

# *Trans* fatty intakes during pregnancy, infancy and early childhood

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## Abstract

All of the essential  $n - 6$  and  $n - 3$  fatty acids accumulated by the fetus must be derived by transfer from the maternal circulation, and ultimately must originate from the maternal diet. After birth, the breast-fed infant receives essential fatty acids via mother's milk, or human milk substitutes and later complementary foods. *Trans* fatty acids (TFA) may have adverse effects on growth and development through interfering with essential fatty acid metabolism, direct effects on membrane structures or metabolism, or secondary to reducing the intakes of the *cis* essential fatty acids in either mother or child. TFA are transported across the placenta and secreted in human milk in amounts that depend on the maternal dietary intake. Inverse associations have been shown between TFA and the essential  $n - 6$  and  $n - 3$  fatty acids in newborn infants, human milk and preschool children. This support the need to reduce industrially produced *trans* fatty acids (IP-TFA) and improve dietary fat quality, particularly by increasing intake of  $n - 3$  fatty acids.

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## 1. Introduction

*Trans* fatty acids (TFA) are present in the diet from two sources, the partial hydrogenation of fats and oils containing *cis* unsaturated fatty acids by industry, and in the milk and meat of ruminant animals as a result of biohydrogenation of fatty acids in the rumen. Whereas TFA can represent as high as 60% of the fatty acids in some shortenings and products made thereof, TFA typically represent 2–5% of the fatty acids in dairy fats and ruminant meats [1]. The estimated average intakes of TFA in Western countries in the 1980s and 1990s were in the range of 2.5–13 g/person/day, with average intakes generally higher in the U.S. and Canada than in Europe [2]. Up until about 2000, 80–90% of dietary TFA in the U.S. and Canada was derived from partially hydrogenated fats, with the remainder derived from dairy fats and ruminant meats [2,3]. However, reductions in the use of partially hydrogenated fats by the food industry has resulted in a decrease in the consumption of IP-TFA in many countries [4].

Arachidonic acid (C20:4 $n - 6$ , ARA) and docosahexaenoic acid (C22:6 $n - 3$ , DHA) are critically important in pre- and post-natal growth and development. Because ARA is found in cell membrane phospholipids throughout the body and is important as an eicosanoid precursor, in second messenger, cell signaling pathways and in cell division, ARA influences growth and development through multiple pathways. DHA is selectively accumulated in the amino phospholipids of membranes in the retina and brain grey matter and is important for visual and neural function [5]. ARA and DHA are synthesized from the dietary essential fatty acids linoleic acid (C18:2 $n - 6$ , LA) and alpha linoleic acid (C18:3 $n - 3$ , ALA), respectively, through  $\Delta 6$  and  $\Delta 5$  desaturation reactions, that occur primarily in the liver. Dietary patterns that compromise  $n - 6$  and  $n - 3$  fatty acid intakes, or alter the metabolism or incorporation of  $n - 6$  and  $n - 3$  fatty acids into developing tissues may, therefore, have adverse effects on fetal and infant development. TFA have the potential to have adverse effects on growth and development in several ways: through inhibition of the desaturation of LA and ALA to ARA and DHA, further metabolism of *trans* monoenoic,  $n - 6$  or  $n - 3$  fatty acids into unusual fatty acid isomers that are incorporated into tissues and disrupt membrane function or eicosanoid pathways, or through destruction of LA

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and ALA during industrial hydrogenation leading to loss of LA and particularly ALA from the food supply. This paper reviews exposure to TFA during growth and development secondary to maternal diet in pregnancy and lactation, and through the early childhood diet.

## 2. Placental fatty acid transfer and fetal development

Although several studies have pointed to mechanisms to facilitate preferential transfer of ARA and DHA across the placenta [6], it is clear that industrially created and naturally occurring TFA derived from the maternal diet are transferred to the developing human fetus [7,8]. Furthermore, the concentrations of TFA, as well as LA, ALA, ARA and DHA in maternal plasma lipids are significantly, and positively correlated with the level of the same fatty acid in infant plasma and umbilical cord lipids at birth [6,8], suggesting that maternal-fetal transfer, and thus fetal exposure is dependent on the concentration of the given fatty acid in the maternal plasma, and thus dietary intake. Studies with healthy pregnant women in Canada found mean concentrations of 4.0% TFA in maternal plasma triglycerides at 36 weeks gestation and 2.9% TFA in their newborn infants' plasma triglycerides at birth; however, the range of TFA concentrations was wide, with as high as 7.9 and 12.8% TFA in the maternal and infant plasma triglycerides, respectively [8]. Studies with adults have demonstrated that high amounts of TFA, similar to those intakes demonstrated in pregnant women and the developing infant before birth, have adverse effects on total cholesterol, total cholesterol/HDL cholesterol and inflammatory markers [9,10]. Some evidence has also been published to show that TFA alter expression of genes related to insulin sensitivity and risk of type 2 diabetes [11], which is also relevant in gestation and growth. Data to show differences in lipid metabolism or plasma lipids due to high exposure to TFA in pregnant women or infants, however, has not been published. Analysis of dietary intakes in Canada in 2000 estimated that at that time the mean intakes of TFA among pregnant women was 3.4–3.8 g/person/day, representing about 1.3% of total energy intakes, while the mean daily intakes of LA and ALA were 11.2 and 1.6 g/person, respectively [3,8]. However, the intake of TFA varied widely, with a range of intakes of 0.7–11.3 g/day, representing 0.2–3.2% total energy [3]. The major dietary sources of TFA were bakery foods which provided 33% of TFA intakes, while fast foods and snacks, breads, and margarines and shortenings provided 22, 10 and 8% of the total intake of TFA [3]. These studies show that the mean concentrations of TFA in maternal and newborn infant plasma triglycerides are similar to the concentration in the dietary fat (about 3–5% of total TFA), that intakes of TFA vary widely with some individuals having very high intakes and that the intake of TFA exceeds that of the essential  $n - 3$  fatty acids by more than two-fold.

Numerous experimental and clinical studies have provided evidence that DHA is important for visual and neural

development, particularly during early development [5]. In animals, inadequate maternal  $n - 3$  fatty acid intakes result in decreased accumulation of DHA in the fetal brain, altered neurotransmitter metabolism and decreased performance on tasks of learning behavior. Recent studies in humans also suggest that maternal DHA status during pregnancy is positively associated with neural development in the infant [12,13]. Further, in prematurely born infants ARA and DHA are positively associated with growth and indices of visual and neural development, respectively [5]. Some studies have shown an inverse association between ARA and infant birth weight and length of gestation, as well as between TFA and length of gestation and birth weight [8,14]. However, since TFA were inversely related to LA and LNA in the maternal plasma, women with higher intakes of TFA from foods containing partially hydrogenated fats may also have lower dietary intakes of LA and ALA [8]. Experimental studies provided evidence of reduced maternal plasma and liver DHA, reduced maternal liver desaturase enzyme activities, and reduced fetal DHA, but in the context of feeding with high amounts of TFA and low intakes of essential fatty acids. Whether or not the intakes of TFA interfere with LA or ALA metabolism in humans is uncertain, although it is clear that intakes of  $n - 3$  fatty acids are low among women and young children following western diets [3,8,15].

## 3. Human milk and infant development

Human milk is the sole source of nutrition for the exclusively breast-fed infant and provides all of the essential fatty acids needed for the infant's growth and development. On average, mature human milk provides 3.7 g fat/100 ml, representing about 50% of the dietary energy intake of the young infant. The high fat content of human milk results in higher exposure to fatty acids, relative to body weight and as a percent of total energy intake than may be apparent from the fatty acid distribution in human milk. A large number of studies have documented the presence of TFA from partially hydrogenated oils and from ruminant meats and milks in human milk [7,16,17]. Further, dietary intervention studies have shown rapid changes in the secretion of TFA into human milk with addition or removal of TFA isomers from the diet of lactating women [7]. These studies clearly show that the breast-fed infant is not protected from exposure to TFA through mechanisms in the mammary gland for selective fatty acid secretion. This is further emphasized by the highly significant linear relationship between the concentration of TFA in mothers' milk and in the plasma triglycerides of breast-fed infants' ( $r=0.82$ ,  $P<0.001$ ), again showing that maternal TFA intake directly determines exposure of the infant [17]. Analyses of mature human milk in Canada in the late 1990s found a mean concentrations of 7.1 g TFA, with a range of 2.2–18.7 g TFA/100 g milk fatty acids [17]. Chen et al. [16] also found as high as 17.2 g TFA in human milk fat in Canada.

The exposure of breast-fed infants to TFA can be estimated from the range of TFA in human milk, assuming 50% energy from fat, and an intake of 780 ml/day by the breast-fed infant. In our studies, breast-fed infants consumed 1.1–9.5% energy from TFA, equivalent to 0.7–5.4 g/day/infant, with mean values of 3.5% energy and 2.0 g/day in Canada in the 1990s [17]. The implications of the high intakes of TFA by breast-fed infants is not known. The major dietary sources of TFA among the mothers at that time were bakery products and breads (34% of intake) and snacks and fast foods (25% of intake) [3].

In 2003, Canada became the first country to introduce food labeling of the TFA content per serving on food labels; this food labeling became mandatory for all packaged foods in the retail sector in December 2005. Industry has responded rapidly and partially hydrogenated fats have been replaced in many foods, such as breads, cookies, crackers and in frying operations. In recent analysis, the mean concentration of TFA (excluding conjugated linoleic acids) in human milk in Canada was 5.3, with a range of 2.9–8.8 g/100 g milk fatty acids (unpublished data). Thus, while the lower range of TFA in human milk has not changed, the upper limit has decreased over 50% from 18.7 to 8.8 g/100 g over the last 6 years, reflecting the decrease in industrial use of partially hydrogenated fats in many foods in Canada. Using the approach taken by Chen et al. [16] of applying equations to describe the relationship between TFA in human milk and dietary intake, the estimated mean intake of TFA, assuming 30% energy from fat, is 2.7% of dietary energy with a range of 1.5–4.5% total energy. Using this approach, Chen et al. [16] estimated that TFA represented an average of 1.1, 3.9 and 7.7% of total dietary energy intakes among women grouped as having low (3.1 g/100 g), medium (6.9 g/100 g) or high (12.4 g/100 g) TFA in their milk fat in 1995. These findings indicate that the major impact of reducing TFA from industrial sources has been to shift the upper range of intakes downwards, by at least 50%.

#### 4. Early child development

Relatively little information is available on the dietary fat intakes of preschool children, although this age group is vulnerable to nutritional deficiencies due to the high requirements for essential nutrients to support continuing rapid growth and development. Recently, we showed that preschool children in Canada consumed an average 33% energy from fat, with 13, 12, 3.6 and 0.7% energy from saturated, monounsaturated fat, LA (C18:2 $n-6$ ) and ALA (C18:3 $n-3$ ), respectively [15]. The mean intake of TFA was 4.8 g/day, representing 1.8% of total energy intakes, with a 5th–95th percentile range of intake of 1.5–10 g/child/day. As in adults, the distribution of intakes was skewed, with some children consuming very high amounts of TFA. A significant inverse linear trend ( $P < 0.05$ ) between the intake of TFA and DHA status, when assessed using the red blood cell phos-

phatidylethanolamine, suggests that TFA may interfere with the formation of DHA from LNA or that diets high in TFA are also those diets that are low in  $n-3$  fatty acids. Although little attention has yet been given to the quality of fat in the diet of preschool children, important processes of neural function continue to develop through early childhood [5]. Notably, the RBC DHA levels in children 1.5–5 years of age are lower than those in infants fed infant formulas lacking DHA, and in whom advantages in increasing visual acuity and measures of neural development have been shown following improvements in their DHA status [5,16].

#### 5. Summary

Infants are exposed to TFA before and after birth by transfer of fatty acids originating from the maternal diet across the placenta and by secretion in human milk. The similar concentrations in mother and child suggest the absence of regulatory mechanisms to protect the developing infant from adverse effects of high maternal intakes of TFA. The use of partially hydrogenated fats and oils by industry, particularly in baked and processed foods that are widely consumed by women and children resulted in exposure to TFA in amounts shown to have adverse health effects on blood lipids and inflammatory markers in adults. In addition, high exposure to TFA is consistently related to lower levels of DHA, a fatty acid that is crucial for normal neural development and function. These considerations support strategies to effectively remove TFA from industrial sources from the diet of pregnant and lactating women, and young children, while improving dietary intakes of the  $n-3$  fatty acids.

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