

# Neonatal Cholesterol Provided by Breastmilk and the Gap in Nutrition Support Solutions

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**Introduction:** Neonatal parenteral nutrition (PN) and enteral nutrition (EN) research is limited regarding cholesterol. Cholesterol is vital in development of the nervous system, synthesis of vitamins, bile acids, lipoproteins, and hormones, and has potential long term cardioprotective effects. Measurement of human breastmilk cholesterol concentration has consisted of small individual samples, finding levels more robust than that provided by infant EN or PN. Re-examining a large global cohort is the first step in targeting cholesterol in nutrition support solutions.

**Hypothesis:** Breastmilk cholesterol levels will differ among populations and exceed EN and PN levels.

**Methods:** In a large (n=360) prospective, longitudinal –Global Exploration of Human Milk (GEHM) cohort study we examined cholesterol concentrations of human milk from three distinct urban populations in Shanghai, China, Mexico City, Mexico and Cincinnati, USA. Enrollment was limited to healthy mothers of term, singleton infants. Sample collection was standardized as a full breast expression during a 4 hour window (9am-1pm) at 4 weeks of infant age. Milk was saponified in alcoholic KOH, sterol extracted, and mass of cholesterol measured by gas liquid chromatography GC using stigmasterol as an internal standard.

**Results:** Breastmilk cholesterol concentration (mg/100mL) differed significantly between all sites with the highest levels in Cincinnati followed by Mexico City and Shanghai (median; IQR): 14.2; 6.2, 10.3; 5.6, 9.5; 4.8, respectively (p<0.001). Among the sample as a whole, breastmilk cholesterol levels were significantly different between BMI classes, with higher classes having higher levels (P=0.001). The median concentration of cholesterol from normal weight mothers (BMI 18.5-24.9) in the large cohort was 10.75 mg/100mL, which is significantly higher than EN (1.7-3.8 mg/100 mL) and PN (0 mg/100mL). A cumulative deficit of about 1500 mg cholesterol in a formula or parenteral fed infant would be realized as compared to a healthy nursing infant over four weeks.`

**Conclusions:** Human milk cholesterol levels, provided via a milk fat globule membrane (MFGM), are significantly greater than that provided by PN or EN and result in a gap of intake in the non-nursing infant. Future studies are imperative to determine appropriate infant PN and EN modification to include cholesterol.

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