meaningful heart rate records to be obtained. A minimum of 2 hours of FHR recording was obtained in only 27 pregnancies or 50% of the preterm labors that led to delivery.

The incidence of intrapartum fetal asphyxia, the limitations in the clinical prediction of the preterm fetus at risk, and the possible significance of such insults suggest that routine umbilical cord blood gas and acid-base analysis of preterm deliveries <34 weeks' gestation would be appropriate at this time.

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Hypertriglyceridemia and hypoxemia in small-for-gestational-age fetuses

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Plasma triglyceride concentration and blood oxygen tension were measured in samples obtained by cordocentesis from 35 small- and 54 appropriate-for-gestational-age fetuses at 18 to 36 weeks' gestation. In the appropriate-for-gestational-age fetuses there was an exponential decrease in plasma triglycerides with gestation. Some small-for-gestational age fetuses were hypertriglyceridemic and the degree of this biochemical disturbance was significantly correlated with the degree of fetal hypoxemia. (AM J OBSTET GYNECOL 1990;162:382-6.)

Key words: Cordocentesis, fetal hypoxemia, fetal triglycerides, small-for-gestational-age fetus, fetal blood

In a study aimed at the detection of familiar hyperlipoproteinemia, Tsang et al.[1] measured umbilical cord plasma triglyceride concentration. An incidental finding of this study was the association between cord blood hypertriglyceridemia and maternal-fetal problems including maternal hypertension, prolonged duration of labor, umbilical cord around the infant's neck, meconium-stained amniotic fluid, post-term delivery, and decreased 1-minute Apgar scores. It was suggested that all these variables are associated with chronic or acute antepartum or intrapartum fetal anoxia and that cord blood triglyceride measurement might provide a quick, inexpensive, and easily available approach to semiquantitation of antepartum or intrapartum fetal distress. Furthermore, it was speculated that measurement of cord blood triglycerides may prove to be a useful predictor of future growth and development.

The aim of this study is to measure the plasma triglyceride concentration and oxygen tension in samples obtained by cordocentesis from appropriate- (AGA) and small-for-gestational-age (SGA) fetuses and examine whether intrauterine hypoxia is associated with fetal hypertriglyceridemia.

Patients and methods

Reference ranges for fetal plasma triglyceride concentration with gestation were constructed by analysis of samples obtained by cordocentesis from 54 AGA

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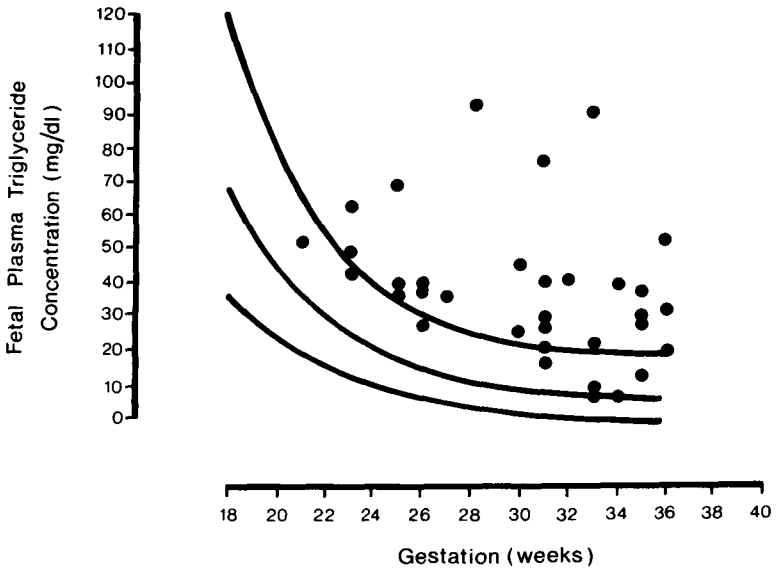

Fig. 1. Reference range (mean and individual 95% confidence intervals) of fetal plasma triglyceride concentration with gestation, which was constructed from the study of 54 AGA fetuses (●). Also shown are umbilical cord plasma triglyceride concentrations obtained from six elective cesarean (○) and 12 vaginal (△) deliveries at term.

fetuses undergoing prenatal diagnosis at 18 to 36 (mean, 26) weeks' gestation.[2] The mean blood Po_2 and glucose concentrations were 41 (SD, 9) mm Hg and 3.68 (SD, 0.65) mmol/L, respectively, and the individual values for each of these AGA fetuses were within the 95% normal ranges for gestation.[3, 1] The indications for cordocentesis were prenatal diagnosis of inherited blood disorders (8), maternal rubella infection (2), fetal karyotyping because of late booking in mothers of advanced age (10), or ultrasonographic detection of fetal malformations (renal, 21; duodenal atresia, 4; pulmonary cyst, 1; hydrocephalus, 8). In all cases the fetal karyotype was normal. Furthermore, none of these fetuses had the blood disorder or infection for which they were tested.

Fetal blood was also obtained by cordocentesis from 38 women referred to our unit at 21 to 36 (mean, 30) weeks' gestation for fetal karyotyping and blood gas analysis because of ultrasonographic evidence of severe fetal growth retardation. Gestational age in both AGA and SGA fetuses was calculated by Nägele's rule and confirmed by an ultrasonographic scan in early pregnancy. In SGA fetuses the abdominal circumference was 2 to 6 (mean, 4.1) SD below the normal mean for gestation. In 20 (57%) cases there was oligohydramnios, defined by the absence of any pocket of amniotic fluid >1 cm in diameter, and in nine (26%) cases the amniotic fluid was subjectively considered to be reduced. In three of the SGA fetuses the karyotype was abnormal (two cases of triploidy and one case of trisomy 21) and data from these fetuses were not analyzed. All the mothers were healthy and on screening had negative test results for antinuclear factor, toxoplasmosis, rubella, cytomegalovirus, and syphilis. There were no drug or alcohol abusers but 11 patients were cigarette smokers. Pregnancy-associated hypertension was present in seven (20%) of the cases at the time of cordocentesis.

Cordocentesis was performed as an outpatient procedure without maternal fasting or sedation. The umbilical cord vessel sampled was identified as artery or vein by the ultrasonographically detected turbulence after the intravascular injection of 200 μl of normal saline solution.[2] The fetal origin of blood was subsequently confirmed by Kleihauer testing. Maternal blood was taken from an antecubital vein immediately before fetal blood sampling. Fetal blood (250 μl) was collected into heparinized syringes and blood gas analysis was performed with a Radiometer ABL 330 blood gas analyzer (Copenhagen, Denmark). Umbilical venous cord and maternal venous blood were also obtained after 12 vaginal and 6 elective cesarean deliveries at 38 to 40 weeks' gestation from women with uncomplicated pregnancies.

The study was approved by the hospital ethical committee and informed consent was obtained from the patients. The indications for cordocentesis in the conditions described are reviewed elsewhere.[2]

For determination of plasma triglycerides, blood was centrifuged (200 *g* at 4° C) and the plasma stored at −70° C for subsequent analysis. Triglycerides were measured with 10 μl of plasma by a fully enzymatic

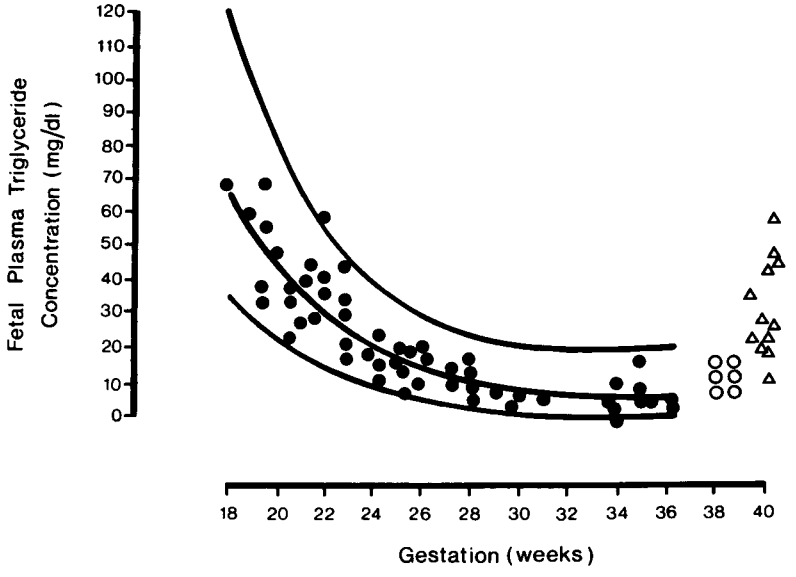

Fig. 2. Individual values of plasma triglyceride concentration of 35 SGA fetuses are plotted on the reference range (mean and individual 95% confidence intervals) with gestation.

colorimetric procedure (Triglycerides N, Wako Pure Chemicals Ltd., West Germany) performed on a discrete automated analyzer (Cobas MIRA, Roche Diagnostics Ltd., Basel, Switzerland). The intraassay coefficient of variation was 1.5%.

Statistical analysis. Statistical analysis was performed with a statistical package for personal computers (P. Royston, Timberlake Clark Ltd., London, England). In the AGA group, the distribution of the data of fetal plasma triglyceride concentration was skewed and was made gaussian by logarithmic (base 10) transformation. The relationship between fetal plasma $\log_{10}$ triglyceride concentration and gestation was adequately described by a quadratic polynomial model. To produce the reference ranges of plasma triglyceride concentration in mg/dl with gestation the limits of the calculated reference range in logarithms were subjected to an antilogarithmic transformation. Because blood Po_2 and plasma triglyceride concentration change with gestation in AGA fetuses, the degrees of hypertriglyceridemia and hypoxemia in SGA fetuses were defined as the number of SD of observed plasma triglyceride concentration and blood oxygen tension from the normal mean for the corresponding gestation; these were expressed as Δ log triglyceride and Δ Po_2, respectively.[3] The unpaired Student t test was applied to test for differences in the mean Δ log triglyceride in the AGA and SGA groups, and for comparison of the vaginally delivered and ceserean groups.

Results

In the AGA group the fetal plasma triglyceride concentration decreased exponentially with gestation (Fig. 1) and the relationship was well fitted by a quadratic model

$$[y = 4.249 - 0.18x + 0.00269x^2$$

where $y = \log_{10}$ (triglyceride concentration + 10), x = completed weeks of gestation]. The maternal plasma triglyceride concentration increased linearly with gestation [$y = 1.919 + 0.01x$, where $y = \log_{10}$ (triglyceride concentration + 3), x = weeks] and there was no correlation between maternal Δ log and fetal Δ log triglyceride concentrations ($r = 0.03$, $n = 54$). For the samples collected at delivery, there was no significant difference between vaginal and ceserean delivery groups in mean maternal plasma log triglyceride concentration ($t = 0.73$, $p > 0.47$), but the mean fetal plasma log triglyceride concentration was 84% higher (95% confidence intervals = +14% to +196%) in the group delivered vaginally (Fig. 1; $t = 2.55$; $p < 0.05$). The mean fetal plasma triglyceride concentration in SGA fetuses was 68% higher (95% confidence intervals = +44% to +96%) than the AGA fetuses (Fig. 2; $t = 6.65$, $p < 0.0001$), but there was no difference in the maternal triglyceride concentrations in the two groups ($t = 0.43$, $p > 0.66$). In addition, the degree of hypertriglyceridemia in SGA fetuses correlated significantly with the degree of hypoxemia (Fig. 3; $r = 0.43$, $n = 35$, $p < 0.01$). There was no significant correlation between the degree of hypertriglyceridemia and gestational age ($r = 0.05$, $p > 0.75$).

Comment

Fetal plasma triglyceride concentration decreases exponentially with gestation. This observation is compat-

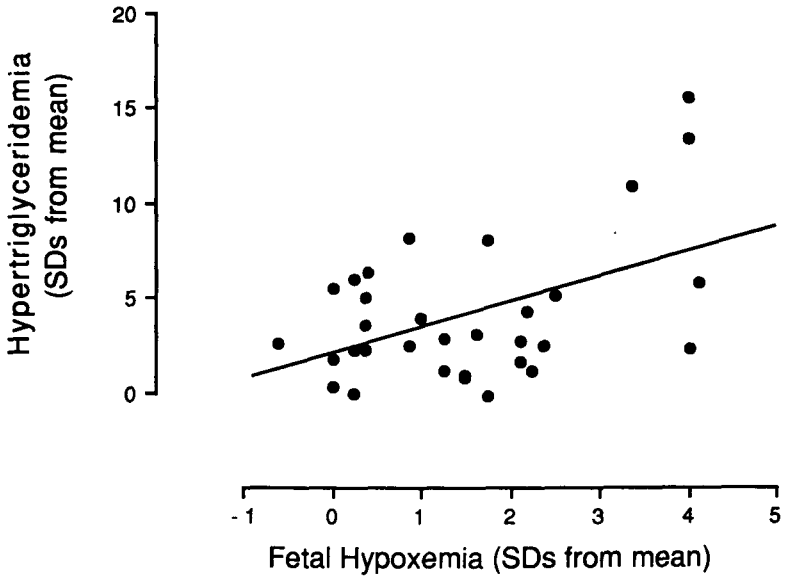

Fig. 3. Relationship of hypertriglyceridemia (triglyceride difference from normal mean from gestation in SDs) and hypoxemia (difference in oxygen tension from normal mean for gestation in SDs) in 35 SGA fetuses.

ible with reported values in cord blood at the time of delivery. Thus, premature infants of 25 to 26 weeks' gestation have higher cord triglyceride concentration than that of those delivered after 27 weeks' gestation.[5] The absence of significant correlation between fetal and maternal triglyceride concentrations suggests that there is no significant transplacental transport of this lipid, and that the fetal plasma triglyceride concentration reflects fetal metabolism. Fetal tissues are capable of triglyceride synthesis from ≥12 weeks' gestation.[6] However, deposition of adipose tissue begins after 24 weeks' gestation and increases exponentially, so that at 32 weeks' gestation the fetal fat content is 3.5%, and at 40 weeks' gestation 16% of the body weight.[7] Therefore, the observed decrease in plasma triglyceride concentration with gestation may be a result of increased use by the fetus for deposition into adipose tissue.

The cord plasma triglyceride concentration at elective ceserean section is similar to the levels in samples obtained by cordocentesis in late gestation. However, the plasma concentration in samples obtained from the umbilical cord at vaginal delivery (similar to that reported in previous studies), is significantly higher than that after cesarean section.[1, 8] Therefore, the stress of labour is associated with an increase in plasma triglycerides, probably as a result of catecholamine-mediated lipolysis.

The finding of hypertriglyceridemia in some SGA fetuses and the significant correlation between the degree of this biochemical disturbance with the degree of fetal hypoxemia provide evidence for the hypothesis of Tsang et al.[1] and other investigators[8, 9] that the plasma triglyceride concentration in cord blood at delivery may be an indicator of antepartum hypoxia. Hypertriglyceridemia may be a result of lipolysis of fetal fat stores. The energy requirements of the fetus are normally met largely by the oxidation of glucose. Because some SGA fetuses are hypoglycemic it is possible that in these fetuses lipids are mobilized from fetal adipose tissue to provide an alternative substrate for oxidation, thereby making more glucose available for metabolism in the brain.[10] Alternatively, in SGA fetuses there may be decreased use of circulating triglycerides. This is analogous to the finding in SGA and premature infants that have a reduced ability to clear triglycerides from their circulation after the administration of intralipid.[5, 11, 12] We have previously shown that hypoxemic SGA fetuses tend to be hypoglycemic and hypoinsulinemic.[4, 13] Because insulin promotes tissue uptake and deposition of lipids, the hypoinsulinemia of SGA fetuses could be responsible for the observed hypertriglyceridemia.[14]

In AGA fetuses, the plasma triglyceride concentration decreases exponentially with gestation, probably reflecting increased uptake into adipose tissue. In SGA fetuses, there is a correlation between hypertriglyceridemia and hypoxemia. However, it is uncertain whether fetal hypoxemia is causative of hypertriglyceridemia or that both factors are related to the degree of uteroplacental insufficiency. The differential contribution of these two mechanisms may be determined by examination of the effect of maternal hyperoxygenation and correction of the fetoplacental hypoxia on the fetal plasma triglyceride concentration.[15] Furthermore, to determine whether hypertriglyceridemia is a

result of lipolysis or reduced use of lipid it would be necessary to measure the fetal blood glucose and plasma glycerol, nonesterified fatty acid, and insulin concentrations, in addition to the triglyceride concentration and oxygen tension in SGA fetuses.

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