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Original Article

Characterization of chylomicron in preterm infants

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Abstract ***Background*:** The aim of this study was to investigate cholesterol and triglyceride levels in the chylomicron fraction of preterm infants at birth and during the early postnatal period.

***Methods*:** The subjects consisted of 133 infants (81 boys and 52 girls): 74 were term infants born at 37–41 weeks of gestation and 59 were preterm infants born at 29–36 weeks of gestation. Cholesterol and triglyceride in the chylomicron fraction were measured using high-performance liquid chromatography.

***Results*:** Compared with term infants, preterm infants had higher cholesterol and lower triglyceride in the chylomicron fraction, both in cord blood and at 1 month after birth. Thus, the chylomicron triglyceride/cholesterol ratio was significantly lower in preterm infants than in term infants in cord blood and at 1 month of age. On single regression analysis the chylomicron triglyceride/cholesterol ratio correlated positively with gestational age at birth ($r = 0.331$, $P = 0.0003$) and at 1 month ($r = 0.221$, $P = 0.0119$).

***Conclusions*:** Preterm infants have a less-lipidated chylomicron composition at birth and at 1 month of age. Some prenatal factors may persist to influence chylomicron lipidation during the early postnatal period.

Key words chylomicron, lipid composition, preterm infant.

Human fetuses have a unique lipoprotein profile, with respect to both quantity and quality, compared with adults. In cord blood, cholesterol is lower and the relative proportion of high-density lipoprotein (HDL) as opposed to low-density lipoprotein (LDL) is much higher.[1] Triglyceride (TG) is also lower, and the distribution is equal to LDL and very low-density lipoprotein (VLDL) fractions.[2] Interestingly, chylomicron (CM) can be detected in cord blood before oral feeding begins.[3] The main function of CM is the transport of fat from the intestine to the liver. During the period of transition from the intrauterine fetal environment to the extrauterine neonatal environment, the nutrient source switches from the placenta to breast milk, which contains high amounts of fat (>50% calories as lipid). Thus, the human fetus must be equipped to efficiently absorb dietary fat and produce CM to transport lipids before birth. Functional development of the human fetal intestine has been investigated using human fetal jejunal explants. These experiments confirmed that human fetal intestine tissue produces and secretes apolipoprotein (apo) B-48 and CM.[4,5]

In the present study, we measured the lipoprotein profile in cord blood from term and preterm infants, especially cholesterol and TG in the CM fraction (CM-C and CM-TG, respectively). We also investigated postnatal changes during the first month of life. In addition, we evaluated the impact of gestational age on CM composition.

Methods

This study was conducted from September 2004 to March 2010 in the maternity ward of Nihon University and subjects were recruited during pregnancy. Only those signing informed consent were enrolled, and after all cases of asphyxia were excluded, 133 infants (81 boys and 52 girls) born by vaginal delivery or cesarean section were included. Of these, 74 were term infants born at 37–41 weeks of gestation and 59 were preterm infants born at 29–36 weeks of gestation. Indications for cesarean section were breech presentation, past history of cesarean section, and preclinical causes. All of the mothers were healthy, and their pregnancies were without complications. At birth, the umbilicus was double clamped and cord blood was sampled from the umbilical vein. At 1 month of age, venous blood was obtained by venipuncture just before feeding. Total cholesterol (TC), HDL cholesterol (HDL-C), and TG were measured by enzymatic methods. Cholesterol and TG in the CM fraction were measured on high-performance liquid chromatography (HPLC) with gel permeation columns (LipoSEARCH; Skylight-Biotec, Akita, Japan).[6,7] Feeding information (i.e. exclusively breast-fed; exclusively formula-fed; or mixed breast- and formula-fed) was obtained from each mother 1 month after each child's birth. No human milk fortifier was used in this study. Written informed consent was obtained from all of the parents, and the study was approved by the University Ethics Committee (Nihon University, Itabashi Hospital, Tokyo, Japan).

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Statistical analysis

Statistical analysis was conducted with STATVIEW (version 4.5; Abacus Concepts, Berkeley, CA, USA). Data are reported as mean ± SE. Differences in measured parameters between term and preterm infants were analyzed using Mann–Whitney *U*-test, and differences in CM-C and CM-TG between the three milk-feeding categories were analyzed on analysis of variance (ANOVA). Sex distribution was analyzed using chi-squared test. Birthweight was analyzed using z-score. The correlation coefficients were determined on single and multiple regression analyses. $P < 0.05$ was considered significant.

Results

Subject characteristics

In cord blood, TC was lower in term infants than in preterm infants. There were no differences in HDL-C or TG between term and preterm infants. At 1 month, one preterm and three term infants were dropped from the study. TC and HDL-C were lower in preterm infants than in term infants, whereas there was no difference in TG between term and preterm infants (Table 1).

Lipid composition of CM

The CM-C and CM-TG could not be detected in the cord blood of 17 infants (12.8%; three preterm and 14 term) and in 20 infants (15.0%; eight preterm and 12 term), respectively, because the levels were below the lower limit of detection (0.01 mg/dL). In four infants (one preterm and three term), both CM-C and CM-TG were <0.01 mg/dL. At 1 month, we could measure CM-C and CM-TG in all of the infants. CM-C at birth correlated positively with that at 1 month in both preterm infants ($r = 0.377$, $P = 0.0035$) and term infants ($r = 0.515$, $P < 0.0001$), while CM-TG correlated positively with that at 1 month in preterm infants ($r = 0.289$, $P = 0.0321$), but not in term infants ($r = 0.029$, $P = 0.9981$).

Table 2 lists the 10th, 25th, 50th, 75th, and 90th percentiles for CM-C and CM-TG in preterm and term infants. Compared with term infants, preterm infants had higher CM-C and lower CM-TG both in cord blood and at 1 month of age. To evaluate the lipid composition of CM, the TG/C ratio (CM-TG/C) was calculated. In cord blood, CM-TG/C was significantly lower in preterm infants (2.53 ± 0.67) than in term infants (8.35 ± 1.21; $P = 0.0001$). At 1 month, CM-TG/C had increased significantly in both preterm and term infants. CM-TG/C was still lower in preterm infants (18.78 ± 3.74) than in term infants (32.41 ± 2.90; $P < 0.0001$). CM-TG/C at birth correlated positively with that at 1 month in preterm infants ($r = 0.289$, $P = 0.0321$) but not in term infants ($r = 0.077$, $P = 0.5690$). In addition, on single regression analysis, CM-TG/C correlated positively with gestational age at birth ($r = 0.331$, $P = 0.0003$) and at 1 month ($r = 0.221$, $P = 0.0119$) when the two groups of infants were combined. The relationship between birthweight Z score (BWz) and CM-TG/C as also analyzed, showing a significant positive association at birth ($r = 0.274$, $P = 0.0029$) but not at 1 month ($r = 0.100$, $P = 0.2578$).

On multiple regression analysis including gestational age and BWz as predictors for CM-TG/C, at birth, both gestational age ($\beta = 0.796$, $P = 0.0030$) and BWz ($\beta = 1.444$, $P = 0.0330$; $r = 0.381$, $P = 0.0001$) were significant independent predictors, while at 1 month, only gestational age ($\beta = 1.986$, $P = 0.0223$), but not BWz ($\beta = 1.055$, $P = 0.6372$; $r = 0.225$, $P = 0.0383$) was a significant predictor.

We obtained information about milk feeding for 67 term infants (90.5%) and 35 preterm infants (59.3%). There were no significant differences in CM-C or CM-TG between the three milk-feeding categories in either term or preterm infants. The relationship between CM-C and CM-TG in term and preterm infants is shown in Figure 1, demonstrating the altered lipid composition of the CM fraction in preterm infants at birth and at 1 month.

Table 1 Subject characteristics

	Preterm infants $n = 59$ Mean ± SE	Term infants $n = 74$ Mean ± SE	*P*-value
Male : Female	39:20	42:32	0.2725
Gestational week	33.9 ± 0.2	38.7 ± 0.2	**<0.0001**
Birthweight (g)	1948.5 ± 54.2	2978.6 ± 58.2	**<0.0001**
Birthweight Z-score	−0.6 ± 0.1	0.1 ± 0.1	**0.0014**
Cord blood			
TC (mg/dL)	75.9 ± 2.8	66.3 ± 1.9	**0.0058**
Triglyceride (mg/dL)	26.4 ± 1.9	26.4 ± 1.6	0.7702
HDL-C (mg/dL)	36.7 ± 1.5	36.8 ± 1.3	0.9603
1 month			
TC (mg/dL)	109.4 ± 2.5	131.7 ± 3.1	**<0.0001**
Triglyceride (mg/dL)	83.0 ± 6.1	70.1 ± 3.6	0.1514
HDL-C (mg/dL)	46.6 ± 1.6	60.7 ± 1.7	**<0.0001**

Bold, $P < 0.05$. HDL-C, high-density lipoprotein cholesterol; TC, total cholesterol.

Table 2 Chylomicron cholesterol and triglyceride levels

	Preterm infants ($n = 59$)		Term infants ($n = 74$)	
	CM-C (mg/dL)	CM-TG (mg/dL)	CM-C (mg/dL)	CM-TG (mg/dL)
Cord blood				
10th %tile	0.01	0.00	0.00	0.00
25th %tile	0.02	0.01	0.01	0.01
50th %tile	0.03	0.03	0.01	0.09
75th %tile	0.11	0.11	0.02	0.23
90th %tile	0.18	0.30	0.06	0.43
At 1 month	$n = 58$		$n = 71$	
10th %tile	0.03	0.68	0.02	0.68
25th %tile	0.06	0.95	0.05	1.11
50th %tile	0.25	1.37	0.08	2.17
75th %tile	0.37	2.19	0.13	3.36
90th %tile	0.47	3.41	0.18	4.90

C, cholesterol; CM, chylomicron; TG, triglyceride.

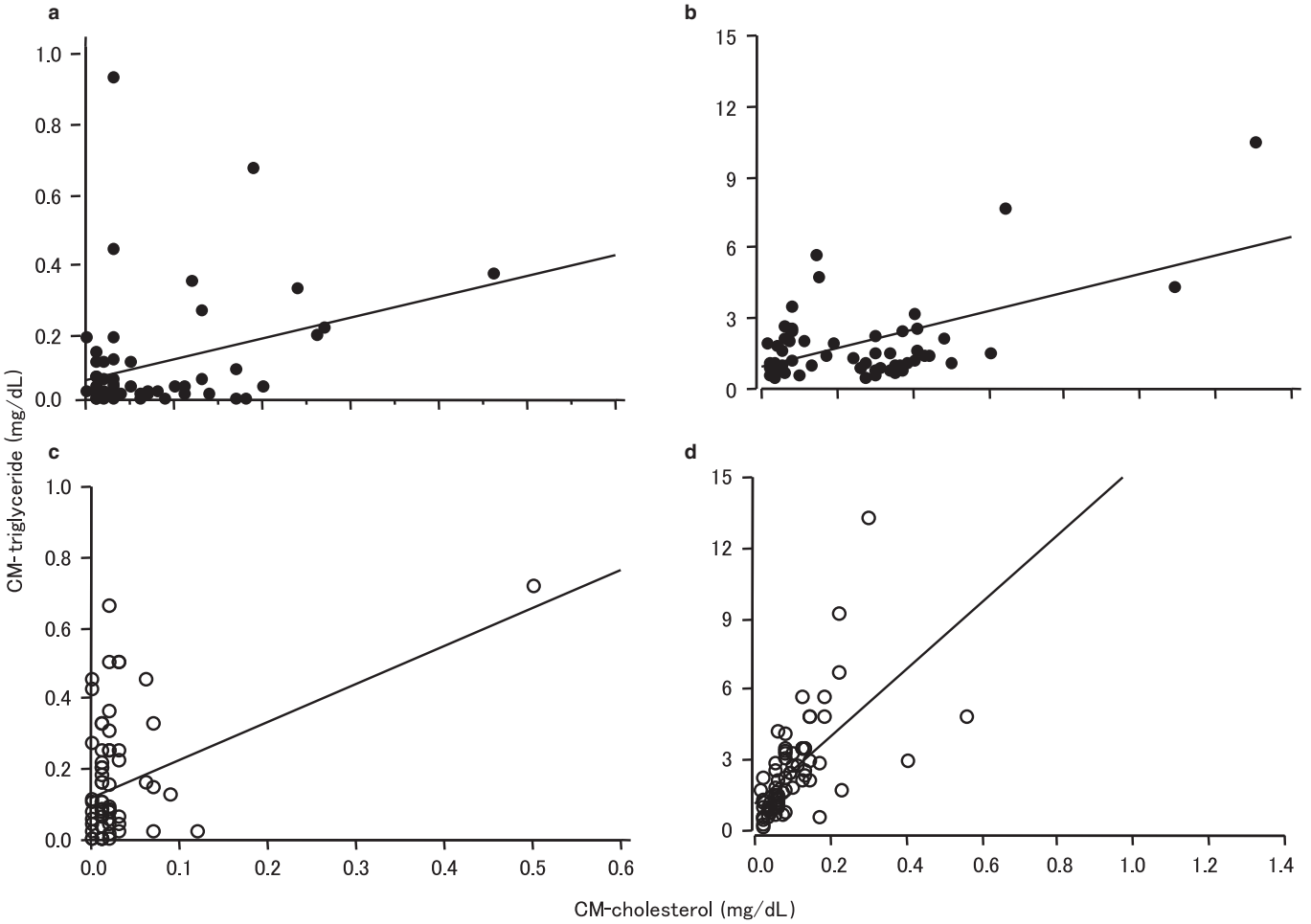

Fig. 1 Relationship between triglyceride and cholesterol in the chylomicron (CM) fraction in (a,b) preterm and (c,d) term infants at (a,c) birth and (b,d) 1 month of age. (a) $r = 0.308$, $P = 0.0174$; (b) $r = 0.553$, $P < 0.0001$; (c) $r = 0.383$, $P = 0.0008$; (d) $r = 0.597$, $P < 0.0001$.

Discussion

To the best of our knowledge, this is the first investigation of the lipid composition of CM in preterm infants. We found that at 1 month of age, after oral feeding has been established, preterm infants had higher cholesterol and lower TG in CM compared with term infants. Furthermore, in preterm infants, the alteration in the composition of CM observed at 1 month was already detectable in cord blood before the initiation of oral feeding. Therefore, the CM composition at 1 month may be determined by some prenatal factors, as well as by dietary fat.

The functional development of the human gastrointestinal tract has been investigated in *ex situ* experiments with fetal gastrointestinal tract tissue.[8] At 10 weeks of gestation, the percentage of edited intestinal apoB transcripts encoding apoB-48 is approximately 10%; it then increases progressively to nearly adult levels (80%) at term.[9] Human fetuses at 18 weeks of gestation have abundant lymphatic vessels in the stomach, small intestine, and rectum.[10] In addition, the human fetus shows effective swallowing at as early as 15 weeks of gestation.[11] Taken together, this suggests that the human fetal intestine may be developed enough to absorb fat in the second trimester. The present findings confirm that human fetal intestine can absorb lipids and secrete CM into the fetal circulation, even in preterm infants born in the third trimester.

The cholesterol and TG reference ranges of lipoprotein subclasses (including CM measured on HPLC) for healthy Japanese men and women were reported recently.[7] Compared with the reference ranges, the 25th and 75th percentiles of CM-C and CM-TG in cord blood were markedly lower in term infants. At 1 month, the 25th and 75th percentiles of CM-C were still lower, but CM-TG had reached adult fasting levels in term infants. Thus, the CM fraction in term infants is more TG rich than in adults. In the previously published healthy adult study, all blood samples were collected ≥8 h after overnight fast.[7] In contrast, in the present study, we obtained blood samples immediately before milk feeding: approximately 3–4 h after the last feed. The present results suggest that term infants may be well equipped to tolerate the frequent high-fat load provided by milk.

A novel finding of the present study is the alteration of the CM composition in preterm infants. CM-TG/C was lower in preterm infants, suggesting that the CM were less lipidated. The maturation of gastrointestinal function in neonates was investigated previously in infant pigs, because of their similarity to human infants.[12,13] The lipidation of CM in neonates is mainly regulated by microsomal triglyceride transfer protein (MTP) and apoA-IV.[13] MTP is a 97 kDa heterodimeric protein (two large M subunits and two small P subunits) that is most abundantly expressed in small intestinal enterocytes and hepatocytes.[14] MTP principally transfers TG to nascent apoB to promote lipoprotein formation. Postnatally, expression of the MTP large subunit in pig jejunum paralleled the intake of a high-fat breast milk diet and declined after weaning. In preterm pigs, however, enteral feeding did not induce intestinal MTP mRNA and activity.[13] The present finding that human preterm neonates have less lipidated CM after milk feeding has begun, is in accordance with what is known of the intestinal development of preterm pigs. Furthermore, in newborn pigs, apoA-IV increases MTP activity and induces the packaging of more TG into CM particles.[15] MTP and its regulation by apoA-IV may also be important in human neonatal fat absorption. Importantly, we found that impaired lipidation of CM in preterm infants is already apparent in cord blood. Preterm infants can absorb fat and secrete CM in the uterus, but the functions of CM lipidation may not be fully developed, and the immaturity remains at 1 month of age. Further investigations are required to establish the exact mechanisms by which the alteration in lipid composition of CM in human preterm infants persists after oral milk feeding has begun.

In the present study, we found that four infants had markedly low CM-C and CM-TG <0.01 mg/dL in cord blood. Their serum lipid profiles, cord blood TC, HDL-C, or TG, and 1 month blood TC, HDL-C, TG, CM-C, CM-TG, or CM-TG/C, did not differ from those of the other infants in the present study. Further clinical evaluations may provide some insight regarding the interpretation of CM-C and CM-TG in cord blood.

In conclusion, preterm infants had higher cholesterol and lower TG in the CM fraction compared with term infants. This characteristic CM composition was observed at birth and at 1 month of age. Therefore, some prenatal factors persist to influence CM lipidation during the early postnatal period. Further investigations are necessary to evaluate the clinical utility of CM composition measurements for preterm infants.

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Disclosure

The authors declare no conflict of interest.

Author contributions

T.O. and S.H. designed the study; Shigeru T. and Shori T. supervised the study; N.N. and S.H. collected data; N.N., A.S. and T.O. analyzed the data. A.S. and T.O. drafted the paper. All authors reviewed and approved the final manuscript.

References

1 Bansal N, Cruickshank JK, McElduff P, Durrington PN. Cord blood lipoproteins and prenatal influences. *Curr. Opin. Lipidol.* 2005; **16**: 400–8.
2 Yonezawa R, Okada T, Kitamura T *et al.* Very low-density lipoprotein in the cord blood of preterm neonates. *Metabolism* 2009; **58**: 704–7.
3 Pagnan A, Cerutti R, Donadon W *et al.* Cord blood cholesterol, triglycerides and lipoprotein electrophoresis in 124 Italian infants. *Ric. Clin. Lab.* 1976; **6**: 259–66.
4 Glickman RM, Rogers M, Glickman JN. Apolipoprotein B synthesis by human liver and intestine *in vitro*. *Proc. Natl Acad. Sci. USA* 1986; **83**: 5296–300.
5 Thibault L, Ménard D, Loirdighi N, Levy E. Ontogeny of intestinal lipid and lipoprotein synthesis. *Biol. Neonate* 1992; **62**: 100–7.
6 Okazaki M, Usui S, Ishigami M *et al.* Identification of unique lipoprotein subclasses for visceral obesity by component analysis of cholesterol profile in high-performance liquid chromatography. *Arterioscler. Thromb. Vasc. Biol.* 2005; **25**: 578–84.
7 Furusyo N, Ai M, Okazaki M *et al.* Serum cholesterol and triglyceride reference ranges of twenty lipoprotein subclasses for healthy Japanese men and women. *Atherosclerosis* 2013; **231**: 238–45.
8 Ménard D. Functional development of the human gastrointestinal tract: Hormone- and growth factor-mediated regulatory mechanisms. *Can. J. Gastroenterol.* 2004; **18**: 39–44.
9 Patterson AP, Tennyson GE, Hoeg JM, Sviridov DD, Brewer HB Jr. Ontogenetic regulation of apolipoprotein B mRNA editing during human and rat development *in vivo*. *Arterioscler. Thromb.* 1992; **12**: 468–73.
10 Jin ZW, Nakamura T, Yu HC, Kimura W, Murakami G, Cho BH. Fetal anatomy of peripheral lymphatic vessels: A D2-40 immunohistochemical study using an 18-week human fetus (CRL 155 mm). *J. Anat.* 2010; **216**: 671–82.
11 Grassi R, Farina R, Floriani I, Amodio F, Romano S. Assessment of fetal swallowing with gray-scale and color Doppler sonography. *Am. J. Roentgenol.* 2005; **185**: 1322–7.
12 Sangild PT, Petersen YM, Schmidt M *et al.* Preterm birth affects the intestinal response to parenteral and enteral nutrition in newborn pigs. *J. Nutr.* 2002; **132**: 2673–81.
13 Buddington RK, Sangild PT, Hance B, Huang EY, Black DD. Prenatal gastrointestinal development in the pig and responses after preterm birth. *J. Anim. Sci.* 2012; **90** (Suppl 4): 290–8.
14 Hussain MM, Rava P, Walsh M, Rana M, Iqbal J. Multiple functions of microsomal triglyceride transfer protein. *Nutr. Metab. (Lond)* 2012; **9**: 14.
15 Yao Y, Lu S, Huang Y *et al.* Regulation of microsomal triglyceride transfer protein by apolipoprotein A-IV in newborn swine intestinal epithelial cells. *Am. J. Physiol. Gastrointest. Liver Physiol.* 2011; **300**: G357–63.

早産児におけるカイロミクロンの特性について

ジャロウ綾子

【背景】 DOHad（Developmental Origins of Health and Disease）という、「将来の健康や特定の病気へのかかりやすさは、胎児期や生後早期の環境の影響を強く受けて決定される」という概念がある。具体的には、低出生体重児は成人になり糖尿病や高血圧、高脂血症など、いわゆるメタボリックシンドロームを発症するリスクが高くなること言われている。また、近年の新生児医療の進歩により新生児死亡率は低下し、超低出生体重児においても生存率が高まった。一方で、新生児期の疾患に起因する後遺症のために精神発達遅滞、運動障害を生じることも少なくない。ヒトの大脳はほとんどがリン脂質でできており、早産児（新生児）における脂肪酸、脂質代謝特性を明らかにし、適切な脂質栄養法を確立することは後遺症のリスクの軽減につながる可能性がある。新生児は成人と比較し、質と量の観点から独自のリポ蛋白プロファイルを有し、これまでの研究で我々は、正期産児と早産児の臍帯血や出生後早期のリポ蛋白プロファイルの変化に関して検討を行ってきた。今回、カイロミクロン（CM）分画の中のコレステロール（C）濃度とトリグリセライド（TG）濃度を測定し、正期産児と早産児で比較検討を行った。

【方法】2004 年 9 月 1 日から 2010 年 3 月 31 日に当院で合併症のない母体から出生し、仮死を除外した在胎 37 週から 41 週の正期産児 74 名と在胎 29 週から 36 週の早産児 59 名の 133 名（男：女 ＝ 81:52）を対象とした。臍帯血と生後 1 か月時の空腹時静脈血にて、CM、TC、TG をゲルろ過 HPLC（高速液体クロマトグラフィー）法で測定した。これらを早産児と正期産児とで比較検討した。出生体重との関係については、Z スコアを用いて検討をおこなった。Z-スコアは、標準偏差の数が母平均より上または下である度合いで、その絶対値が大きければ大きい程、分布の平均値からのずれが大きいことを示す。なお、本研究は日本大学医学部附属板橋病院の臨床研究倫理審査委員会で承認され（承認日 平成 17 年 12 月 16 日）、参加する親から書面によるインフォームドコンセントを得た。

【結果】 早産児では、正期産児と比較して臍帯血と生後 1 か月の静脈血の両者において CM-TG / C 比は有意に低値であった（$p<0.001$）。単相関分析において在胎週数は、出生時(臍帯血)の CM-TG / C 比（$r=0.331$、$p<0.003$）、生後 1 か月（静脈血）の CM-TG / C 比（$r=0.221$、$p<0.0119$）と強い正相関を示した。

【考察】経口哺乳開始前の臍帯血において、早産児と正期産児とでは、CM の脂質構成に相違が認められた。正期産児と比べると、早産児は生後 1 カ月で明らかに CM 中の C は高く、TG は低値であることがわかった。早産児では生後 1 か月の CM の構成脂質内容は、出生後の哺乳内容に影響されると同時に、何らかの出生前の胎内因子による影響を受けることが推察された。ブタ早産児において、腸管栄養の際に小腸のミクロソームトリグリセリド転送蛋白（microsomal triglyceride transfer protein : MTP）mRNA の発現やその活性が誘導されないとの報告があり、早産児の哺乳開始後の CM の TG 取り込み低下のメカニズムは、ブタの場合と同様に腸管機能の成熟の遅れとして、MTP に関連する TG の転送障害が推測される。

また、食事中の TG は、小腸内で胆汁酸とミセルを形成し、膵リパーゼの作用により脂肪酸とグリセロール（またはモノアシルグリセロール）に分解され、小腸上皮細胞内に取り込まれる。小腸上皮細胞内に取り込

まれた脂肪酸とグリセロールは TG に再合成され、MTP によって小胞体の内腔に輸送、アポ-48 に転送され、アポ A-I や A-IV、C 群とともに、原始 CM が合成される。膵リパーゼ活性は正期産児と比較し、早産児でより低下していることが知られている。膵リパーゼの活性低下により、小腸上皮細胞内に取り込まれる脂肪酸やグリセロールが少ないことで、TG の再合成が進まず、早産児における CM-TG が低値であった可能性も考えられる。

早産児では臍帯血と 1 か月後 CM-TG/C が低値であり、TG が低値であったが、LPL（lipoprotein lipase）活性が早産児で亢進していることが原因かは不明である。当施設の吉川、岡田らの先行研究[1]においては、低出生体重児では出生直後は正期産児と比べて LPL 活性はむしろ低下しているが、生後 1 か月になると LPL 活性は catch-up し、血漿中の VLDL(very low-density lipoprotein)-TG を細胞内へ取り込むことによる皮下脂肪厚の増大が推測されたと報告されている。VLDL のこのような動態の影響が CM にでている可能性もあるが、小腸粘膜細胞における CM の形成（lipidation）の段階でも低出生体重（早産）が影響した結果であるかは今後の研究の課題である。

母体-胎盤－胎児の生理的構造関係において、リポ蛋白はそのままでは胎盤を通過せず、LDL (low-density lipoprotein)レセプターや VLDL レセプターを介して取り込まれ、水解と再合成を経て臍帯血に分泌される。妊娠糖尿病では VLDL レセプターの発現の増強と臍帯血での TG 上昇が報告されている。胎児の血清脂質は母体より約 1/3 低い値に保たれており、脳などで必要なコレステロール(TC)は胎児が合成していると考えられる。また胎児においては、肝の LDL レセプター活性の増加は、在胎週数と正の相関を示 し、血中の LDL コレステロール濃度とは負の相関にある。当施設の長野、岡田らの先行研究[2]において、新生児の TC の組成について、正期産児と早産児の出生時と生後 1 か月の静脈血を比較した研究が行われている。この研究では、TC 中の VLDL、LDL、HDL (high-density lipoprotein)、さらに粒子の大きさによる構成について調べられている。正期産児では、出生時（臍帯血）の TC と比較して、生後1ヶ月では全ての分画において、数値が上昇していた。早産児では、出生時の LDL が正期産児と比較して特に高かった。正期産児と早産児とでは、TC のプロファイルが異なり、また出生時と生後 1 か月で TC の増減も異なることがわかっている。

また、正期産児と早産児において、消化管機能と肝代謝機能の発達の程度は児の在胎週数で異なり、早い在胎週数で出生すれば、臓器の機能はより未熟である。膵リパーゼ活性は正期産児と比較し、早産児でより低下していることが知られている。膵リパーゼの活性低下により、小腸上皮細胞内に取り込まれる脂肪酸やグリセロールが少ないことで、TG の再合成が進まず、早産児における CM-TG が低値であった可能性も考えられる。

動物を用いた研究を含めて、早産と CM 形成に関連した研究は極めて少ない。今後の研究で、早産児における CM 分画への脂質の転送障害と経腸栄養が確立した 1 か月の新生児期にも CM への TG 転送障害が続いている正確な機序を明らかにする必要がある。

【結論】新生児の CM 中のコレステロール（C）とトリグリセリド（TG）について、明らかにした。早産児では出生時と生後 1 か月時で、CM における TG の組み込みが有意に低いことが分かった。経口摂取が始まってもなお TG 組成は低値であることから、このメカニズムには、出生前の要因が影響していると考えられた。

【文献】

1) Yoshikawa K, Okada T, et al. Association between serum lipoprotein lipase mass concentration

and subcutaneous fat accumulation during neonatal period. European Journal of Clinical Nutrition 2010; 64: 447–453.

2) Nagano N, Okada T, et al. Early postnatal changes of lipoprotein subclass profile in late preterm infants. Clinica Chimica Acta 2012; 413: 109–112.