg/kg) was readministered after 12 h if FiO_2 remained > 0.21.
- ✓ 29⁰-33⁶ w GA infants treated with CPAP and nebulized surfactant had a reduced need for intubation in the first 72 h compared to CPAP alone.

Early CPAP and need for Intubation and Ventilation

Yee, et al Paediatr Child Health. 2011 16(10):633.

- ✓ Fourteen studies were reviewed. Eleven studies provided varying degrees of supportive evidence (level of evidence 3 to 4) that the use of primary CPAP can reduce the need for intubation and mechanical ventilation.
- ✓ Avoidance of intubation and mechanical ventilation is more likely in mature infants >27 weeks' gestation.

Does Avoiding Intubation Prevent BPD?

Fischer&Buhrer Pediatrics 2013 Nov;132(5):e1351-60

Schmolzer et al, BMJ 2013 Oct 17;347:f5980.

- ✓ Reviewed 7 trials – 3289 infants
- ✓ Avoiding intubation reduced death or BPD
- ✗ OR = 0.83, (.71 - .96)
- ✓ 4 trials – 2782 infants
- ✓ CPAP alone associated with decreased death or BPD
- ✗ OR= 0.9, (.82 - .98)

At what point should infants on CPAP be intubated for Surfactant?

Dargaville et al Neonatology 2013;104(1):8-14. doi

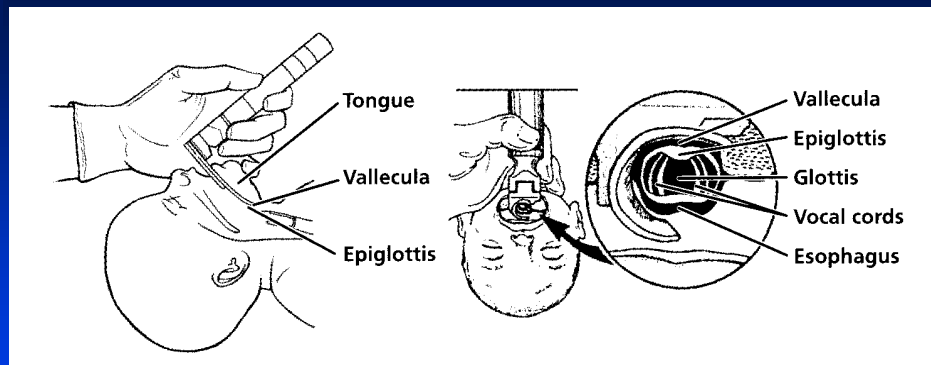
- ✖ CPAP failure was predicted by an $FiO_2 > .3$ in first few hours of life
- ✖ CPAP failure was associated with a higher risk of death or bronchopulmonary dysplasia at 25-28 weeks' gestation (CPAP-F 53% vs. CPAP-S 14%, relative risk 3.8, 95% CI 1.6, 9.3) and a substantially higher risk of pneumothorax at 29-32 weeks.

Intubation in DR

- Often done as emergency when infant cannot be stabilized and for very compromised infants
- Not surprising that intubation is associated with increased risk of IVH
- Aly et al showed that intubation in the DR increased Severe IVH (OR=2.7, CI 1.1-6.6, P=0.03).

Aly et al Brain Dev. 2012 Mar; 34(3):201-5.)

Neonatal Intubation



Intubation of Preterm Neonate

- **Current guidelines suggest use of premedication including paralytic for non-emergent intubations**
- **Our experience has shown that intubations are shorter and more successful when used**
- **However Do Not use in presence of facial dysmorphism, micrognathia, cleft palate etc**
- **Will obliterate spontaneous breathing and will result in fall in ventilation and increase CO₂ unless compensated for**

DR and NICU Intubation of ELBW Infants ***More Difficult - Lane et al J Pediatr 2004; 145:67***

- ✗ DR Intubation success rate-per-attempt was 39% for infants ≤ 28 weeks, and 54% for infants >28 weeks**
- ✗ NICU success rate was 32% for ≤ 28 weeks, and 60% for infants >28 weeks in the NICU**
- ✗ 17% of infants of ≤ 28 weeks were intubated on the first attempt compared with 53% for infants of >28 weeks**

DR Intubation

O'Donnell, C. P.F. et al. Pediatrics 2006;117:e16

- ✗ Deterioration during intubation occurred in 4 of 24 attempts < 30 seconds vs 20 of 27 > 30 seconds**
- ✗ Fall in SpO₂ and HR greater in infants whose SpO₂ $< 70\%$ when intubated**
- ✗ The mean SpO₂ was 70% at intubation**
- ✗ 17/25 (68%) deteriorated if SpO₂ $< 70\%$ vs 8/26 (31%) $> 70\%$**
- ✗ We believe that this is too low and that bag and mask should be given till the SpO₂ $> 85\%$ before attempting intubation**

Intubation for Resuscitation of ELBW Infant

- ✓ **We need to emphasize better stabilization for ELBW infants**
- ✓ **Immediate attempts at intubation before attempts at stabilization are probably inappropriate!**
- ✓ **Early intubation may allow early baro/volutrauma**
- ✓ **Prophylactic surfactant is effective at 15 minutes and early surfactant is also beneficial < 2 hours!**

Physiologic Response to Intubation

**Kelly, M. A. and Finer, N. J *Pediatr.* 1984 Aug;
105:303-9**

- **All attempts are associated with fall in SaO₂, HR, increase followed by decrease in BP, except in ELBW where BP falls very quickly**
- **Laryngoscope in mouth triggers responses**
- **Longer the attempt – worse are effects!!**
- **All of these can be prevented or reduced with premedication with atropine, a muscle relaxant and a narcotic or anesthetic agent**

Premedication- Current Use

Singh et al E-PAS2014:3844.618

Jackson et al, E-PAS2014:2939.545

Chandrasekharan et al E-PAS2014:328

- **Single center review - Used in approx 50%, less by faculty**
- **They did not report improved success with premed and noted increased PaCO₂ with paralysis**
- **Single center review demonstrated decrease ventilation and increase PaCO₂ with paralysis, more with surf**
- **A survey of US NICUs with a 40% response rate reported that**
- **Premedication with analgesics were routinely used for elective intubations in 67% of US NICUs surveyed (40% response rate) compared with 97% of all Level III UK NICUs (100% response rate).**

Premedication and Neonatal Intubation

Kumar et al. Pediatrics. 2010; 125(3):608-615;

AAP Guideline

- **Neonatal Intubation associated with marked physiologic instability**
- **Reviewed medications used**
- **Developed guideline which recommended that for non-emergent intubations premedication including a paralytic is recommended**
- **Still not practiced for majority of intubations**

Canadian Pediatric Society – Fetus and Newborn Committee

Barrington et al, Paediatr Child Health. Mar 2011

- ✓ **Recommend a vagolytic, a rapid acting narcotic, and a rapid acting short duration muscle relaxant**
- ✓ **If the decision is made to intubate using a potent opiate but without muscle relaxation, we recommend that a muscle relaxant be drawn up in the correct dosage and be available for use in case of chest wall rigidity.**

Current Premedication use in Neonates

Durrmeyer et al, Pediatric Crit Care Med. 2013 May;14(4):e169-75.

- **Evaluated use of premedication and whether it followed current recommendations in French Neonatal Units in 2005-2006.**
- **Premedication use prior to neonatal intubation was not systematically used and when used it was most frequently inconsistent with recent recommendations.**

Current Premedication use in Neonates

Wheeler et al, J Paediatr Child Health 2012

Nov;48(11):997-1000

- All tertiary care neonatal units in Australia and New Zealand use premedication for Intubation
- 93% use paralytics
- This is quite different from US units!!

Neonatal Intubation Distributions by Premedication and Location.

Le et al J Perinatology 2014 Jun;34(6):458-60

	LOCATION	INTUBATION ATTEMPTS	SUCCESSFUL ATTEMPTS	SUCCESS RATE (Median %)
No Premedication	DR + NICU	1136	402	22
	DR	916	333	25
	NICU	220	69	25
Premedication Paralysis Subgroup	NICU	1558	669	43 [*]
	NICU	1372	615	45 [*]
TOTAL		2694	1071	36

^{*} p < 0.05 when comparing to no premedication group.

Difficult Neonatal Intubations: Causes

- ✗ Most of these are a result of failing to perform the procedure correctly
- ✗ Commonest errors are:
 - ✗ Lack of good exposure – overextension, improper holding of laryngoscope, prying, not lifting, lack of adequate cricoid pressure, poor vision because of short focal length, wrong blade size or shape – I try to avoid distal curve
 - ✗ Failure to use appropriate premed

Why Does Intubation Fail ?



- The primary reason for intubation failure in tiny infants, and larger babies with abnormal airways, is VISION !
- Vision can be improved
 - Glasses or Loupes – Not well accepted
 - Video – Expensive, large, difficult to use.

Difficult Neonatal Airway The Very Preterm Infant

- Laryngoscopes and blades are too big!!
- These infants have small mouths and it is difficult to get a clear view of the larynx
- When the ETT is inserted there is very little space to see
- Seeing is difficult because the focal distance for these infants is very short
- None of the current videolaryngoscopes have appropriate size and curvature – not useful for < 800gm infant



Difficult Neonatal Airway The Very Preterm Infant

- At age 30, you can clearly see something 13 cm in front of your eye
- By age 50 this has become 40 cm
- When holding a laryngoscope, the blade is 6 cm, and most operators eyes are about 6-10 cm away from proximal end of blade
- Thus if you are > 40, you will have trouble seeing something clearly at < 20 cm

Difficult Neonatal Airway

- We have placed a number of sets of magnifiers (3X) in the DR and NICU
- For me they are life saving
- For most who try them, the airway becomes much easier to recognize
- We now have a videolaryngoscope – Storz with a 19 inch screen



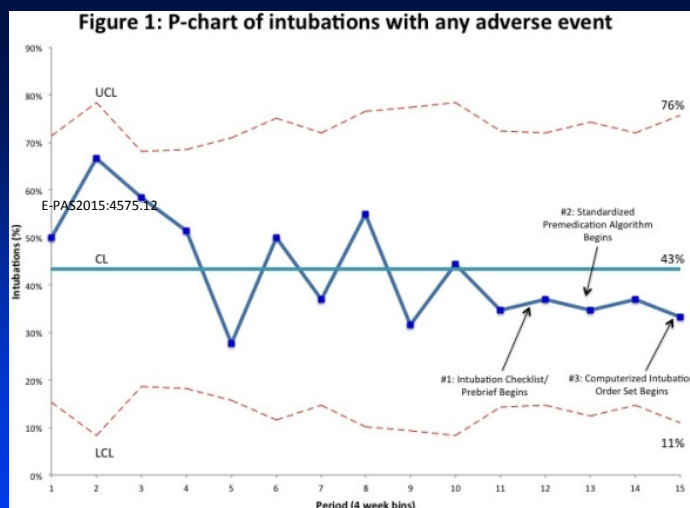
Adverse Events with Neonatal Intubation

Hatch et al PAS – 2015 E-PAS2015:4575.12

- 273 neonatal intubations reviewed
- Reported a severe adverse event rate of 8.8% and a 35% rate of non-severe events which included difficult bag and mask ventilation – 7.3% and esophageal intubation of 21.4%.
- Hypotension was most frequent severe adverse event – 3.7% of intubations.
- Adverse events most frequently associated with emergent intubations following unplanned extubation.

Adverse Events with Neonatal Intubation

Hatch et al PAS – 2015 E-PAS2015:4575.12

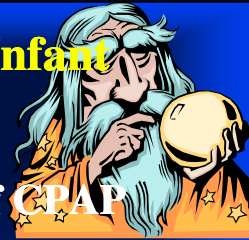


Hypotension with Premedication for Intubation

Tran et al. PAS 2015 EPAS 2015 1574.544
Nishisaki A et al Crit Care Med. 2013;41(3):874-85.

- 2/3 of infants premedicated for intubation developed significant hypotension after premedication, with a fall off $\geq 20\%$ following blade insertion
- Following intubation, an additional 11/31 decreased their MAP 21-51%.
- A large multi-center cohort study of childhood intubations reported that adverse events occurred in 20% of intubations,
- Hypotension receiving intervention was the most common severe event in children, occurring in approximately 3%

Respiratory Support for the ELBW Infant 2014



- ✓ **Whenever possible give infant a trial of CPAP**
- ✓ **Consider early caffeine**
- ✓ **If infant reaches failure criteria – probably ideally FiO_2 consistently $> .35$, consider the least invasive approach for surfactant administration**
- ✓ **Fine catheter/angiocath, brief intubation followed by extubation, aerosol in future if studies support**
- ✓ **Continued support including nutrition, noninvasive ventilation – not yet proven!**