



# Research Week 2023

## Physiological responses and disposition of lipids following fetal Intralipid 20® infusion

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### Keywords

prematurity, parenteral nutrition, nutrition, lipids

### Abstract

#### Introduction

Premature infants are exposed to a high lipid environment at earlier developmental stages than is normal, either via fat-rich breastmilk or by intravenous lipid emulsion parenteral nutrition (PN). Premature infants receiving PN sometimes develop pathologies, including PN-associated liver disease (PNALD), lipid embolism of the lung, and increased cardiac stiffness. We studied physiological responses to Intralipid 20® and lipid disposition in the fetal blood, liver, lung, heart, and placenta in fetal sheep at 85-90% of gestation (equivalent to 36 weeks in humans), eliminating confounding factors associated with preterm birth.

#### Methods

Ewes carrying twin fetuses underwent sterile surgery at  $119 \pm 1$  days of gestational age (dGA; term=147 dGA) to implant fetal vascular catheters. After 6 days surgical recovery, one fetus from each twin pair received Intralipid 20® (per manufacturer's recommendations for premature infants) for 8 days, ramping up from  $0.7 \pm 0.1 \text{ g kg}^{-1} \text{ d}^{-1}$  to  $2.8 \text{ g}^{-1} \text{ kg}^{-1} \text{ d}^{-1}$ . Fetal hemodynamic parameters were continuously monitored, arterial blood gases and contents measured daily, blood was separated and stored for lipid analysis, and tissues were collected at necropsy. Statistical significance was determined at  $P < 0.05$ .

#### Results

The fetal physiological response to Intralipid 20® was limited: hemodynamic pressures, heart rate, hematocrit, arterial pH,  $\text{CO}_2$  and  $\text{O}_2$  were unaffected. Intralipid 20® infusion increased circulating glucose and plasma protein levels, plasma triglycerides, cholesterol and phospholipids, as well as many lipid species in red blood cells. Fetal body and organ weights were unaffected, except liver weight increased by 18%. Intracellular fat droplets (Oil Red O staining) were more abundant in livers of treated fetuses.

## Summary

Fetal lipid emulsion PN has minimal impact on hemodynamic physiology and, not unexpectedly, increases circulating plasma lipids and incorporation of lipids into red blood cells. Interestingly, lipid uptake and incorporation into lipid droplets is localized to the liver, with heart, lungs and placenta grossly unaffected.