Effects of gestational alcohol exposure on the fatty acid composition of umbilical cord serum in humans[1–3]

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ABSTRACT This study examined the effects of maternal periconceptional alcohol intake on polyunsaturated fatty acid (PUFA) concentrations in human neonates. The area percentage of each fatty acid in cord blood serum from 12 infants born to control women (who consumed <2 mL absolute ethanol/d) was compared with that of 9 infants born to women whose periconceptional alcohol intake averaged ≥30 mL absolute ethanol/d. Periconceptional alcohol use was associated with a 30% increase in the proportion of docosahexaenoic acid (22:6n−3) in cord blood (3.0% of total lipid in control infants compared with 3.9% in alcohol-exposed infants; $P < 0.01$). The rise in the proportion of 22:6n−3 was responsible for increases in the ratio of n−3 to n−6 fatty acids and the ratio of long-chain n−3 to n−6 fatty acids ($P < 0.055$). Examination of the lipid-class fatty acid profile indicated that serum lipid alterations were localized to the cholesterol esters; 22:6n−3 in the cholesterol esters of alcohol-exposed infants increased 54% ($P < 0.011$) and arachidonic acid increased 55% ($P < 0.005$). The relative fatty acyl composition of maternal serum showed a significant increase in 18:0 fatty acids in the alcohol-exposed group (25%, $P < 0.005$) but there were no changes in the other fatty acids. The increase in the proportion of 22:6n−3 was unexpected but is consistent with the hypothesis that this essential lipid may be conserved selectively. These results imply that the lifelong neurobehavioral and sensory dysfunction in fetal alcohol syndrome and other alcohol-related neurodevelopmental disorders may be due in part to PUFA dysregulation. *Am J Clin Nutr* 2000; 71(suppl):300S–6S.

KEY WORDS Docosahexaenoic acid, DHA, polyunsaturated fatty acids, PUFAs, lipids, ethanol, alcohol in pregnancy, gestational alcohol exposure, neonate, fetus, umbilical cord serum

INTRODUCTION

Ethanol is a potent modulator of lipid metabolism and is known to alter the fatty acid profiles of many organs (1, 2). For example, concentrations of arachidonic acid, docosahexaenoic acid (22:6n−3), or both may be decreased in the liver (3) or brain (4, 5) of animals after chronic alcohol exposure. Decreases in these long-chain polyunsaturated fatty acids (LCPUFAs) have also been observed in the blood of alcoholics (2). Alterations in LCPUFA concentrations in cells and organs lead to changes in physiologic function. The loss of 22:6n−3 in particular from the central nervous system (CNS) may lead to suboptimal CNS development and function (6–8). For example, Uauy et al (9) observed decreased visual acuity in premature infants fed a formula based on corn oil (high in n−6 fatty acids) compared with infants supplemented with marine oil (containing long-chain n−3 fatty acids). Carlson and Werkman (10) observed reductions in performance on measures related to visual attention and memory by using the Fagan test at 12 mo of age in infants fed a vegetable oil–based formula compared with infants supplemented with marine oil during the first 2 mo of life. Autopsy studies showed that human infants fed vegetable oil–based formulas that contained neither arachidonic acid nor 22:6n−3 had significantly lower brain 22:6n−3 concentrations than did infants who were breast-fed (11, 12). Taken together, these studies indicate that a failure to supply adequate 22:6n−3 during critical periods of development can lead to suboptimal CNS maturation and cognitive dysfunction, visual dysfunction, or both (13). Failure to supply these LCPUFAs during late fetal development, when there is a surge in arachidonic acid and 22:6n−3 accumulation in the CNS accompanying the brain growth spurt (14), may lead to adverse neurochemical consequences.

Alcohol abuse during pregnancy may lead to alcohol-related neurodevelopmental disorders (ARNDs; 15), which are commonly manifested as impairment of cognitive function and behavior (16). Fetal alcohol syndrome (FAS) is characterized by prenatal and postnatal growth retardation and morphologic abnormalities in addition to CNS involvement, which may include mental retardation (16). The CNS dysfunctions associated with intrauterine alcohol exposure may be related, in part, to alterations in PUFA metabolism and deposition. Alterations in

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22:6n−3 concentrations may contribute to CNS impairment because of the functional significance of this fatty acid for CNS development, as noted above (6–10, 13).

Gestational alcohol abuse may compromise essential fatty acid (EFA; 18:3n−3 and 18:2n−6) status in 2 ways. First, pregnancy stresses maternal EFA status (17, 18) because the mother must supply all of the fatty acids needed for fetal and placental growth. It is also known that the placenta transports individual PUFAs selectively, each with its own selectivity factor (17), and alcohol can disturb placental transport (19). Second, alcohol increases fatty acid catabolism (2, 20) and, depending on the dose and frequency of alcohol abuse, may lead to decreased concentrations of LCPUFAs (1, 2). This suggests that pregnant women who abuse alcohol may have infants with lower LCPUFA concentrations in several organs, including the brain, perhaps due to altered lipid metabolism. Supporting this argument are the recent findings of Burdge et al (21), who showed that newborn guinea pigs have marked reductions in 22:6n−3 concentrations in brain phospholipids as well as a loss of the behavioral righting reflex after daily in utero alcohol exposure, and that the deficit is partially reversed when alcohol exposure is paired with tuna-oil supplementation.

This preliminary investigation examined, for the first time, the effects of alcohol use during pregnancy on serum PUFA concentrations in human neonates. Profiles of both umbilical cord and maternal serum PUFAs were examined in neonates and mothers with relatively high amounts of periconceptional alcohol exposure and in control subjects.

SUBJECTS AND METHODS

Subjects

Informed consent for the acquisition and use of umbilical cord and maternal blood samples was obtained upon admission into the study in accordance with a protocol approved by Wayne State University Institutional Review Board. Medical and social histories of all patients were obtained upon initial presentation for prenatal care in an antenatal clinic. Socioeconomic status was measured by using a modified Hollingshead 2-factor (occupation and education) index of social position (22). Detailed histories of alcohol and cigarette use in the periconceptional period and during pregnancy were obtained from the mothers upon admission to prenatal care and at each subsequent visit. Participants were recruited based on alcohol consumption, which was determined from their acknowledged drinking histories obtained by screeners skilled at eliciting drug and alcohol histories in structured, scripted interviews (23). The structured interview included the full-scale Michigan Alcoholism Screening Test (24) and T-ACE scales (25). Participants were categorized according to the estimated milliliters of absolute alcohol consumed per day (AAD) around the time of conception and were assigned to either the control group or the alcohol group. Subjects who reported periconceptional alcohol consumption within the range of 0–1.8 mL AAD were assigned to the control group (n = 14 mothers and 12 infants). Women with periconceptional alcohol intake ≥30.0 mL AAD were assigned to the alcohol group (n = 13 mothers and 9 infants). Maternal blood samples were obtained from participants after delivery by venipuncture and umbilical cord blood samples were collected from the placental portion of the umbilical vein into a serum-separator evacuated tube after clamping the umbilical cord. Both cord and maternal serum samples were stored at −70°C until analysis. Most of the serum samples from the mothers and infants included in this study were also used in a study of carbohydrate-deficient transferrin, reported elsewhere (26).

Serum extraction, derivatization, and analysis

From each serum sample, 200 μL were extracted by using the method of Bligh and Dyer (27) for total lipids after the addition of 20 μg of the internal standard tricosanoic acid. Lipid-class separation was performed by using the method of Agren et al (28) with Bakerbond SPE* aminopropylsilane bonded silica gel columns (JT Baker Inc, Phillipsburg, NJ). All lipids were transmethylated according to the procedure of Morrison and Smith (29) by using a 14% wt:vol solution of boron trifluoride in methanol. The resulting fatty acid methyl esters were analyzed by using the method of Salem et al (3) with a Hewlett-Packard 5890 gas chromatograph (Hewlett-Packard, Palo Alto, CA) with a 10:1 split injection ratio on a 0.25 mm × 30 m DB-FFAP capillary column (J&W Scientific, La Palma, CA) using flame ionization detection. Data were expressed as a percentage of total fatty acid weight (% by wt) or referenced to an internal standard and expressed as an absolute concentration.

Statistical analysis

Statistical analysis was performed using the nonparametric Mann-Whitney U test with a Bonferroni/Dunn correction. A value of $P < 0.01$ was considered significant to compensate for multiple testing between groups.

RESULTS

Clinical features

A total of 27 mothers and 21 neonates (including 20 mother-infant pairs) participated in this study; 74% of the subjects were African American. Maternal demographic, pregnancy, and alcohol intake data are summarized in **Table 1**. Maternal age ranged from 17 to 41 y. The median age was 20.0 y for control subjects and 27.5 y for women in the alcohol group (Table 1). Fifty-five percent of the women had not completed a high school education, but most (70%) had continued beyond the tenth grade. There were no significant differences in socioeconomic status between the 2 groups. Forty-five percent of the control mothers and 63% of mothers in the alcohol group were smokers. All were multiparous and had experienced fewer live births than pregnancies due to either spontaneous or voluntary abortions.

Periconceptional alcohol consumption by all measures was significantly greater in the alcohol group than in the control group. The women in both groups reported that they reduced their alcohol consumption once they became aware of their pregnancies (data not shown), and ≈75% of the control subjects reported abstaining from drinking throughout pregnancy. Control subjects who continued drinking reported an average 93% decrease in alcohol consumption throughout the remainder of gestation. Women in the alcohol group who continued to drink during pregnancy reported an average daily decrease of 50%. This may have

TABLE 1
Demographic and clinical characteristics of subjects

	Control group (n = 14)	Alcohol group (n = 13)
Age (y)	21.8 ± 1.32 (20.0)	26.6 ± 2.16 (27.5)
Level of education (y)	11.3 ± 0.43 (11.0)	11.2 ± 0.46 (11.0)
Socioeconomic status[1]	3.8 ± 0.36 (4.0)	4.0 ± 0.5 (5.0)
Previous pregnancies (n)	2.6 ± 0.41 (3.0)	4.3 ± 0.62 (4.5)
Live births (n)	0.6 ± 0.39 (0.0)	1.5 ± 0.63 (1.0)
Cigarettes smoked/d	8.2 ± 3.3 (0.0	10.6 ± 4.91 (6.5)
Alcohol consumed in periconceptional period (mL/d)	0.06 ± 0.06 (0.0)	56.9 ± 8.87[2] (53.23)
Alcohol consumed during pregnancy (mL/d)	0.03 ± 0.03 (0.06)	23.66 ± 0.03[2] (7.2)
Alcohol consumed during pregnancy (mL/drinking day)	0.89 ± 0.59 (0.0)	124.21 ± 41.7[2] (97.59)
Alcohol consumed 2 wk before delivery (mL/d)	0.0 ± 0.0 (0.0)	9.17 ± 3.84[3] (2.07)
Proportion of drinking days 2 wk before delivery	0.0 ± 0.0 (0.0)	0.09 ± 0.04 (0.04)
Number of days subjects drank during pregnancy (n)	1.0 ± 0.7 (0.0)	36.9 ± 10.9[2] (34.0)
Total amount of alcohol consumed during pregnancy (mL)	3.84 ± 2.66 (0.0)	2702.4 ± 304.6[2] (2568.61)
Total score on the T-ACE scale for risk drinking (25)	0.18 ± 0.60 (0.0)	1.3 ± 0.6 (1.0)

[1] $\bar{x}$ ± SEM; median in parentheses. Socioeconomic status was determined with the Hollingshead 2-factor index of social position (22). This scale combines the educational level and occupation of the individual and spouse to define a social class.
[2,3] Significantly different from control group, [2] $P < 0.005$; [3] $P < 0.05$.

been due in part to obligatory counseling, which involved advice that reducing or ceasing intake of alcohol and other drugs would improve their babies' health. Only those women who reported the highest consumption of alcohol continued to drink alcohol near the end of pregnancy. Fifty-one percent of women in the alcohol group consumed alcohol during the 2-wk period before delivery, drinking a 2-day average of 13.0 mL/d (range: 41.4–81.62) for an average of 2 drinking days (range: 1–4; data not shown) within that 2-wk period. Both the reported proportion of drinking days during pregnancy and the amount of alcohol consumed per drinking day across pregnancy showed a pattern of binge drinking.

Fatty acyl composition of neonatal serum

As shown in **Table 2,** there were no significant differences in the fatty acid distribution of cord blood serum between women in the alcohol and control groups, with the exception of 22:6n−3. Periconceptional ethanol use in the alcohol group resulted in a 30% increase in the proportion of 22:6n−3, from an average of 3.0% in control subjects to 3.9% in the alcohol group. The increased proportion of 22:6n−3 was responsible for marginally significant increases in both the n−3 to n−6 ratio and the long-chain n−3 to n−6 ratio (P = 0.055). Similar trends were observed when the serum fatty acyl profiles were analyzed in terms of absolute concentrations (**Table 3**). Significance was not reached, due in part to the slight decline in the overall fat concentration.

Fatty acyl composition of lipid classes from neonatal cord serum

Examination of the fatty acyl profile of the major lipid classes in cord serum revealed significant rearrangements of n−3 and n−6 groups within cholesterol esters. As shown in **Table 4,** the

TABLE 2
Fatty acid weight percentage of serum total lipid extracts from human cord blood after intrauterine alcohol exposure

Fatty acid	Control group (n = 12)	Alcohol group (n = 9)
Nonessential (% by wt)	22.3 ± 0.4[1]	21.8 ± 0.7 (−2.2)
16:0		
16:1n−7	3.4 ± 0.2	3.0 ± 0.3 (−11.8)
18:0	9.0 ± 0.2	9.0 ± 0.3 (0.0)
18:1n−9	16.3 ± 0.7	15.3 ± 0.8 (−6.1)
18:1n−7	3.1 ± 0.1	2.8 ± 0.1 (−9.7)
20:3n−9	0.25 ± 0.02	0.20 ± 0.03 (–20.0)
Total nonessential	54.4 ± 3.5	52.1 ± 3.4 (−4.2)
n−6 Polyunsaturated (% by wt)	9.7 ± 0.5	9.4 ± 0.6 (−3.1)
18:2		
18:3	0.24 ± 0.03	0.23 ± 0.02 (−4.2)
20:2	0.6 ± 0.11	0.5 ± 0.08 (−16.7)
20:3	2.4 ± 0.80	2.3 ± 0.14 (−4.2)
20:4	13.8 ± 0.5	14.7 ± 0.7 (6.5)
22:4	0.62 ± 0.04	0.61 ± 0.04 (−1.6)
22:5	1.2 ± 0.11	1.1 ± 0.08 (−8.3)
Total n−6 polyunsaturated	28.6 ± 2.0	28.8 ± 2.1 (0.7)
n−3 Polyunsaturated (% by wt)	0.12 ± 0.03	0.09 ± 0.05 (−25.0)
18:3		
20:5	0.17 ± 0.03	0.14 ± 0.02 (−17.6)
22:5	0.22 ± 0.02	0.24 ± 0.02 (9.1)
22:6	3.0 ± 0.17	3.9 ± 0.28[2] (30.0)
Total n−3 polyunsaturated	3.5 ± 0.2	4.4 ± 0.4 (24.5)
n−3:n−6	0.12	0.15 (25.0)
Total lipids (mg/g)	1.83 ± 0.07	1.71 ± 0.13

[1] $\bar{x}$ ± SEM; Percentage difference between the alcohol-exposed infants' and control infants' values in parentheses.
[2] Significantly different from control group (Mann Whitney U test with Bonferroni/Dunn post hoc analysis), $P < 0.01$.

TABLE 3
Fatty acid concentration of serum total lipid extracts from human cord blood after intrauterine alcohol exposure[1]

Fatty acid	Control group (n = 12)	Alcohol group (n = 9)
Nonessential (μg/g serum)		
16:0	442 ± 21	400 ± 31 (−9.5)
16:1n−7	68 ± 6	56 ± 8 (−17.8)
18:0	178 ± 9	165 ± 9 (7.4)
18:1n−9	324 ± 83	278 ± 19 (−14.3)
18:1n−7	62 ± 4	50 ± 2[2] (19.6)
20:3n−9	4.5 ± 0.3	3.6 ± 0.6 (−20.0)
Total	1079 ± 70	952 ± 63 (−11.7)
n−6 PUFA (μg/g serum)		
18:2	191 ± 13	172 ± 16 (−10.1)
18:3	4.3 ± 0.7	4.1 ± 0.4 (−4.7)
20:2	11 ± 2.7	8 ± 1.2 (−24.3)
20:3	47 ± 2.9	42 ± 1.7 (−10.1)
20:4	271 ± 15	266 ± 14.8 (−1.8)
22:4	12 ± 1	11 ± 0.9 (−8.9)
22:5	24 ± 2.8	21 ± 1.3 (−13.8)
Total	560 ± 40.2	524 ± 39 (−6.4)
n−3 PUFA (μg/g serum)		
18:3	2.3 ± 0.6	1.5 ± 0.9 (−34.8)
20:5	7.3 ± 0.8	7.2 ± 1.1 (−1.4)
22:5	3.8 ± 0.4	4.0 ± 0.7 (5.3)
22:6	60 ± 3	71 ± 11 (19.7)
Total	73 ± 3.8	84 ± 10 (15.1)
n−3:n−6	0.13	0.16 (23.0)
Total lipid (mg/g)	1.83 ± 0.1	1.71 ± 0.13

[1] $\bar{x}$ ± SEM; percentage difference between the alcohol-exposed infants' and control infants' fatty acid values in parentheses.
[2] Significantly different from control group (Mann Whitney U test with a Bonferroni/Dunn post hoc analysis), $P < 0.01$.

weight percentage of arachidonic acid was increased in the total lipid extracts of cholesterol esters by 55.5%, from 10.8% in control infants to 16.8% in infants exposed to alcohol. The rise in arachidonic acid significantly increased the total n−6 PUFAs in alcohol-exposed infants by 24.0%.

There was a significant increase in the percentage of α-linolenic acid (18:3n−3) in the cholesterol esters of alcohol-exposed infants as compared with control infants; 18:3n−3 rose from 0.14% (control subjects) to 0.42% (alcohol-exposed subjects), a 3-fold increase in this EFA. Moreover, there was a 54.8% increase in 22:6n−3 in the cholesterol-ester fraction of alcohol-exposed infants; the percentage of 22:6n−3 rose from 0.84% in the control group to 1.26% in the alcohol-exposed group. The changes in 18:3n−3 and 22:6n−3 brought about a 44.4% increase in the total n−3 fatty acids and a 52.9% increase in the n−3 to n−6 ratio in the cholesterol esters of alcohol-exposed infants. No significant differences were found in other lipid classes (**Table 5**).

Fatty acyl composition of maternal serum

The fatty acyl composition of maternal serum samples, expressed as weight percentages, revealed a significant increase

TABLE 4
Fatty acid weight percentage of serum cholesterol esters in human cord blood after intrauterine alcohol exposure

Fatty acid	Control (n = 10)	Alcohol (n = 7)
Nonessential (% by wt)		
16:0	17.8 ± 0.7	15.31 ± 0.4 (−14.0)
16:1n−7	5.5 ± 0.4	4.5 ± 0.2 (−18.1)
18:0	3.5 ± 0.3	2.8 ± 0.2 (20.0)
18:1n−9	27.5 ± 1.1	26.1 ± 1.0 (−5.1)
18:1n−7	3.5 ± 0.4	3.3 ± 0.2 (−5.7)
20:3n−9	0.4 ± 0.07	0.2 ± 0.01 (−50.0)
Total	62.1 ± 1.9	54.2 ± 2.2 (−12.7)
n−6 Polyunsaturated (% by wt)		
18:2	13.4 ± 0.9	14.5 ± 1.3 (−8.2)
18:3	0.55 ± 0.06	0.54 ± 0.02 (−1.8)
20:2	0.12 ± 0.01	0.26 ± 0.06 (−116.7)
20:3	1.0 ± 0.04	1.1 ± 0.07 (−10.0)
20:4	10.8 ± 0.9	16.8 ± 0.6[2] (55.5)
22:5	0.32 ± 0.02	0.27 ± 0.02 (−15.6)
Total	26.2 ± 1.5	32.5 ± 1.2[3] (24.0)
n−3 Polyunsaturated (% by wt)		
18:3	0.14 ± 0.02	0.42 ± 0.09[2] (200.0)
22:6	0.84 ± 0.07	1.26 ± 0.14[3] (54.8)
Total	0.90 ± 0.11	1.68 ± 0.2[2] (44.4)
n−3:n−6	0.03 ± 0.004	0.05 ± 0.006[2] (52.9)

[1] $\bar{x}$ ± SEM; Percentage difference between the alcohol-exposed infants' values and control infants' values in parentheses.
[2,3] Significantly different from control group (Mann Whitney U test with a Bonferroni/Dunn post hoc analysis), [2] $P < 0.005$; [3] $P < 0.0167$.

TABLE 5
Fatty acid profile of serum cholesterol esters, triacylglycerols, phospholipids, and total lipid extracts from human cord blood after intrauterine alcohol exposure[1]

Fatty acid	Cholesterol esters	Triacylglycerols	Phospholipids	Total lipid extracts
20:4n−6 (% by wt)				
Control group (*n* = 10)	10.8 ± 0.9	5.3 ± 0.5	14.7 ± 0.4	13.8 ± 0.5
Alcohol group (*n* = 7)	16.8 ± 0.6[2]	5.8 ± 0.3	15.2 ± 0.8	14.7 ± 0.7
22:6n−3 (% by wt)				
Control group (*n* = 10)	0.84 ± 0.07	2.0 ± 0.3	4.0 ± 0.2	3.0 ± 0.2
Alcohol group (*n* = 7)	1.3 ± 0.1[2]	2.5 ± 0.4	4.6 ± 0.3	3.9 ± 0.3[2]
n−3:n−6				
Control group (*n* = 10)	0.03 ± 0.004	0.11 ± 0.01	0.17 ± 0.01	0.12 ± 0.01
Alcohol group (*n* = 7)	0.05 ± 0.006[2]	0.13 ± 0.02	0.19 ± 0.02	0.15 ± 0.01[2]

[1] $\bar{x}$ ± SEM.
[2] Significantly different from control group (Mann Whitney *U* test with a Bonferroni/Dunn post hoc analysis), $P < 0.0167$.

in 18:0 in the alcohol group (data not shown). There were no significant differences between groups in the other fatty acids.

DISCUSSION

This study examined the effects of periconceptional alcohol consumption on the fatty acid profile of neonates. The results show that alcohol use during pregnancy affects the distribution of fatty acids in the cord serum by increasing the proportion of 22:6n−3. These results provide evidence that maternal alcohol consumption alters fatty acid metabolism in the human fetus. However, the results must be qualified in several respects. Our analyses were performed at the end of pregnancy, by which time maternal drinking was markedly diminished. This was due, in part, to the counseling provided to the women, a necessity for the ethical treatment of pregnant women who drink alcohol. Nevertheless, it appears that this low amount of alcohol consumption was associated with increased cord plasma 22:6n−3 concentrations.

Alcohol consumption has generally been found to decrease PUFA concentrations, purportedly by inhibiting the elongation and desaturation of n−3 and n−6 precursors (30). However, 2 rodent studies as well as 1 human study have reported that chronic alcohol exposure led to increases in brain 22:6n−3 concentrations, even though most of the studies found declines. These seemingly disparate data can be better understood if interpreted with a new hypothesis concerning the mechanism of ethanol action on fatty acid metabolism (31, 32). In this view, the main effect of ethanol is to stimulate fatty acid catabolism. Fatty acid anabolism is then stimulated in vivo by a feedback mechanism in an adaptive response that serves to maintain tissue PUFA concentrations. This hypothesis has gained direct support from controlled dietary experiments of in vivo fatty acid metabolism in both cats and rhesus monkeys (31, 32), as well as from recent observations in alcoholic patients (N Salem Jr, J Hibbeln, B Wegher, and R Pawlosky, unpublished observations, 1999). In this view, the intensity of the alcohol stimulus is critical in determining the outcome when measured in terms of fatty acyl composition. Low doses of alcohol, repeated infrequently, may lead to stimulation of fatty acid metabolism, thereby increasing, for example, 22:6n−3 concentrations. However, in the case of alcoholism in which high alcohol consumption is typically repeated frequently, fatty acid catabolism overwhelms the rates of fatty acid elongation, desaturation, and transport and therefore tissue concentrations of LCPUFAs decline.

With this perspective, our finding of increased cord blood 22:6n−3 concentrations after in utero alcohol exposure may be interpreted to be a result of low amounts of maternal ethanol intake, leading to stimulation of fatty acid anabolism. This metabolic stimulation could explain the small increase in the 22:6n−3 concentrations. However, it would be predicted that relatively high amounts of in utero alcohol exposure would lead to reductions in tissue and blood concentrations of 22:6n−3.

Of course, the biochemical status of a fetus is complex because of its interactions with the mother's system. Differences in serum lipids between the 2 groups may reflect modifications in fatty acid transport or uptake. Alcohol has been shown to modify placental physiology and thereby alter nutrient flow from mother to fetus (33–36). For example, alcohol interferes with the transport of zinc and glucose (33, 34), and leucine incorporation into proteins was significantly lower in placentas of alcoholic women compared with those of abstainers (35). The placenta selectively sequesters arachidonic acid into phosphoglycerides for export into the fetal circulation (36). In particular, Ruyle et al (37) showed selective uptake of various fatty acids, including 22:6n−3, across the rat placenta, a process that may be modified by alcohol abuse.

A related hypothesis is that the rise in 22:6n−3 concentrations in the alcohol-exposed infants may reflect reductions in the capacity of other organs to accumulate 22:6n−3 from the blood. This hypothesis proposes that there are lower amounts of 22:6n−3 in, for example, the brains of alcohol-exposed infants. In a recent study by Burdge et al (21), feeding adult female guinea pigs alcohol both before and throughout pregnancy led to decreases in phospholipid 22:6n−3 concentrations in the brains of the newborn offspring, although the plasma and liver PUFA contents were unchanged. Evidence from a study performed in our laboratory indicated that alcohol administration during pregnancy increased serum 22:6n−3 concentrations in rat fetuses at gestational age 20 d, but that the percentage of this fatty acid was significantly decreased in the brain. (YM Denkins and N Salem Jr, unpublished observations, 1996).

In the present study, most (74%) of the women who participated were African American, a population with a higher likelihood of exhibiting ARNDs than whites (16), and this may have increased the probability of observing accompanying biochemical differences between the groups. FAS is the most severe consequence of intrauterine alcohol exposure, consisting of birth weight below the 10th percentile, phenotypically distinct facial anomalies, and CNS dysfunction (16). The rate of occurrence of FAS in African Americans is 7 times higher than that in whites, despite the fact that abstinence among African American women is significantly higher

(38) and the frequency of alcohol intake is significantly lower than that of white women. Among those who abuse alcohol, African American women more frequently exhibit binge-drinking behavior, drinking ≥5 drinks per occasion but in fewer episodes than their white counterparts (39). It has been postulated that the high peak blood alcohol concentrations associated with this type of drinking behavior put infants born to this population at significantly greater risk for alcohol-related birth defects such as FAS or ARNDs (16), which may contribute to differences in biochemical features. Although these results do not separate the effects of drinking from those of withdrawal, they show the effect of limited gestational alcohol exposure on the neonatal serum lipid profile.

Our results are not explained by the greater number of previous pregnancies in the alcohol group than in the control group (Table 1; $P < 0.06$), because maternal and neonatal 22:6n−3 concentrations in humans would be expected to decrease with successive pregnancies, not to increase as found here, based on the previous work of Hornstra et al (40). One other study reported elevated 22:6n−3 concentrations in cord plasma; Al et al (41) found that 22:6n−3 concentrations in umbilical plasma phospholipids were significantly higher after a pregnancy complicated by pregnancy-induced hypertension than after a normal pregnancy. However, the increased serum 22:6n−3 concentrations of the alcohol-exposed infants in the present study differ in that the change in 22:6n−3 concentrations was localized mainly to the cholesterol esters. There were no changes in phospholipids or triacylglycerols in these infants (Table 5). Pregnancy-induced hypertension has been shown to contribute to low birth weight and preterm delivery (42). Although alcohol-associated hypertension is common among women who drink heavily (43–45), the effect of alcohol abuse on the course of hypertensive pregnancies has not been studied adequately. However, Mankes et al (46) showed that alcohol administration during pregnancy increased hypertension, caused multiple birth defects, and increased fetal mortality in both normotensive and spontaneously hypertensive rats. The authors did not measure lipid composition.

Further study is needed to evaluate whether higher amounts of alcohol intake produce qualitatively similar results in terms of fatty acyl composition. Additional research is also needed to examine interactions between maternal alcohol intake and both maternal diet and infant outcomes.

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