

## **Vitamin A**

### **Rationale**

Vitamin A is the generic name for a group of fat soluble compounds that exhibit the biological properties of the primary alcohol, retinol. Retinol metabolites exhibit potent and site specific effects on gene expression and lung growth and development.

Vitamin A is involved in the growth and differentiation of many cells and maintains the integrity of the epithelial cells of the respiratory tract. If a fetus is deprived of vitamin A, normal lung development does not occur. Accumulation of Vitamin A typically occurs in the third trimester and, therefore, premature infants have decreased hepatic stores. In comparison to term infants, premature infants less than 32 weeks gestation have decreased plasma concentrations of both Vitamin A and retinol-binding protein (RBP). RBP is a specific carrier protein that vitamin A binds to in plasma. Inadequate provision and delivery of Vitamin A postnatally may exacerbate the problem.

Vitamin A must be given intramuscularly because vitamin A deficiency cannot be restored to normal levels by being added to enteral or parenteral nutrition. Administration of Vitamin A through intravenous alimentation solutions is unreliable because it irreversibly oxidizes and loses biologic activity when exposed to light.

The appropriate concentration of plasma vitamin A in premature infants is not known. Concentrations below 200 micrograms/L (0.70 micromol/L) have been considered as deficiency in premature infants and concentrations below 100 micrograms/L (0.35 micromol/L) as indicating severe deficiency and depleted liver stores.

Deficiency of Vitamin A in laboratory animals has shown impairment of branching and alveolar development in the lung. Deficiency produces histopathological changes in the respiratory tract that include necrotizing tracheobronchiolitis and squamous metaplasia. After the lung is formed, deficiency of vitamin A can cause a loss of Clara cells, goblet cells, and ciliated cells making the airway more susceptible to infection and injury. These changes can be reversed with restoration of adequate vitamin A status. Similar changes have been observed in ventilated infants with chronic neonatal lung injury. This suggests that Vitamin A deficiency may contribute to such injury in neonates and vitamin A supplementation may facilitate healing and recovery. Some studies have shown that infants developing chronic lung disease have lower concentrations of vitamin A than infants that do not develop chronic lung disease.

Vitamin A has been found safe and effective in a large multicenter trial. Vitamin A is potentially toxic with raised intracranial pressure and vomiting described in infants receiving large doses. Adults and children with chronic hypervitaminosis A have had bone and joint pain, mucocutaneous lesions, and hepatic dysfunction, but this has not been recognized in preterm infants.

Current research supports the use of Vitamin A supplementation in VLBW infants requiring early respiratory support. It has been reported that there would be one fewer

infant with chronic lung disease for every 14 or 15 infants treated with vitamin A supplementation.

**Currently**, we are using Vitamin A therapy in our unit for:

- all infants <1000 grams
- infants 1000-1250 grams if ventilated >24 hours

**Dose:**

5000 IU (0.1cc) IM on M-W-F x 4 weeks

May be discontinued prior to 4 weeks of treatment if the infant reaches full enteral feeds (150 cc/kg/day of premature infant formula or 120 cc/kg/day of premature infant formula with 1cc/day of Poly-vi-sol)

**References**

1. Tyson JE, Wright LL, Oh W, et al. Vitamin A supplementation for extremely-low-birth-weight infants. *N Engl J Med* 1999;340:1962-1968.
2. Shenai JP. Vitamin A supplementation in very low birth weight neonates: rationale and evidence. *Pediatr* 1999;104:1369-1374
3. Hazinski, Thomas A. Vitamin A Treatment for the Infant at Risk for Bronchopulmonary Dysplasia. *Neoreviews* 2000 1: 11-15
4. Darlow BA, Graham PJ. Vitamin A supplementation for preventing morbidity and mortality in very low birthweight infants (Cochrane Review). In: *The Cochrane Library*, 4, 2000