SURFACTANT ADMINISTRATION IN THE NEONATE

by

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SURFACTANT ADMINISTRATION IN THE NEONATE

BEHAVIORAL OBJECTIVES

UPON COMPLETION OF THE READING MATERIAL, THE PRACTITIONER WILL BE ABLE TO:

1. List the proven benefits of surfactant administration.
2. Define the cause of respiratory distress syndrome (RDS).
3. Recall the physiologic functions of surfactant.
4. Explain the difference between prophylactic administration and rescue or therapeutic administration of surfactant.
5. Define the indications for prophylactic administration of surfactant.
6. Define the indications for therapeutic administration of surfactant.
7. State the two clinical indicators of RDS.
8. State the two contraindications for surfactant administration.
9. List the physiologic hazards and complications of surfactant administration.
10. List the procedural hazards and complications of surfactant administration.
11. List the expected outcomes of surfactant administration.
12. Compare and contrast dosing of Survanta and Curosurf.
13. List the steps in preparation for instillation of surfactants.
14. List the steps for surfactant instillation.
15. Outline the required parameters to be monitored before, during and after surfactant administration.
16. Identify one alternative method of surfactant administration.
This course is for reference and education only. Every effort is made to ensure that the clinical principles, procedures and practices are based on current knowledge and state of the art information from acknowledged authorities, texts and journals. This information is not intended as a substitution for a diagnosis or treatment given in consultation with a qualified health care professional.
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PREFACE

Our practice of neonatal care has changed dramatically, in part, due to the creation of exogenous surfactants. When I began practice in 1975, the cause and mechanism of respiratory distress syndrome (RDS), then called hyaline membrane disease (HMD), was still under speculation. The first successful surfactant replacement therapy was reported in 1980. A 1985 respiratory therapy textbook does not even mention the possibility of surfactant replacement in the treatment of RDS. Prevention by means of inhibiting premature labor and administration of glucocorticoids to accelerate lung maturity were the two main foci of treatment for RDS at that time.

Neonatal textbooks in the early 1990’s reflected the new hope of surfactant replacement therapy. The success of this treatment became established as a standard of care for neonates with RDS.

In 1990, the United States Food and Drug Administration (FDA) released colfosceril palmitate for use in preterm infants with RDS. Shortly thereafter, other types of surfactants became available: Exosurf® (synthetic surfactant) and Survanta® (modified natural surfactant). Also available domestically are Curosurf® (natural surfactant) and Infrasurf® (natural surfactant). Administration techniques, adverse effects and benefits have been re-thought since then. Further research has revealed the remarkable value of this therapy. Surfactant therapy has substantially decreased mortality and respiratory morbidity in those infants with respiratory failure secondary to surfactant deficiency.

Additional diseases in which to administer these medications and resolved issues regarding the safety and efficacy of exogenous surfactant are discussed. In 2008, the American Academy of Pediatrics Committee on Fetus and Newborn stated that “Secondary surfactant deficiency also contributes to acute respiratory morbidity in late-preterm and term neonates with meconium aspiration syndrome, pneumonia/sepsis, and perhaps pulmonary hemorrhage. Surfactant replacement may be beneficial for these infants.”

This course is designed to explain the evolution of surfactant replacement therapy and assist in the training of clinicians who administer exogenous surfactant. Instillation of medications into the airway via endotracheal and tracheostomy tubes is a professional responsibility of Respiratory Therapists and other allied health personnel for at least three decades. Beta-2 adrenergic bronchodilators are administered for bronchospasm treatment, N-acetylcysteine as a mucolytic which helps dissolve purulent mucus; lidocaine to decrease laryngospasm and other medications including those used in resuscitation efforts are administered via this route.
INTRODUCTION

Respiratory Distress Syndrome (RDS)

Respiratory Distress Syndrome (RDS), even in 1994, is estimated to be the cause of 30% of neonatal deaths and 70% of all preterm deaths. It was called hyaline membrane disease (HMD) when I began in the profession of Respiratory Care. Many variables contribute to a surfactant deficiency, but prematurity of the pulmonary system seems to be the number one reason for RDS. RDS in itself is another topic.

Long-term implications of RDS include bronchopulmonary dysplasia (BPD). There are five stages of BPD: mild, moderate, severe, chronic, and advanced. Essentially, BPD is to infants what COPD is to adults. The highest incidence of BPD is in infants who suffered from RDS. The treatment for RDS is thought to be the primary cause of BPD. High ventilating pressures, high FIO₂ requirements, presence of patent ductus arteriosus (PDA) and fluid overload are all contributing factors in the development of BPD. Prevention of RDS is avoidance of prematurity. Often times, this is not a controllable factor.
Surfactant Administration in the Neonate

Hypoventilated lungs, “ground glass”, air bronchogram formation at the periphery.
CXR compliments of xrayxredits.com

Exogenous Surfactants in Respiratory Distress Syndrome

Infants at risk for RDS demonstrate improved clinical outcomes when natural surfactant extract is intratracheally administered prophylactically. The groups of infants that are the focus of this Meta-analysis (Meta-analysis refers to the analysis of analyses...the statistical analysis of a large collection of analysis results from individual studies for the purpose of integrating the findings) are intubated infants of less than 30 weeks of gestation age. Prophylactic
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administration of natural surfactant has proven to:

1. Decrease the risk of air leak syndromes such as pneumothorax and pulmonary infiltrate with eosinophilia (PIE).

2. Decrease in the incidence of infant mortality.

3. Decrease the risk of bronchopulmonary dysplasia (BPD).

4. Decrease death.

5. Improve oxygenation as demonstrated by improved alveolar-arterial oxygen difference, arterial/alveolar oxygen ratio and decreased FIO₂ requirements.

6. Improve ventilation as demonstrated by decreased mean airway pressures (MAP) and improved ventilator efficiency index.

7. Incidence of infants surviving to go home is significantly higher with prophylactic administration than with rescue-therapy administration.

Meconium Aspiration Syndrome (MAS)

Meconium Aspiration Syndrome CXR
Compliments of Virtual Children’s Hospital of Iowa
Meconium aspiration syndrome is due to fetal asphyxia that mostly affects the term or post-term neonate, with post term infants at higher risk. The theory is that a period of fetal asphyxia causes the fetal anal sphincter to relax and causes increased peristalsis of the fetal intestine. Due to this relaxation, fecal matter is released into the amniotic fluid. The fetus gasps and aspirates in response to the asphyxiating episode. The meconium laced amniotic fluid is now in the trachea and possibly the lower airways. There are subsequent consequences of this aspiration such as a chemical pneumonitis and hypoxia/hypercarbia due to V/Q mismatching.

Vasospasm of the pulmonary vasculature in response to the outlined situation leads to persistent pulmonary hypertension (PPH). In other words, fetal circulation continues, bypassing the lungs, which leads to a worsening clinical and outcome picture; persistent fetal circulation (PFC). Bilateral infiltrates and air trapping predisposes the lung to air leak syndromes and are additional causes of pulmonary hypertension.
Exogenous Surfactants in Meconium Aspiration Syndrome

Meta-analysis has additionally proven that administration of exogenous surfactant is of benefit to infants with meconium aspiration syndrome (MAS). One study demonstrated that multiple doses of surfactant decreases the number of neonates treated with extra corporeal membrane oxygenation (ECMO). In the study, infants a/A oxygen ratio improved which decreased the need for ventilatory support, therefore allowing these infants to avoid ECMO. One study demonstrated a reduction in hospital stay for those infants given surfactants to treat MAS. The Canadian Pediatric Society recommends a “Grade A” (highest level) recommendation for surfactant administration for intubated infants with meconium aspiration syndrome requiring more than 50% O₂.

HISTORY

In the 1960s, researchers tried to aerosolize dipalmitoylphosphatidylcholine (DPPC) to neonates with respiratory distress syndrome (RDS). No beneficial effect could be demonstrated with this method of administration. Dr. Enhorning and coworkers were able to demonstrate the first successful animal model of surfactant replacement therapy in 1972. They administered a natural surfactant extract from lavaging the lungs of mature rabbits directly into the trachea of immature rabbits. Alveolar expansion and improvement in lung compliance was noted. After this breakthrough, clinical trials in the neonate began.
A variety of surfactant products have been manufactured, both synthetic and natural. The initial synthetic surfactant used on neonates was Exosurf®. Curosurf® and Survanta® are natural surfactants.

As research continues, biochemical engineering has discovered four proteins in surfactant, SP-A, SP-B, SP-C and SP-D. It has been found that one of these proteins, SP-B, when recombined with appropriate phospholipids, is best at sustaining surfactant activity. It also appears that SP-C is significant in effective surfactant function. SP-B binds to DPPC, prevents its’ collapse into little liposomal balls and allows it to work up to fifty hours.

SP-A may be a determinant for the predisposition of the neonate to RDS. SP-D may be responsible in the control of infection.

Lysine (K) and hydrophobic leucine (L) formulated into a peptide surfactant (KL4) has shown to increase pulmonary function in animals to normal range within 12 hours. Lavage with KL4 removed part of the inflammatory exudates and re-expanded the alveoli in MAS patients. Research is continuing throughout research centers in the United States.

University of California at San Francisco researchers holds a patent on the use of nonionic hydrophilic polymers or carbohydrates to reduce surfactant inactivation in pulmonary surfactant therapy. Studies have shown that up to 30% of infants given exogenous surfactant do not respond to treatment. The reason for this is thought to be inactivation of the surfactant. Inactivation of surfactant may be a key factor in the etiology of ARDS. These investigators have discovered that the inactivation of surfactants can be significantly reduced by administration of nonionic hydrophilic polymers or carbohydrates. Conditions that, according to the researchers, could benefit greatly from the administration of surfactant plus these polymers or carbohydrates or from the polymers and carbohydrates alone include IRDS, meconium aspiration pneumonia, ARDS, cystic fibrosis, severe asthma, bronchiectasis and pneumonia.

**NATURAL SURFACTANT**

By far, one of the biggest challenges that face the premature infant is lack of natural surfactant. A deficiency or dysfunction of pulmonary surfactant causes RDS. Not only is the lack of surfactant an issue in the premature neonate, but also the overall immaturity of all organ systems contributes to the development of RDS. Surfactant production is easily disrupted by hypoxemia, hypothermia and acidosis in the premature infant, but fairly stable in infant of at least 35 weeks gestation.
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Surface Tension

Surface tension is the force acting on the surface of a liquid, tending to minimize the area of the surface. Quantitatively, it is the force that appears to act across a line of unit length on the surface. Surface tension is also known as interfacial force; interfacial tension; surface tensity.

Surfactants act to reduce the surface tension of a liquid. The surface tension of water is 72 dyne/cm; a surfactant can reduce this to a value in the range of 30-50 dyne/cm.

Composition of Pulmonary Surfactant

Pulmonary surfactant first appears at the same time as the development of Type II pneumocytes. Pulmonary surfactant is predominantly dipalmitoylphosphatidylcholine (DPPC), or phosphatidylcholine, PC, which is also called lecithin, with lesser amounts of other phospholipids (sphingomyelin) including phosphatidylglycerol (PG), phosphatidylethanolamine and phosphatidylinositol. Pulmonary surfactant also contains neutral lipids and distinct surfactant proteins. The proteins critical to surfactant composition have been named SP-A, SP-B, SP-C and SP-D. Further research has shown us that the proteins act as a first-line defense against invading microorganisms and play a role in allergic diseases such as asthma by binding with aeroallergens. After production, pulmonary surfactant is stored in the lamellar inclusion bodies of the cell. It has a half-life of about ten hours.

Surfactant Production and Lung Maturity

Surfactant production may begin as early as week 20, during the canalicular, third stage, of lung development. The canalicular period is week 17 through 26, when the terminal and respiratory bronchioles multiply and the alveoli start to form. The Type I and Type II alveolar cells (pneumocytes) are differentiated. Type I becoming the alveolar capillary membrane, Type II evolve into surfactant producing cells. Note that when Type II cells are damaged, they divide into Type I cells. It is not sufficient for pulmonary surfactant to be present in order to have viable lung tissue. The capillaries have to be close enough to the alveoli to provide gas exchange.
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via the a-c membrane. It is thought that although the capillaries are present at weeks 20 to 21, they are not close enough to participate in gas exchange with the alveoli until weeks 24-25. True alveoli are formed during the fourth and fifth stages of lung development in the 32 to 34 week range. It is during this period that the alveolar Type II cells produce mature surfactant.

The initial surfactant is said to be present at 22 weeks. It isn’t until around the 35 week that mature surfactant is present. This is also when phosphatidylglycerol (PG) appears. The level of sphingomyelin stays fairly constant throughout gestation. Comparison of the amount of lecithin to sphingomyelin is called the L/S ratio and is one way to determine fetal lung maturity.

A lecithin to sphingomyelin ratio (L/S ratio) of 2:1 occurs near 35 weeks gestation and most likely coincides with production of mature surfactant.

Another indicator of the presence of mature surfactant is the amount of PG in the amniotic fluid. If PG is present, it indicates that the lung probably possesses mature surfactant.

The combination of the L/S ratio and the presence of PG in the amniotic fluid are called the lung profile and using this as a predictor of lung maturity is more accurate than using just the L/S ratio or the presence of PG alone.

Research has developed other methods for determination of lung maturity, but the lung profile, at present, is the most widely used and accepted.

Physiologic Functions of Surfactant

1. Lowers surface tension
2. Ability to rapidly absorb, spread and reform a monolayer in the dynamic conditions associated with the respiratory cycle
3. Enhances capillary circulation, normalizing ventilation/perfusion ratios
4. Protection of the alveolar tissues against barotraumas
5. Aids in the evacuation and regulation of lung fluids
6. Improves bronchial clearance
7. Acts as a barrier to inhaled agents
8. Stabilizes the conducting airways
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INDICATIONS FOR SURFACTANT REPLACEMENT

Prophylactic administration is defined as surfactant given down the ETT prior to the first breath or immediately after delivery room intubation and stabilization.

Rescue or therapeutic surfactant administration is given after the initiation of mechanical ventilation in infants with clinically confirmed RDS.

Prophylactic Indications for Respiratory Distress Syndrome (RDS):

1. Infants at risk of developing RDS due to prematurity-related surfactant deficiency. This may be defined as due to short gestation (less than 27 weeks). Treatment should be accomplished as soon after delivery as possible, following intubation and clinical ascertainment of proper ETT placement.

2. Infants ≥ 27 weeks and < 30 weeks gestation should receive surfactant without delay if they require intubation and supplemental oxygen for respiratory failure.

3. Infants ≥ 30 weeks gestation should receive surfactant therapy if they require mechanical ventilation and have a diagnosis of RDS.

4. Infants who have laboratory evidence of surfactant deficiency such as: a lecithin/sphingomyelin (L/S) ratio less than 2:1, bubble stability test which indicates lung immaturity or the absence of phosphatidylglycerol (PG).

Guidelines for Additional Doses in Respiratory Distress Syndrome (RDS):

1. Infants who are < 30 weeks gestation with the diagnosis of RDS should be administered a bolus 6-12 hours after the first dose if they continue intubated on mechanical ventilation, regardless of the inspired oxygen concentration.

2. Infants who are ≥ 30 weeks gestation with the diagnosis of RDS should receive a second dose of surfactant as a bolus 6-12 hours after the first dose if they continue intubated on mechanical ventilation and require > 30% inspired oxygen. If the infant remains intubated with an inspired oxygen concentration between 21-29%, a second dose of surfactant may be considered.

3. Preterm infants with RDS and worsening oxygenation 6-12 hours after the second dose of surfactant may be considered for additional dosing. (A total of 4 doses maximum is recommended.)
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Rescue or Therapeutic Indications:

Infants who require intubation and mechanical ventilation due to:

1. Increased work of breathing as demonstrated by increased respiratory rate, substernal and suprasternal retractions, grunting and nasal flaring

2. Increasing FIO₂ requirements as noted by pale or cyanotic skin color, agitation, and decreases in PaO₂, SpO₂, SaO₂ or TCO₂

And

3. Have clinical evidence of RDS including:
   - CXR characteristic of RDS
   - MAP greater than 7 cmH₂O to maintain adequate oxygenation

Other specific indications:

1. Primary pulmonary hypertension
2. Meconium aspiration syndrome
3. Neonate with RDS and with an a/A ratio of less than 0.22

\[ \text{a/A} = \frac{\text{PaO₂}}{\text{FIO₂ (713) – PaCO₂}} \]

CONTRAINdications

1. Presence of congenital anomalies incompatible with life beyond the neonatal period
2. Respiratory distress in neonates with laboratory evidence of lung maturity

HAZARDS AND COMPLICATIONS

Physiologic:

- Apnea
- Mucus plugs
- Barotrauma resulting from increase in lung compliance following surfactant replacement and failure to change ventilator settings accordingly.
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Procedural:

- Plugging of ETT by surfactant
- Hemoglobin desaturation and increased need for supplemental oxygen
- Bradycardia due to hypoxia
- Tachycardia due to agitation with reflux of surfactant into the ETT
- Pharyngeal deposition of surfactant
- Administration of surfactant to only one lung
- Administration of suboptimal dose secondary to miscalculation

ADDRESSING CONCERNS OF THE PAST

Meta-analyses concluded that with prophylactic administration of natural surfactant does not influence the risk one way or the other of:

1. Patent ductus arteriosus (PDA)
2. Intraventricular hemorrhage (IVH)
3. Severe (Grade III oar IV) intraventricular hemorrhage
4. Retinopathy of prematurity (ROP)

Raju reported in 1993 that there was a small increase in pulmonary hemorrhage associated with the use of surfactants. It is thought that this complication may be in fact, hemorrhagic pulmonary edema secondary to massive ductal shunting.

Treating the PDA and appropriate ventilatory management may prevent pulmonary hemorrhage.

No other side effects of surfactant administration have been reported.

LIMITATIONS OF METHOD

If surfactants are administered pre-confirmation of ETT placement by definitive measures (CXR), such as in the delivery or C-section room, the result may be inadvertent administration to only one lung or to the stomach. Administration of surfactants should not delay stabilization of the neonate. Suctioning via the ETT should be held for one to two hours after administration of the surfactant.
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EXPECTED OUTCOMES

1. Decreased FIO₂ requirements
2. Decreased work of breathing (WOB)
3. Increased lung volumes as noted by CXR
4. Improvement in CXR overall-clearer lung fields
5. Improved compliance, airway resistance, tidal volume, minute ventilation and FRC
6. Decreased mechanical ventilation requirements such as PIP, PEEP and MAP
7. Improved arterial/alveolar PO₂ (a/A PO₂)

Photo compliments of Ross Laboratories.

PRACTICAL APPLICATION

COMMON INITIAL CLINICAL QUESTIONS

Who/Where are surfactants administered?

Surfactants are administered by neonatologists and trained respiratory therapists:

1. During transport situations
2. In the delivery or C-section rooms
3. In the neonatal intensive care unit (NICU)
How are surfactants handled and stored?

Both Curosurf® and Survanta® should be stored in a refrigerator at 36-46° F. Before use, the vial should be slowly warmed to room temperature and gently turned upside-down, in order to obtain a uniform suspension. **DO NOT SHAKE**.

Unopened, unused vials of Curosurf® or Survanta® that have been warmed to room temperature can be returned to refrigerated storage within 24 hours for future use. **Do not warm to room temperature and return to refrigerated storage more than once.** Protect the vials from light. Each single-use vial should be entered only once and the vial with any unused material should be discarded after the initial entry.

What are the different types and brands of exogenous surfactants?

There are several brands of exogenous surfactants to choose from. Desired qualities of exogenous surfactant include: SP-B-High surfactant apoprotein B content and excellent surface activity.

Although there are several choices for the Neonatologist, past studies have proven that modified bovine surfactant extract results in better outcomes for the infant with RDS than do synthetic surfactants.

However, two recently completed trials comparing protein containing synthetic surfactants to animal derived surfactant extract, showed there was no statistically different clinical differences in death and chronic lung disease between the two. Clinical outcomes between the two groups were similar.

- **Exosurf®** (colfosceril palmitate) is a fully synthetic surfactant preparation, which lacks the hydrophobic apoproteins that are in natural surfactants. It is manufactured by Glaxo Wellcome and initially approved by the FDA in 1990. Colfosceril palmitate is also known as DPPC. This surfactant also contains cetyl alcohol as a spreading agent, Tyloxapol, to disperse the DPPC and cetyl alcohol and sodium chloride is added to adjust osmolality. Ingredients include 85% DPPC, 9% hexadecanol, and 6% tyloxapol.

- **Bovine Lipid Extract Surfactant (bLES)** is a natural surfactant consisting of bovine surfactant lipids and proteins extracted from calf lung lavage. The manufacturer is bLES Biochemicals. Its’ composition is 75% PC, 1% SP-B and SP-C.

- **Alveofact®** - a bovine surfactant preparation composed of 99% PL, 1% SP-B and SP-C.

- **Infrasurf®** - calf lung surfactant extract containing DPPC, tripalmitin, SP-B 290 g/ml, and SP-C 360 g/ml.

- **Calf Lung Surfactant Extract (CLSE)** - similar to Infrasurf®.
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- **Venticute®** - a surfactant preparation based on recombinant rSP-C formulated by Nycomed was granted “Fast Track” designation by the FDA for reduction of mortality in patients with severe acute pneumonia or gastric aspiration leading to intubation, mechanical ventilation and severe oxygenation impairment in 2007. There is a multi-national clinical trial in process. This product is now targeted for the non-neonatal patient group also.

- **Lucinactant (Surfaxin KL₄)** - surfactant that contains KL₄, which is a synthetic peptide, which mimics SP-B and DPPC. Discovery Labs announced FDA acceptance of Surfaxin in 2004 and in 2005, the FDA approved it for treatment of BPD.

- **Curosurf® (poractant alfa)**

  ![](image.compliments)

  Picture compliments of Dey Laboratories

Curosurf® is available in two vial sizes, 1.5 and 3.0 ml. The initial dose for Curosurf® is 200 mg (2.5 ml)/kg; subsequent doses 100 mg (1.25 ml)/kg. It is composed of minced pig lung and contains DPPC, SP-B and SP-C (unknown amount).

<table>
<thead>
<tr>
<th>Neonate Weight in Grams</th>
<th>Curosurf® Initial Dose</th>
<th>Curosurf® Subsequent Dose</th>
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<tbody>
<tr>
<td>700</td>
<td>1.8 ml</td>
<td>0.9 ml</td>
</tr>
<tr>
<td>900</td>
<td>2.3 ml</td>
<td>1.1 ml</td>
</tr>
<tr>
<td>1100</td>
<td>2.8 ml</td>
<td>1.4 ml</td>
</tr>
<tr>
<td>1300</td>
<td>3.3 ml</td>
<td>1.6 ml</td>
</tr>
<tr>
<td>1500</td>
<td>3.8 ml</td>
<td>1.9 ml</td>
</tr>
<tr>
<td>1700</td>
<td>4.3 ml</td>
<td>2.1 ml</td>
</tr>
<tr>
<td>1900</td>
<td>4.8 ml</td>
<td>2.4 ml</td>
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Up to 2 subsequent doses of 1.25 ml/kg birth weight can be administered at 12-hour intervals if indicated.
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The indications for subsequent dosing of Curosurf® are, neonates who remain intubated and require mechanical ventilation and supplemental oxygen.

- Survanta® (beractant) and Survanta® TA

Survanta is a bovine surfactant preparation containing both SP-B and SP-C proteins. The composition is DPPC, tripalmitin, SP-B <0.5%, SP-C 99% of TP wt/wt. It is deemed a modified natural surfactant. This exogenous surfactant is manufactured by mincing the lungs of adult cows; removing all contaminants and then adding back DPPC, surface-active agents and spreading agents. Survanta® is available in 4 and 8 ml. vials. The dose is 100 mg/kg or 4 ml/kg. based on the neonate’s birth weight. Survanta® is manufactured by Ross Products Division, Abbott Laboratories Inc.

PRACTICAL APPLICATION

Preparation for instillation of surfactants

1. Verify physician’s order for administration of surfactant
2. Review the infant’s clinical record
3. Wash hands
4. Gather necessary equipment
   - Surfactant (Survanta® or Curosurf®)
   - Alcohol prep pad
   - 10 cc luer lock syringe with a 20 gauge needle
SURFACTANT ADMINISTRATION IN THE NEONATE

- 5 French end-hole catheter (feeding tube)
- Sterile gloves
- Sterile suture removal kit

Administration of surfactant will be initiated upon the written or telephone order from a neonatologist. The order for administration of surfactant will be written in the order section of the infant’s clinical record. Survanta® or Curosurf® will be administered in accordance with manufacturer’s recommendations and the following procedure.

Steps for surfactant instillation

1. Determine the total dose of surfactant being used.

2. Preparation of the feeding tube is done with sterile technique.

3. Slowly withdraw the entire contents of the vial into a sterile plastic syringe through a large gauge needle (at least 20 gauge). **DO NOT FILTER SURFACANT AND AVOID SHAKING.**

4. Attach the pre-measured and cut (at 8 cm) 5 French end-hole catheter to the syringe. Fill the catheter with surfactant. Expel excess surfactant through the catheter so the total dose to be given remains in the syringe.

5. Before administering surfactant, assure proper placement and patency of the ETT and perform a clinical assessment of the infant. At the discretion of the clinician, the ETT be suctioned before administration of surfactants. Stabilize the neonate before proceeding with dosing.

6. Ventilation prior to dosing should be provided by mechanical ventilation or rarely manual ventilation with bag to ETT. To lessen the risk of experiencing hypoxia during instillation, that the ventilator settings be changed to 60 breaths/minute, inspiratory time 0.5 seconds and FIO₂ of 1.0 during initial dose (unless rescue immediately post birth). Sufficient PIP should be used to provide adequate gas exchange and chest wall movement.

   Ventilator settings recommended during subsequent dosing include increasing FIO₂ by 0.20 or an amount sufficient to prevent hypoxia and rate adjusted to 30 breaths/minute with an inspiratory time less than 1.0 second. If the infant’s pretreatment rate is 30 or greater; rate should not be lessened for the purpose of surfactant administration.

   Manual ventilation **should not be** used to administer repeat doses of surfactants. During the dosing procedure, ventilator settings may be adjusted at the discretion of the clinician to maintain appropriate oxygenation and ventilation.
After completion of the dosing procedure, resume usual ventilator management and clinical care.

7. Each Survanta® or Curosurf® dose should be administered in two aliquots, with each aliquot administered into one of the two main stem bronchi by positioning the neonate with either the right or left side dependent.

At this writing (2008), there is actually no evidence that supports the need to place the infant in multiple positions during administration of surfactant. There is also no evidence that suggests that a bolus or slow infusion is more effective than the other.

The tip of the 5 F feeding tube should be inserted into the infant’s ETT with the tip positioned distally in the ETT. The catheter tip should not extend beyond the distal tip of the ETT.

The neonate is disconnected from assisted ventilation for each half dose so that the surfactant-filled catheter can be passed to the end of the ETT for direct tracheal instillation. Each half-dose is instilled over 2 to 3 seconds.

The neonate is ventilated for a minimum of 30 seconds or until stable between each half dose.

8. During dosing patient position, vigor, heart rate, chest expansion/movement, skin color, SpO₂, TCOM if applicable, ETT patency /position and placement and position of delivery device should be monitored.

If heart rate slows, the infant becomes dusky or agitated, TCO₂ falls more than 15% or surfactant backs up in the ETT, dosing should be slowed or halted and, if necessary, the PIP, ventilator rate, and/or FIO₂ increased.

In the event of any severe adverse reactions, discontinue treatment immediately and notify the physician. Remain at the bedside and provide appropriate support until the neonate is stable or another respiratory therapist or the neonatologist relieves you. The clinician should be aware that rapid improvements in lung function might require immediate reductions in FIO₂ and/or PIP and ventilator rate.
MONITORING DURING ADMINISTRATION OF SURFACTANT

<table>
<thead>
<tr>
<th>TIME</th>
<th>FIO₂ AND VENTILATOR SETTINGS</th>
<th>HR</th>
<th>SpO₂</th>
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Monitoring after surfactant administration

The infant should be closely monitored for 30 minutes after the procedure. It is suggested that ABG’s be drawn approximately one hour post administration of surfactant. Arterial blood gases, chest radiograph, ventilator setting requirements, pulmonary mechanics/volumes, heart rate, chest movement, skin color, vigor, breath sounds and blood pressure should be monitored after dosing with surfactant.

1. Suctioning should not be performed for a minimum of one hour after surfactant is administered except when dictated by clinical necessity. Rales and moist breath sounds may occur transiently and are not an indication that the infant needs to be suctioned. Infants, whose ventilation becomes markedly impaired during or shortly after dosing, may have mucus plugging in the endotracheal tube, particularly if pulmonary secretions were prominent prior to drug administration.

2. Additional doses of surfactant may be given at six to twenty-four hour intervals if indicated for persistent or recurrent O₂ requirement of 30% or more as early as 2 hours after initial dose,
or more commonly, 4-6 hours in neonates who demonstrate increased ventilator requirements or in those who fail to improve after initial dose.

Alternative methods of administration

An ETT with a connector that has a side port may also be used for the administration of surfactants. These are particularly helpful in the case of micro-preemies or when delivering surfactant right after birth in the delivery or C-section rooms.

Survanta® literature recommends a quarter-dose to each lung quadrant and suggests specific positions for administration to these four areas during surfactant administration.

BARRIERS TO SURFACTANT EFFICACY

1. Albumin inactivates pulmonary surfactant
2. Fibrinogen inactivates pulmonary surfactant
3. Inhalation of cool air disrupts pulmonary surfactant
4. Leaking of plasma proteins

DOCUMENTATION

Documentation will include monitoring variables pre, during and post surfactant administration. The therapist will also document the type of surfactant used, the dose and lot number of medication.

INFECTION CONTROL

Standard precautions should be followed at all times. Aseptic technique is to be practiced during performance of this procedure. If any other CDC transmission-based guideline exists, the CDC precautions must be followed.
**SURFACTANT ADMINISTRATION CLINICAL COMPETENCY**

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- Verifies physician order.
- Reviews neonate's clinical record for possible contraindications and the indications for administration.
- Calculates the dosage required of the surfactant ordered.
- Obtains surfactant from pharmacy.
- Prepares the surfactant by warming to room temperature and gently turning to obtain a uniform suspension.
- Washes hands.
- Assure proper placement of the neonate’s ETT by viewing most recent CXR.
- Assure patency of ETT. Suction if indicated and stabilize.
- Perform a clinical assessment of the neonate.
- Gathers equipment/supplies:
  - Alcohol prep pad
  - 10 cc luer lock syringe with a 20 gauge needle
  - 5 French end-hole catheter (feeding tube)
  - Sterile gloves
  - Sterile suture removal kit
- Uses sterile technique during preparation and instillation process.
- Pre-measure and cut the 5 French end-hole catheter.
- Slowly withdraws the entire contents of the surfactant vial into a sterile plastic syringe through the large gauge needle. Does not filter or shake surfactant. Place on sterile field.
- Attaches the pre-measured and cut 5 French end-hole catheter to the syringe.
- Fills the catheter with surfactant. Expels the excess surfactant through the catheter so the total dose to be given remains in the syringe.
- Divides ml. by one-half to obtain the amount required for each aliquot.
- Set-up monitoring documentation.
- Changes ventilator settings as recommended.
- When neonate is disconnected from assisted ventilation, inserts the tip of the 5 French feeding
**SURFACTANT ADMINISTRATION IN THE NEONATE**

- tube into the neonate’s ETT with the tip positioned distally in the ETT. Ensures that the catheter tip does not extend beyond the distal tip of the ETT.
- Administers one-half of total dose over a 2-3 second period with neonate turned on its’ left side.
- Assisted ventilation is resumed for a minimum of 30 seconds or until stable.
- Administers the last half of total dose over a 2-3 second period with the neonate on its’ right side.
- Resume assisted ventilation.
- During dosing, monitors the neonate’s position, vigor, heart rate, color, chest expansion/movement, skin color, SpO₂, TCOM if applicable, ETT patency/position and placement and position of delivery device.
- In the event of a severe adverse reaction, discontinues surfactant administration and notifies the neonatologist.
- Remains at bedside, monitoring patient and weaning ventilator settings for a minimum of 30 minutes.
- Obtains blood gas one-hour post surfactant administration.
- Does not suction via the ETT for a minimum of one-hour post surfactant administration unless ventilation becomes markedly impaired.
- Documents administration, monitoring values pre-, during and post instillation, the type of surfactant given, the dose and lot number of medication.

**Preceptor signature**

**Therapist signature**

**CLINICAL PRACTICE EXERCISE**

You are called to L & D (labor and delivery) for the birth of a 28-week-old infant. The mother has been having premature contractions unresponsive to tocolytic drugs. Tocolytics such as terbutaline, help slow and hopefully, stop, contractions. The infant is delivered spontaneously, vaginally. You perform initial routine NRP (Neonatal Resuscitation) protocol without incident. After initial stabilization and intubation, the neonatologist requests that you administer exogenous surfactant. The infant weighs 700 gms. Your facility uses Survanta®.
SURFACTANT ADMINISTRATION IN THE NEONATE

What would be your initial step in preparation for administration of surfactant?

Your next step would be to:

While preparing the surfactant, what steps would you take to avoid complications and hazards during administration?

How would you prepare the Survanta® for administration?

Now that you are ready to instill the surfactant, you would now obtain baseline vitals. What would these measurements be?

Which measurements would you or an assistant continue to take during administration of the surfactant?

You are now instilling the surfactant. How would the infant be positioned?

During administration, the infant’s cardiac rate changes from 160-beats/min. to 100 beats/min. What would be your response to this change in vitals?

Now that the instillation of the surfactant is complete, what is the last remaining, essential part of the procedure?
SURFACTANT ADMINISTRATION IN THE NEONATE

SUMMARY

Prematurity of the pulmonary system is the number one cause of respiratory distress syndrome (RDS) in the neonate. The long-term implication of RDS is bronchopulmonary dysplasia (BPD) in the infant, which is similar to COPD in the adult. The best prevention of RDS is to prevent prematurity. Sometime, as we all know, that is not possible. If we are presented with a premature infant, with premature lungs, surfactant administration has been demonstrated to improve clinical outcome.

Prophylactic administration of surfactant has proven to decrease the risk of air leak syndromes, incidence of infant mortality, risk of BPD and death. It is also proven to improve oxygenation, ventilation and incidence of survival.

Infants with meconium aspiratory syndrome (MAS) (RDS Type II) may also benefit from the administration of surfactant.

Research beginning in the 1960’s led to clinical trials in 1972 and subsequently to the exogenous surfactants available to us today. There are both synthetic and natural surfactants available.

Initial surfactant is present at 22 weeks gestation, but it isn’t until about the 35th week, that mature surfactant is present. It is this mature surfactant that contains the appropriate composition to keep the infant’s alveoli expanded. Surfactant lowers surface tension, enhances capillary circulation, normalizing ventilation to perfusion ratios, protects the alveolar tissues against barotraumas, aids in the evacuation and regulation of lung fluids, improves bronchial clearance, acts as a barrier to inhaled agents, stabilizes the conducting airways and provides some immunomodulatory functions. It has the ability to rapidly absorb, spread and reform a monolayer thereby responding to dynamic changes in the respiratory cycle.

Prophylactic and therapeutic administration has separate definitions and indications. Contraindications for the administration of surfactant are twofold; congenital anomalies incompatible with life and no laboratory evidence of lung immaturity. Hazards and complications are physiologic such as apnea, mucus plugs and barotrauma and procedural.

After administration of surfactant, the clinician may expect to see decreased FIO2 requirements, work of breathing and mechanical ventilation requirements. The lung volumes, CXR, compliance, airway resistance, tidal volume minute volume, minute ventilation, functional residual capacity and a/A PO2 are expected to improve.

There are several brands of exogenous surfactants with different dosing procedures and amounts. Many are to be refrigerated and warmed just prior to instillation. Most are not to be shaken. You don’t want to waste any of those bubbles! Each facility, neonatologist and clinician may have his or her administration procedure preference. What is given here is a suggestion, a guideline (if you will) taking into consideration manufacturer’s recommendations for your perusal and adaptation.
SURFACTANT ADMINISTRATION IN THE NEONATE

As our profession increasingly adopts non-invasive ventilation strategies, it is likely that there will be studies challenging the need for intubation. One study of early surfactant administration with extubation to NCPAP was associated with significant reductions in the need for mechanical ventilation, fewer air leak syndromes (such as pneumothorax) and lower incidence of BPD compared with a strategy of later selective surfactant administration and continued mechanical ventilation in infants with RDS. The findings suggested that a lower treatment threshold has a greater advantage than a higher treatment threshold.

CLINICAL PRACTICE EXERCISE DISCUSSION

Initially, you may wish to obtain the Survanta and begin warming the vial, since it can only be warmed manually. You also need to calculate the dosage, as that will determine the size vial obtained. The dosing for Survanta is 4 ml/kg. If the infant weighs 0.7 kg, the dose is then 4 x 0.7 or 2.8 ml. The Survanta® dosing chart reveals that an infant weighing 651-700 gms. is to receive 2.8 ml. as well. You will then choose the smaller, 4-ml. vial.

The next step suggested is to ensure proper placement and patency of the endotracheal tube. Along with this, suctioning may be indicated.

To prevent unnecessary problems, the infant should be stabilized. Ventilator settings adjusted as recommended by the manufacturer and your facilities procedure. To lesson the risk of experiencing hypoxia during instillation, settings should be increased to a FIO₂ 1.0, a frequency of 60 breaths/minute and an inspiratory time of 0.5 seconds.

• Prepare the feeding tube with sterile technique

• Slowly withdraw the entire contents of the vial into a sterile plastic through a large bore needle. **Do not shake. Do not filter.**

• Attach the pre-measured and cut catheter to the syringe. Fill the catheter with surfactant. Expel excess surfactant. Another suggestion at this point is to divide your dose into two aliquots. If you are giving a total of 2.8 ml, that equates to 1.4 ml. per aliquot. Some practitioners like to mark the syringe at the halfway point.

Baseline measurements of breath sounds, chest assessment, cardiac rate, SpO₂ and color are taken. If the infant is on a transcutaneous monitor, TCCO₂ and TCO₂ are also useful monitoring parameters.

During administration, patient position, vigor, cardiac rate, color, chest expansion and movement SpO₂, TCCO₂ and TCO₂ should be watched closely and compared to baselines values.

The most common positioning now is just to turn the infant to one side for one aliquot and the opposite side for the second aliquot.

If all other vitals and measurements are consistent with baseline values, the clinician may opt to
slow down the dosing procedure and allow the neonate to stabilize. If the infant becomes dusky, TCO₂ falls greater than 15% or surfactant backs up in the ETT, dosing should be slowed or halted and, if necessary, ventilator settings may be increased.

The last step in this procedure would be to slowing return the infant to the ventilator settings prior to administration of the surfactant. The infant should be closely monitored and ventilator adjustments made as indicated by blood gases, chest X-ray and clinical assessment.
SURFACTANT ADMINISTRATION IN THE NEONATE

SUGGESTED READING AND REFERENCES


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Dey 2751 Napa Valley Corporate Drive, Napa, CA 94558


Glaxo Wellcome Exosurf® Neonatal Monograph.
SURFACTANT ADMINISTRATION IN THE NEONATE


Hohifeld, J. M. The Role of Surfactant in Asthma. Department of Respiratory Medicine, Hannover Medical School and Department of Immunology, Allergology and Clinical Inhalation, Fraunhofer Institute of Toxicology and Aerosol Research, Hannover, Germany. Respir Res 2002 3(1):4.


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Nycomed Group, Langebjerg 1, Denmark.

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SURFACTANT ADMINISTRATION IN THE NEONATE

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Whittaker, K. Comprehensive Perinatal and Pediatric Respiratory Care
SURFACTANT ADMINISTRATION IN THE NEONATE

POST TEST

DIRECTIONS: IF COURSE WAS MAILED TO YOU, CIRCLE THE MOST CORRECT ANSWERS ON THE ANSWER SHEET PROVIDED AND RETURN TO: RCECS, 16781 VAN BUREN BLVD, SUITE B, RIVERSIDE, CA 92504-5798 OR FAX TO: (951) 789-8861. IF YOU ELECTED ONLINE DELIVERY, COMPLETE THE TEST ONLINE – PLEASE DO NOT MAIL OR FAX BACK.

1. Prophylactic administration of natural surfactant has been proven to:
   a. Prevent meconium aspiration syndrome.
   b. Decrease the risk of air leak syndromes such as pneumothorax and PIE.
   c. Decrease the incidence of congenital diaphragmatic hernia.
   d. None of the above.

2. Prophylactic indications for surfactant replacement include:
   a. Infants at risk of developing RDS due to prematurity-related surfactant deficiency.
   b. Infants with low birth weight (less than 800-1300 grams).
   c. Infants with short gestation (less than 30-32 weeks).
   d. Infants who have laboratory evidence of surfactant deficiency.
   e. All of the above.

3. Physiologic functions of surfactant include:
   a. Lowering surface tension.
   b. Rapidly absorbs, spreads and reforms a monolayer.
   c. None of the above.
   d. All of the above.

4. The primary cause of RDS is:
   a. Deficiency or dysfunction of pulmonary surfactant.
   b. Prematurity of the pulmonary system.
   c. Meconium aspiration.
   d. TTNB

5. Rescue or therapeutic indications for surfactant replacement DO NOT include:
   a. Decreasing FIO₂ requirements.
   b. Increased work of breathing.
   c. Clinical evidence of RDS.
   d. A CXR characteristic of RDS.
SURFACTANT ADMINISTRATION IN THE NEONATE

6. Contraindications for the administration of surfactants include:
   a. Presence of congenital anomalies incompatible with life beyond the neonatal period.
   b. Respiratory distress in neonates with laboratory evidence of lung maturity.
   c. “B” only.
   d. “A” and “B”.

7. **Physiologic** hazards and/or complications of surfactant administration **DO NOT** include:
   a. Apnea.
   b. Pharyngeal deposition of surfactant.
   c. Mucus plugs.
   d. Barotrauma.

8. **Procedural** hazards and/or complications of surfactant administration **INCLUDE**:
   a. Plugging of the ETT by surfactant.
   b. Increased need for supplemental oxygen.
   c. Bradycardia due to hypoxia.
   d. All of the above.

9. Expected outcomes from the administration of surfactant include:
   a. Improvement in CXR.
   b. Decreased work of breathing.
   c. Improved arterial/alveolar PO₂.
   d. All of the above.

10. Monitoring of the neonate during administration of surfactant **DOES NOT** include:
    a. Baseline breath sounds.
    b. Heart rate before, during and after administration.
    c. CVP readings.
    d. SpO₂ before, during and after administration.

11. The **initial** dose of Curosurf for a 1500 gm. neonate is 1.9 ml.
    a. True
    b. False

12. Both Survanta® and Curosurf® are available in two vial sizes.
    a. True
    b. False
SURFACTANT ADMINISTRATION IN THE NEONATE

13. During the initial dose of surfactants, FIO₂ should be set at 1.0.
   a. True
   b. False

14. Survanta® does not have an initial dose recommendation that differs from subsequent dosing.
   a. True
   b. False

15. Aseptic technique is to be practiced during preparation for and administration of surfactants.
   a. True
   b. False

16. It is suggested that blood gases be obtained approximately four hours post administration of surfactants.
   a. True
   b. False

17. Suctioning should not be performed for a minimum of two hours after surfactant administration.
   a. True
   b. False

18. Exogenous surfactant administration has been proven to:
   a. Decrease the incidence of infant mortality.
   b. Decrease death.
   c. Decrease the risk of air leak syndromes.
   d. All of the above.

19. Which of the following is true regarding administration of exogenous surfactants:
   a. You must use a filtered needle when drawing up surfactants.
   b. The endotracheal tube placement must be confirmed prior to administration.
   c. The vial must be shaken well prior to administration.
   d. Sterile technique is not necessary.
20. One acceptable alternative method of surfactant administration is:

a. Intranasally.
b. In-line nebulization.
c. Via a specifically designed side port in an endotracheal tube.
d. None of the above.
SURFACTANT ADMINISTRATION IN THE NEONATE

ANSWER SHEET

NAME____________________________________ STATE LIC #_______________________

ADDRESS_________________________________ AARC# (if applic.)___________________

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SURFACTANT ADMINISTRATION IN THE NEONATE

EVALUATION FORM

NAME:____________________________________________ DATE:________________

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Were the objectives of the course met? _____  _____

Was the material clear and understandable? _____  _____

Was the material well-organized? _____  _____

Was the material relevant to your job? _____  _____

Did you learn something new? _____  _____

Was the material interesting? _____  _____

Were the illustrations, if any, helpful? _____  _____

Would you recommend this course to a friend? _____  _____

What was the most valuable portion of the material?

________________________________________________________________________

What was the least valuable portion of the material?

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