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Elevation of Plasma Lathosterol, as an Indicator of Increased Cholesterol Synthesis, in Preterm (23–32 Weeks Gestation) Infants Given Intralipid

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ABSTRACT. Hypercholesterolemia is common in preterm infants administered 10% Intralipid perhaps because of excess phospholipid in plasma causing efflux of cholesterol from tissues. The purpose of this study was to determine if cholesterol synthesis (as measured by plasma lathosterol) is increased in preterm infants (23–32 wk gestation) during infusion of up to 4 g 10% Intralipid/kg body wt/d. Two groups of infants were studied. Intralipid intake was compared to: *1*) plasma cholesterol in blood sampled over the first 100 d of life (preliminary study, $n = 22$) and *2*) plasma cholesterol, lathosterol, and apo AI and B in blood taken at birth (cord), d 3–4 of life, and at least three additional times over the next 25 d (lathosterol study, $n = 22$). Lathosterol was quantitated by gas liquid chromatography and apo AI and B by immunoprecipitation. In the preliminary study, plasma cholesterol levels rose (to 4.06–10.70 mM) with Intralipid administration. Infants who received <2 g Intralipid/kg body wt/d were not hypercholesterolemic. In the lathosterol study, plasma cholesterol increased (1.86–2.24 mM, $p = 0.06$) and apo AI and B did not change, but lathosterol and the cholesterol:lathosterol ratio decreased (5.24–2.88 μM, $p = 0.01$, and 284–124 10^2 × mmol lathosterol:mol cholesterol, $p = 0.007$, respectively) from birth to d 3–4 ($n = 11$ paired samples). Infants followed longitudinally had increased cholesterol and lathosterol (4- to 7-fold) with increasing Intralipid administration, which decreased after discontinuation of infusion. Apo AI and B decreased upon Intralipid infusion. The results of this study show that 10% Intralipid administration to preterm infants (23–32 wk gestation) results in increased plasma lathosterol. The coincident fall in plasma apo AI and B suggests that the elevated cholesterol synthesis may be extrahepatic. (*Pediatr Res* 31: 186–192, 1992)

Abbreviations

HMG CoA, 3-hydroxy-3-methylglutaryl coenzyme A
apo, apolipoprotein

An increase in plasma cholesterol levels in the 1st wk of life is normal in term infants (1). Postnatal changes in preterm infants are less clear, but there have been many reports of hypercholesterolemia (2–13) beyond the levels observed either *in utero* (14) or in healthy term infants (1). This is attributed to i.v. lipid administration and has also been noted in similarly treated term infants (2, 4, 5, 15) and adults (16, 17). Griffin *et al.* (2) showed that infusion of 10% Intralipid (KabiVitrum Canada Ltd., Newmarket, Ontario, Canada), resulted in elevated plasma cholesterol in neonates, and estimated 50% of the increase was from endogenous sources. Increased efflux of nonesterified cholesterol from tissues to plasma, with accumulation of cholesterol in a lipoprotein known as LpX (2), might result in enhanced cholesterol synthesis to replace membrane cholesterol lost to the plasma. To the best of our knowledge, cholesterol synthesis has not been measured in preterm infants during i.v. lipid feeding.

Cholesterol synthesis is commonly determined by assay of the activity of liver HMG CoA reductase (EC 1.1.1.34) (18), plasma mevalonate (19), or deuterated water incorporation into cholesterol (20). Although not involving liver biopsy, the latter two methods require laborious methodology or blood volumes too large for infant studies. Cholesterol synthesis has also been measured *in vivo* by quantitation of plasma lathosterol, a sterol precursor of cholesterol, by gas-liquid chromatography (21). Plasma concentrations of lathosterol are correlated with the rate of hepatic HMG CoA reductase activity in adult humans (22).

The primary objective of this study was to determine lathosterol levels in preterm infants preceding and during 10% Intralipid administration. Subjects ranged from 23–32 wk gestation, inasmuch as these infants most often require parenteral nutrition with Intralipid. Plasma apo AI and B and nonesterified and total cholesterol concentrations were measured as indicators of HDL, LDL, and LpX. First, a preliminary study was conducted to document the association between plasma cholesterol levels and Intralipid administration at this facility.

MATERIALS AND METHODS

Preliminary Cholesterol Study. Infants. All infants of 24–32 wk gestation admitted between April and August 1989 to the Special Care Nursery of the British Columbia Children's Hospital in Vancouver were followed. Results are given for the 21 infants, with birth weight appropriate for gestational age, for whom at least five plasma samples were obtained (the first within 2 wk of birth). Medical care was given at the discretion of the attending physicians with no regard to this study. Generally, infants were nourished via a peripheral vein immediately after birth with glucose (D5W or D10W; Baxter Corp., Toronto, Ontario, Canada), followed by the inclusion of amino acids (Vamin A or B; KabiVitrum Canada Ltd., Newmarket, Ontario, Canada) and Intralipid (0.5–4 g/kg body wt/d) over the next week. Lipids were mixed with 2 IU heparin/mL and infused at a constant, continuous rate. Expressed breast milk and/or formula (Similac Special Care or Pregestimil, Ross Laboratories, Columbus, OH

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or Enfalac or Prosoybee, Mead Johnson, Belleville, Ontario, Canada) were fed by nasogastric bolus as tolerated. Gestational age, birth weight, sex, daily weight gain, and enteral and parenteral feeding data were recorded.

Samples. Blood was collected by heel prick into capillary tubes for hematocrit analysis as part of the medical care, the tubes were spun and results were read within 2 h of sampling, and plasma was recovered from the tube. Additional samples were acquired when excess plasma remained from other required laboratory tests. Plasma was stored at −70°C. Samples were analyzed for total cholesterol as described below.

Lathosterol Study. Infants. The 22 infants followed in this study were born at 23–32 wk gestation at Grace Hospital and admitted to the Special Care Nursery of the British Columbia Children's Hospital between February and August 1990. A requirement of a concurrent study was that infants be intubated from birth. Infants' medical and dietary history was collected as above. Serum bilirubin and history of prenatal maternal dexamethasone treatment were recorded.

Samples. The umbilical cord was clamped within 2 min of delivery and blood (1 mL) was collected by puncture of the umbilical vein. Blood (0.5 mL) was sampled at 3–4 d of age and, where possible, two to five more times during the next 4 wk by puncture of a vein on the dorsum of the hand at the time of other clinical sampling (approximately 1000 h). Plasma was obtained after centrifugation (3000 rpm, 15 min, 4°C) and stored at −70°C within 4 h of collection.

Sterol Analyses. Plasma nonesterified and total cholesterol (3β-hydroxysterol) levels were determined using enzymatic kits (Diagnostic Chemicals, Ltd.; Charlottetown, Prince Edward Island, Canada). Quality control serum (Sigma Chemical Co., St. Louis, MO) was included in each assay. Sample blanks were assayed if hemolysis was noted. Plasma lathosterol was extracted (21) and quantitated (22) with minor modification. In brief, 5α-cholestane, an internal standard (Sigma Chemical Co.), was added to 50–100 μL plasma and saponified with 50% KOH and methanol (6:94, vol/vol) for 1 h at 80°C. This was then extracted three times with petroleum ether, dried, and silylated with hexamethyldisilane:trimethylchlorosilane:dimethylformamide, 20:2:5, vol/vol/vol (Pierce; Rockford, IL), 5 min at room temperature. Recovered sterols were immediately injected into a Varian 3400 gas-liquid chromatograph equipped with flame ionization detection and a Varian 401 data system (Varian Canada Ltd., Georgetown, Ontario, Canada). Separation was achieved on an RTx-1, 25-m capillary column, 0.25-mm internal diameter, 0.25-μm thickness (Restek, Corp.; Bellefonte, PA). The column oven was programmed to increase from 80°C for 1 min to 120°C (20°C/min), hold for 7 min, rise to 249°C (20°C/min), hold for 15 min, rise to 269°C (20°C/min), and hold for 20 min. The oven was then heated to 320°C before subsequent analyses. The injector and detector were set at 300 and 320°C, respectively, and the carrier gas (helium) flow was set at 1.25 mL/min with an inlet split ratio of 100:1 commencing 0.7 min after the run start. Lathosterol peak identification was confirmed using an authentic standard (Sigma Chemical Co., St. Louis, MO). The interassay coefficient of variation was 11%. Results were calculated as μM lathosterol and the ratio of lathosterol:cholesterol (10^2 × mmol lathosterol:mol cholesterol) (21).

Apolipoprotein Analyses. Plasma apo AI and B were measured by immunoprecipitation (Beckman Array Protein System, Palo Alto, CA).

Statistics. Variations among infants in start, dosage, and duration of Intralipid feeding were unavoidable because this study operated within the confines of the best treatment for each patient. Therefore, the only valid statistical comparisons possible were paired *t* tests between cord and d 3–4 samples because infants' treatments were relatively similar until this point.

Ethics. The study protocols were approved by the clinical screening committees for research and other studies involving human subjects of the University of British Columbia and British Columbia Children's and Grace Hospitals. Informed consent was obtained from all parents to allow their infant's participation in the lathosterol study.

RESULTS

Preliminary cholesterol study. Infants were divided into two groups based on whether or not they had received >2 g/kg body wt/d for more than 2 d. Infants in the i.v. lipid group had a lower mean gestational age and birth weight and began enteral feeds later than infants given negligible i.v. lipid (Table 1). Changes in plasma cholesterol *versus* postnatal age and Intralipid administration of representative infants (Table 2) are plotted in Figures 1 and 2. The clinical profiles of both groups were typical for infants of this degree of immaturity and included hyaline membrane disease, bronchopulmonary dysplasia, septicemia, patent ductus arteriosus, intraventricular hemorrhage, and necrotizing enterocolitis.

Plasma cholesterol levels rose coincident with lipid administration (Fig. 1). The highest level measured for each infant ranged from 4.06 to 10.70 mM. In all cases, cholesterol levels decreased after cessation of i.v. lipid infusion. The highest plasma cholesterol levels found for infants receiving negligible Intralipid was 5.17 mM (Fig. 2).

Lathosterol study. These infants were divided into two not mutually exclusive subsets: 1) those for whom paired cord and d 3–4 samples were available ($n = 11$) and *2*) those from whom at least three additional samples were collected after d 3–4 of age ($n = 10$). Five infants did not fit either group. Paired cord and d 3–4 data were not obtained for subjects if the blood had clotted in the cord before sampling, the infant was too sick for investigation, or the blood sample was too small for analysis. Longitudinal sampling was discontinued as a result of extubation (according to concurrent study protocol) or death. The clinical profiles of the participating infants were similar to those in the preliminary study. Serum bilirubin did not exceed 209 μM (12.2 mg/dL) in any infant.

Cord and d 3–4 subset. The birth weight and gestational age of these infants are shown in Table 3. Two infants were female, two were Oriental, and nine were Caucasian; two were born by cesarean section. The mean plasma cholesterol concentrations of the group of infants studied increased between birth and d 3–4, but there was no change in apo AI or B (Table 3). There was, however, considerable variation among individual infants. Thus,

Table 1. *Characteristics of infant populations (mean ± SD, range)**

	Preliminary study		Lathosterol study
	With i.v. lipid	Without i.v. lipid	(Longitudinal i.v. nutrition)
n	12	9	10
Birth weight (g)	954 ± 343 (655–1800)	1227 ± 170 (955–1475)	1030 ± 172 (665–1225)
Gestational age (wk)	26.0 ± 2.2 (24–31)	28.9 ± 1.3 (28–31)	26.6 ± 1.6 (23–29)
Onset of Intralipid infusion (d)	6.5 ± 2.6 (3–12)		3.9 ± 1.3 (3–7)
Onset of enteral feeds (d)	14.3 ± 8.4 (1–33)	3.1 ± 1.6 ($n = 7$)† (1–5)	6.2 ± 3.2 (3–12)
EBM/formula/mix (%)	42/42/16	38/12/50	40/20/40
Sex (F/M)	5/7	3/6	4/6
Delivery (SVD/CS)	8/4	5/4	5/5
Race (C/O/EI)	10/0/2	8/0/1	8/2/0

* EBM, expressed breast milk; SVD/CS, spontaneous vaginal delivery/cesarean section; C/O/EI, Caucasian/Oriental/East Indian.

† Only eight of nine infants received enteral feeds during the study, and one infant received enteral feeds late, at d 13, and is not included.

Table 2. *Details of infants presented in Figures 1–4*

Infant	Sex	Birth weight (g)	Gestational age (wk)	Delivery	Onset of amino acid infusion (d)	Enteral feeds	Clinical features
A	M	1800	31	SVD	6	EBM d 16–22, Pregestimil d 23–38, d 46–	HMD, BPD, NEC, gastrointestinal surgery d 6, 38
B	M	980	25	SVD	3	SCF 68 d 15–22, SCF 81 d 22–	Severe IVH
C	F	700	24	SVD	2	EBM d 33–57, Prosoybee d 57–	HMD, BPD, NEC, IVH
D	M	720	25	SVD	2	EBM d 8–14, d 24–63, SCF 81 d 62–70, EBM d 71–	HMD, BPD, PIE
E	F	1000	28	CS	2	EBM d 6–36, SCF 81 d 36–46, EBM/SCF 81 d 46–	HMD, BPD, twin
F	M	955	28	CS	2	SCF 68 d 13–34, SCF 81 d 34–	HMD, BPD, NEC
G	F	1130	28	SVD	3	EBM/SCF 68 d 12–	Birth asphyxia, HMD, PIE, pneumonia, IVH, PDA
H	M	1080	28	CS	3	EBM/SCF 68 d 11–12, d 19–	HMD, BPD, NEC, PDA
I	F	925	26	CS	2	EBM/SCF 68 d 2–5, EBM d 5–	HMD, septicemia, PDA
J	M	685	23	SVD	3	SCF 68 d 5–8	Birth asphyxia, HMD, NEC, PDA, spastic quadriplegia
K	M	875	26	SVD	3	EBM d 8–14, d 18–	HMD, BPD, PDA, respiratory infection d 16
L	M	1140	26	SVD	3	EBM d 14–	Septicemia, PDA, inguinal hernia surgery d 8
M	M	920	26	SVD	2	EBM d 5–	HMD, pneumonia, IVH, septicemia
N	M	1025	27	CS	3	EBM/SCF 68 d 4–	Perinatal asphyxia, HMD, BPD, PDA

SVD, spontaneous vaginal delivery; CS, cesarean section; HMD, hyaline membrane disease; BPD, bronchopulmonary dysplasia; PDA, patent ductus arteriosus; IVH, intraventricular hemorrhage; PIE, pulmonary interstitial emphysema; NEC, necrotizing enterocolitis; EBM, expressed breast milk; and SCF, Special Care formula.

the plasma cholesterol decreased in three of 11 infants, showed no change in one of 11 infants, and increased in eight of 11 infants over the first 3–4 d of life (Table 3). The plasma lathosterol concentration and the ratio of lathosterol:cholesterol, however, decreased. There were no differences in any of these parameters between infants whose mothers were (n = 4) or were not given dexamethasone before delivery. The administration of small amounts of Intralipid (<1 g/kg body wt/d, n = 2) before the d 3–4 sampling did not have any discernible effect.

Longitudinal subset. Characteristics of the infants studied are shown in Table 1. Three infants were Oriental and the remainder were Caucasian. Cholesterol, apo AI and B, and lathosterol concentrations and i.v. lipid intake for representative infants (Table 2) are plotted in Figures 3 and 4.

The rise in plasma lathosterol was coincident with the infusion of Intralipid and increase in plasma cholesterol. In the three infants for whom Intralipid was stopped before the final sample was taken, plasma sterol concentrations returned to preinfusion levels (*e.g.* Fig. 3, infant L). Apo AI and B levels either did not change or decreased during Intralipid infusion. In the two infants who received negligible Intralipid (Fig. 4), plasma lathosterol levels increased slightly after birth, but showed no further increase over the 11 d studied. Plasma apo AI increased in one of these infants (M), but cholesterol and apo B did not change appreciatively in either.

DISCUSSION

Cord plasma analyses. The cord plasma cholesterol, apo AI, and apo B concentrations found here are similar to published levels for infants of similar gestational age (3, 23–29). The higher cord plasma cholesterol levels in very preterm than in term infants (25, 26, 28) have been hypothesized to reflect enhanced hepatic cholesterol synthesis related to a spurt in liver growth (14). Our finding that cord lathosterol concentrations are not different in preterm than term (unpublished observation) infants does not support this hypothesis.

Lathosterol concentrations were much more variable among preterm (Table 3) than among term infants (unpublished observation). This may reflect collection of cord plasma from only elective cesarean section births in the term but not the preterm infants, inasmuch as the many variables of labor and delivery that affect cord plasma cholesterol levels (30) might also influence cholesterol synthesis rates. One such variable is maternal dexamethasone administration, which is often given before preterm delivery to reduce neonatal respiratory distress (31). This results in increased total, HDL, and LDL cholesterol and apo AI levels in 26–32 wk gestation infants and has been suggested to be related to enhanced fetal cholesterol synthesis (32). Four infants in our study were exposed to dexamethasone at a wide range of times before birth. Possibly, this contributed to the high degree of variability in the preterm cord lathosterol results.

Cord versus d 3–4. Preterm plasma cholesterol concentrations increased about 20% over the first 3–4 d of life, whereas lathosterol concentrations decreased by about 45%. In term infants sampled at comparable ages, cholesterol increased 40% and lathosterol decreased 10% (unpublished observation). It seems that, irrespective of gestational age, cholesterol synthesis does not increase in the early newborn period. Preterm infants are often in negative energy balance at 3–4 d of age when supported by parenteral nutrition without lipid. Their apparently larger decrease in cholesterol synthesis might be explained by limiting acetyl CoA levels for biosynthetic pathways.

Infants not receiving Intralipid. In agreement with reports for enterally fed preterm infants (23, 28), hypercholesterolemia did not occur in infants given negligible Intralipid. Of further note, lathosterol levels did not increase. The results, however, indicate that enterally fed preterm infants may not experience the increase in plasma cholesterol levels that are typical of term infants and believed to be associated with the onset of oral feeding (1).

Apoprotein analysis of the two infants who received negligible Intralipid showed no notable changes in apo B containing LDL and VLDL. HDL (as indicated by apo AI) levels increased in infant M, but no changes were seen in infant N. Others have

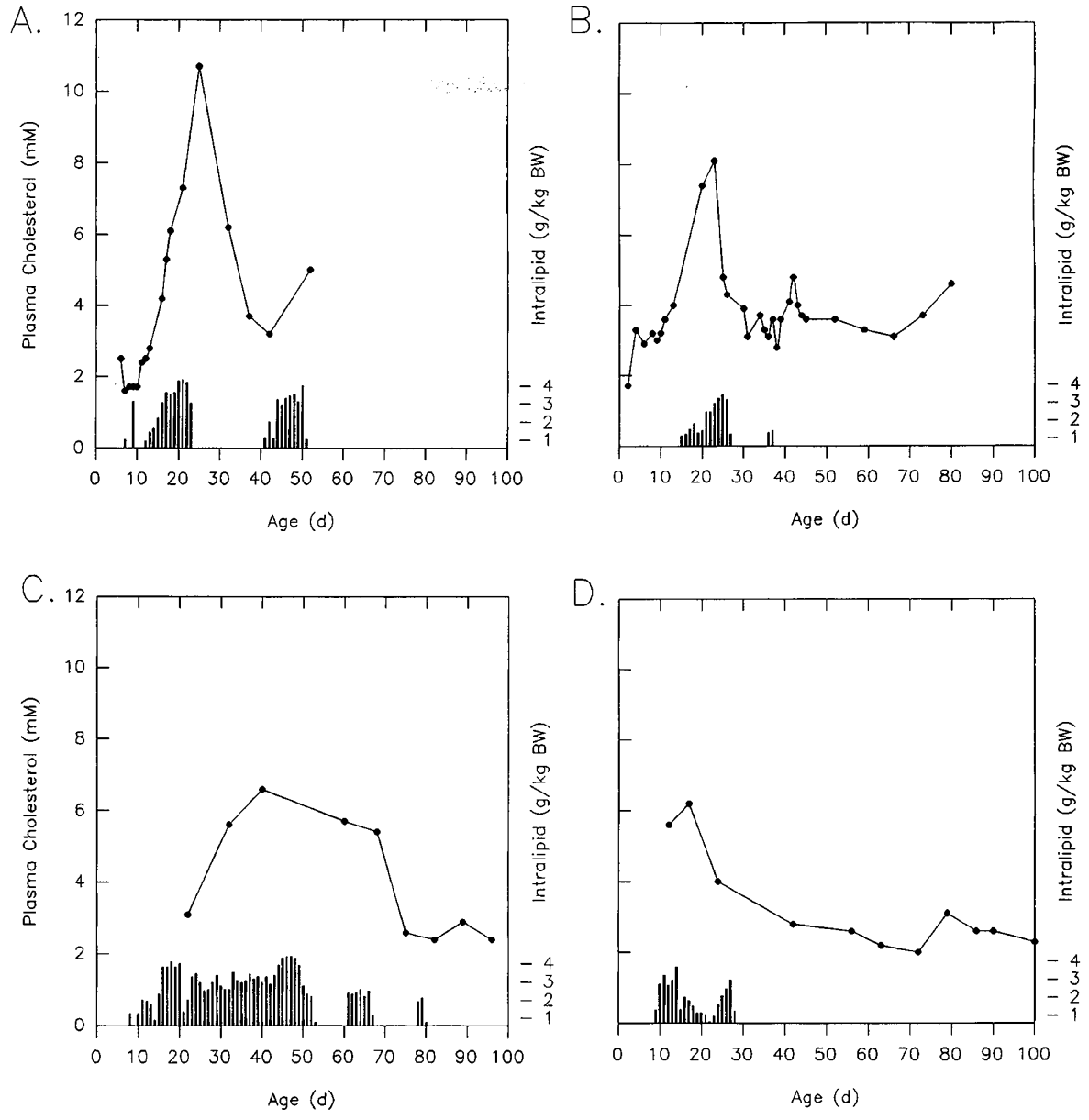

Fig. 1. Plasma cholesterol levels (●) and Intralipid infusion rates (*solid bars*) over the first 100 d of life of four representative preterm infants. Infants are described in Table 2.

reported at least a transient increase in apo AI (28), HDL cholesterol (23, 27, 33), or VLDL or LDL cholesterol (23, 27) in preterm infants given only enteral nutrition in the 1st mo of life.

Infants receiving Intralipid. Intralipid, an emulsion of soybean oil triglyceride and egg yolk phospholipid, is often administered for prolonged periods to infants unable to tolerate adequate enteral nutrition. Its metabolism involves association of the emulsion particles with C apoproteins and triglyceride hydrolysis via lipoprotein lipase (17, 34). The resulting phospholipid-rich vesicles, after inclusion of more C apoproteins, albumin, and equimolar amounts of nonesterified cholesterol, are commonly referred to as LpX particles. Plasma cholesterol levels increase cumulatively when Intralipid is infused (7–10, 12). Griffin *et al.* (2) calculated that, although Intralipid contains about 4 mg cholesterol and 2 mg plant sterols/g triglyceride, at least 50% of the excess plasma cholesterol is derived from endogenous sources. Plant sterols were only slightly elevated in infants given Intralipid for either 24 h or 2.5 mo (2). It seems unlikely, therefore, that the elevation of plasma cholesterol in our study is explained by accumulation of infused plant sterol, which was not discriminated by the plasma cholesterol (3β-hydroxysterol) enzymatic assay used.

Presumptive evidence for accumulation of LpX in this study includes *1*) elevated plasma nonesterified cholesterol levels (data not shown) in infants during Intralipid administration but not in those given negligible Intralipid or fed enterally. (27) and *2*) the failure of apo AI or B to increase during Intralipid infusion (Fig. 3). A decrease in apo AI, with higher AI levels when enteral feeds were introduced, has been reported by others (5). It has been hypothesized that decreased HDL cholesterol levels in adults given parenteral nutrition may be due to the lack of nutritional input at the intestine, a site of apo AI synthesis (35). We found no evidence of increased apo AI with enteral feeding. The reduced apo B levels during Intralipid administration (Fig. 3) could be the result of perturbation of hepatic triglyceride synthesis and secretion of VLDL as hypothesized for adults (35).

The increase in plasma lathosterol levels in concert with Intralipid administration, together with the fall in lathosterol levels upon cessation of lipid infusion, provides the first evidence of increased cholesterol synthesis associated with Intralipid infusion. Lathosterol levels rose to values 4- to 7-fold higher than reported for normal term infants (cord or d 4) or adults, into the range of hypercholesterolemic adults treated with cholestyr-

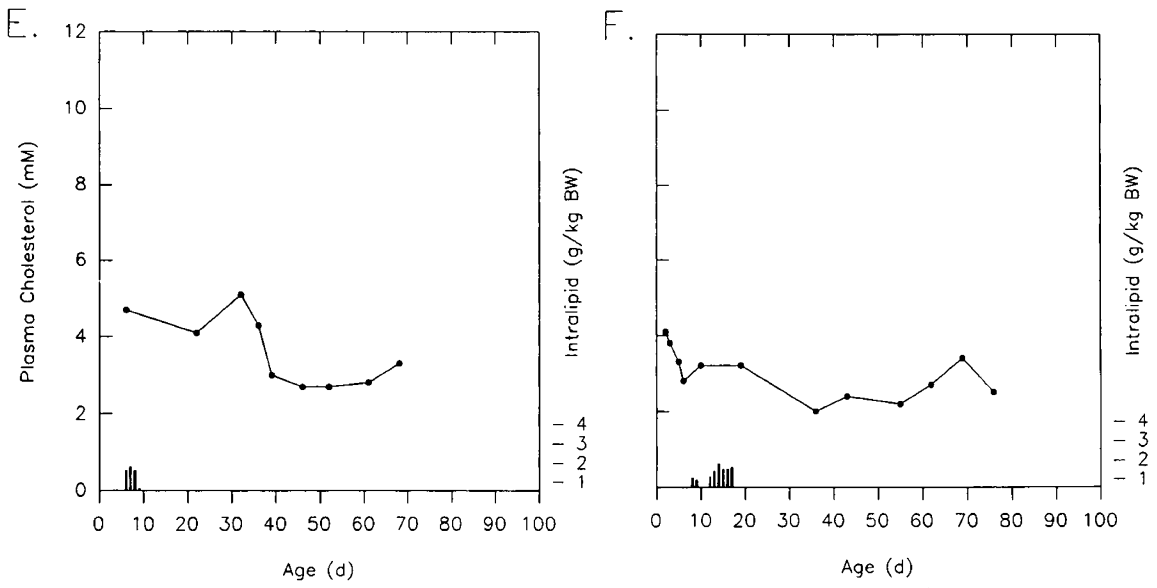

Fig. 2. Plasma cholesterol levels (●) and Intralipid infusion rates (*solid bars*) over the first 100 d of life of two representative preterm infants administered negligible Intralipid, which is defined as >2 g/kg body wt/d for more than 2 d. Infants are described in Table 2.

Table 3. *Levels of cholesterol, apo AI and B, and lathosterol in plasma of preterm infants at birth (cord) and 3–4 d of life**

Infant	Birth weight (g)	Gestational age (wk)	Cholesterol (mM)		Apo AI (g/L)		Apo B (g/L)		Lathosterol (μM)		Lathosterol (10^2 × mmol): cholesterol (mol)	
			Cord	d 3–4	Cord	d 3–4	Cord	d 3–4	Cord	d 3–4	Cord	d 3–4
SW	920	26	1.32	2.53	0.35	0.48	0.22	0.39	3.03	2.48	229	98
AB	975	28	2.12	1.76	0.52	0.44	0.20	0.20	8.90	1.21	419	69
NC	1066	27	1.34	2.74	0.22	0.33	0.28	0.34	2.48	3.28	185	120
NP	685	23	1.60	1.37	0.50	0.40		0.14	7.16	2.07	446	151
JM	1195	29	1.66	1.60	0.50	0.43	0.16		4.97	3.05	300	190
SK	1130	28	1.29	2.43	0.61	0.53	0.09	0.31	1.84	2.01	142	83
JRa	1480	32	2.15	2.51	0.36	0.67	0.17	0.37	4.34	1.84	202	74
JRb	1700	32	3.39	2.53	0.89	0.76	0.36	0.20	4.68	1.73	138	69
MR	1025	27	1.76	2.02	0.56	0.38			2.84	2.30	162	114
EL	875	26	1.19	1.50	0.54	0.56	0.10	0.15	5.17	2.04	435	136
SJ	1050	26	2.64	3.67	0.48	0.49	0.35	0.12	12.23	9.70	464	264
Mean	1100	27.6	1.86	2.24	0.50	0.50	0.21	0.25	5.24	2.88	284	124
SD	282	2.7	0.67	0.68	0.17	0.13	0.10	0.11	3.11	2.33	133	60
n	11	11	11	11	11	11	9	9	11	11	11	11
p†			0.06		0.5		0.5		0.01		0.007	

* Missing values indicate insufficient sample volume for analysis.

† Paired two-tailed *t* tests were performed in all cases except for plasma cholesterol, where a one-tailed test was used.

amine resin (unpublished observations). Increased cholesterol synthesis, measured by hepatic HMG CoA reductase activity, has also been reported in rats given lecithin mesophase infusion (36). However, a similarly induced hypercholesterolemia occurred even in the absence of a functioning liver (37), suggesting that the increased cholesterol synthesis may be extrahepatic. In this regard, Innis and Boyd (38) found that rats infused with Intralipid had increased adipose tissue and skeletal muscle, but decreased hepatic, HMG CoA reductase activity. It thus seems possible that the increased lathosterol levels in the i.v. lipid-infused preterm infant could reflect extrahepatic cholesterol synthesis. This hypothesis is compatible with decreasing apo AI and B levels because the transfer of extrahepatic membrane cholesterol to the plasma would not depend on the secretion of lipoproteins.

Summary. It appears that 10% Intralipid administered to preterm infants (23–32 wk gestation) is accompanied by increased cholesterol synthesis (as measured by plasma lathosterol concentrations), which may be of extrahepatic origin. Several potential complications of i.v. lipid administration to preterm infants have been proposed (39, 40), but the impact of changes in cholesterol synthesis is unknown. Studies in other species have suggested long-term effects on cholesterol homeostasis (41). The potential effect of increased use of two-carbon units for sterol synthesis to other metabolic pathways may also be worth consideration.

Recent studies have shown that i.v. lipid solutions that contain 20% lipid (50% less phospholipid/kJ) or mixtures of medium-chain and long-chain triglycerides minimize or do not elicit hypercholesterolemia in infants (12, 13, 42) or adults (34). The lathosterol methodology described may be of value in defining the effect of these solutions on tissue cholesterol synthesis.

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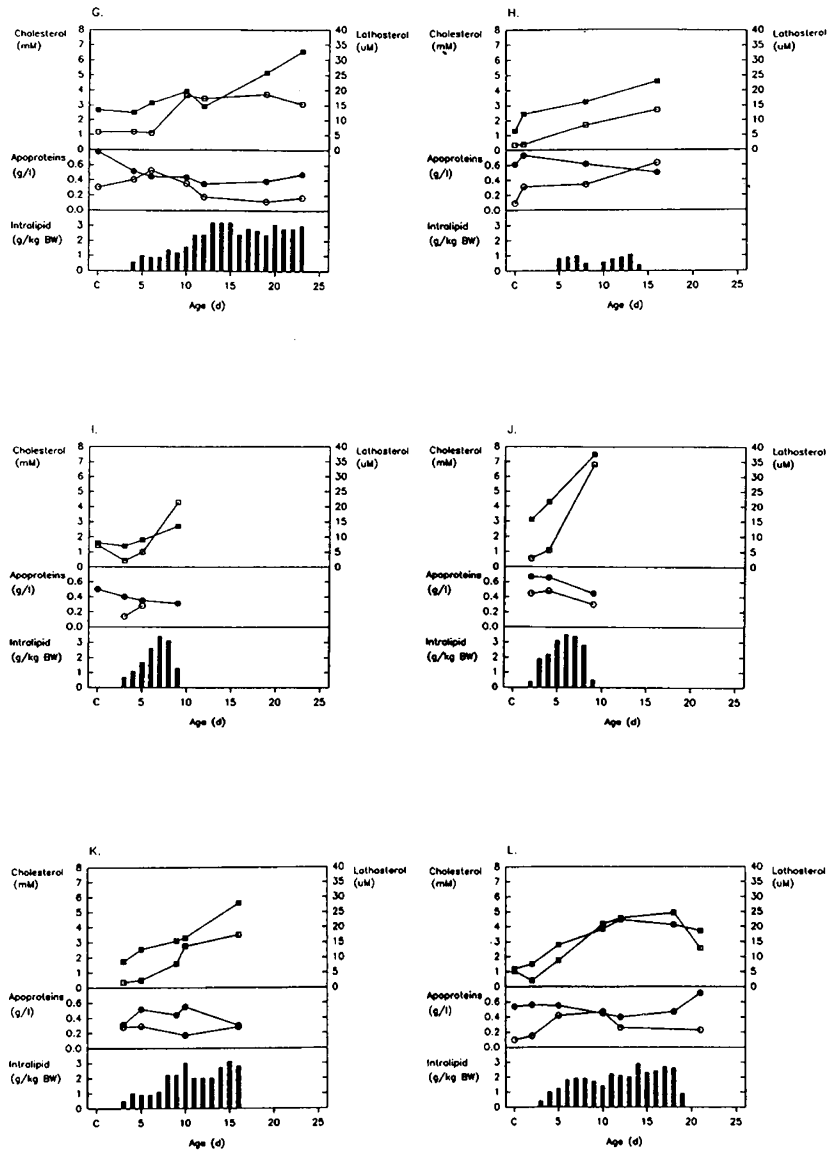

Fig. 3. Plasma cholesterol (■), lathosterol (□), and apolipoprotein AI (●) and B (○) levels and Intralipid infusion rats (*solid bars*) over the first 25 d of life of six representative preterm infants. All available data is plotted. Infants are described in Table 2.

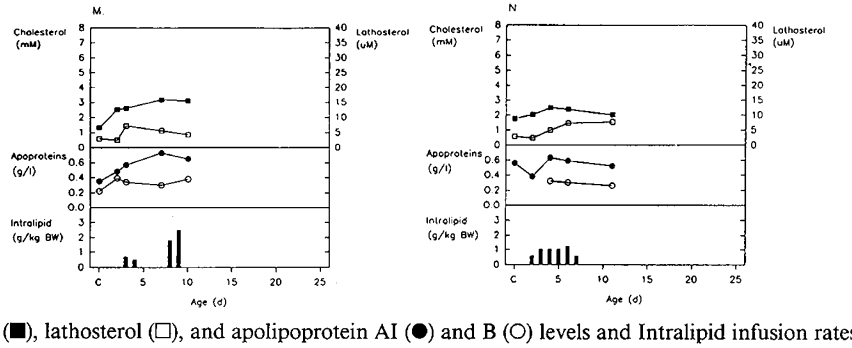

Fig. 4. Plasma cholesterol (■), lathosterol (□), and apolipoprotein AI (●) and B (○) levels and Intralipid infusion rates (*solid bars*) over the first 13 d of life of two representative preterm infants administered negligible Intralipid, which is defined as >2 g/kg body wt/d for more than 2 d. All available data is plotted. Infants are described in Table 2.

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