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n-3 Fatty acid metabolism in women – Reply

The findings reported by Pawlosky *et al.* (2003*a*) are in good agreement with our results, which show greater conversion of α-linolenic acid (LNA; 18: 3*n*-3) to docosahexaenoic acid (DHA; 22: 6*n*-3) in women compared with men consuming their habitual diet (Burdge *et al.* 2002; Burdge & Wootton, 2002). It has long been known that greater oestrogen exposure increases dihomo-γ-linolenic acid and arachidonic acid concentrations in women, which implies increased Δ6- and Δ5-desaturase activities (Ottosson *et al.* 1984). This is consistent with the observation that women taking 30–35 μg ethynyloestradiol/d in a contraceptive pill, which represents an increase in oestrogen exposure compared with the menstrual cycle, had 2·5-fold greater conversion of α-[^{13}C]LNA to DHA than those who did not take synthetic oestrogens (Burdge & Wootton, 2002). One additional important implication of our findings and those of Pawlosky *et al.* (2003*a*) is that the conversion of docosapentaenoic acid (DPA) to DHA, which uniquely requires both Δ6-desaturase activity and peroxisomal β-oxidation, is also modified by gender. This suggests that DHA synthesis may be regulated independently from the activity of earlier steps in the pathway.

There appears to be a reciprocal relationship between partitioning of α-[^{13}C]LNA towards β-oxidation, measured as excretion of $^{13}CO_2$ on breath and C recycling into saturated and monounsaturated fatty acids, and conversion to eicosapentaenoic acid (EPA), DPA and DHA (Burdge & Wootton, 2003). Women, who preferentially use carbohydrate as an energy source (Jones *et al.* 1998), would have a greater availability of α-LNA for conversion to EPA, DPA and DHA. In men, who use fatty acids as an energy source to a greater extent than women (Jones *et al.* 1998), less α-LNA would be available for conversion to long-chain polyunsaturated fatty acids. Together with greater fractional conversion of DPA, preferential partitioning of fatty acids away from β-oxidation may further increase the overall capacity of women for DHA synthesis.

Although there appear to be differences in the sensitivity of the techniques used, these are not so great as to produce differing conclusions about the effects of gender upon α-LNA metabolism. In fact, when [^{13}C]DHA enrichment exceeded background abundance, we could readily detect it (Burdge & Wootton, 2002). We suggest that conversion below this level would be of questionable biological importance. Kinetic analysis of the type described by Pawlosky *et al.* (2003*b*) uses concentrations of labelled fatty acids in plasma as an indirect measure of α-LNA conversion, which is an intracellular process. Since such models ignore partitioning of individual intermediates between lipid pools and different metabolic fates (β-oxidation, storage or further metabolic transformation), there is a tendency towards underestimation of conversion and limited precision.

The key question that remains to be addressed is the biological significance of differences in capacity for DHA synthesis between men and women. It is possible that maintenance of DHA concentrations in tissues in men may depend on dietary sources or recycling to a greater extent than in women. Capacity to up-regulate DHA synthesis under hormonal control in women may be important for satisfying fetal demands for DHA during pregnancy. Plasma phospholipid DHA concentration increases in pregnant women: this may facilitate supply of DHA to the fetus (Postle *et al.* 1995). Up-regulation of DHA synthesis due to rising circulating oestrogen levels may be an important source of DHA to support this increase in maternal plasma DHA concentration. One potential implication is that differences in capacity for DHA synthesis may contribute to the 50 % variation in plasma DHA concentration between women at term (Postle *et al.* 1995). If true, infants born to mothers with a lower capacity for DHA synthesis may be at greater risk of deficit in DHA assimilation. It would then be important to characterise in detail factors that determine capacity for DHA synthesis in women.

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