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Invited commentary

Effects of fat on carbohydrate absorption: more is not necessarily better

Many of us with physiological interests in nutrition specialise in one or other of the macronutrients. This can lead to a blinkered view, since in normal daily life we do not, of course, eat nutrients in isolation. A couple of years ago I commented on the qualitative effects of dietary carbohydrate on fat absorption and appearance in the circulation (Frayn, 1998*a*). Now it seems appropriate to remember that the converse is also true – that dietary fat may affect the absorption and disposition of dietary carbohydrate. This is clearly demonstrated in a paper appearing in this issue, from Normand and colleagues in Lyon and Paris (Normand *et al.* 2001). In an experiment using wheat that has been labelled with ^{13}C by growing it in an atmosphere of $^{13}CO_2$, they show that the rate of appearance of the exogenous glucose in the circulation is markedly altered by the addition of fat to the meal. In particular, a relatively large amount of fat (42 g) leads to a biphasic pattern of glucose concentrations, with a second peak from about 3 h after the meal; plasma insulin concentrations are also elevated during this phase, along with non-esterified fatty acid (NEFA) and triacylglycerol (TG) concentrations. Appearance of the ^{13}C label in the circulation shows late absorption of the dietary carbohydrate, which is, interestingly, incomplete even at 7 h after the high-fat meal. The authors speculate that such a high fat content leads to adverse metabolic changes. A lower amount of fat (17 g), in contrast, could be seen as beneficial since it reduced glucose concentrations in the early phase (0–3 h) after the meal (compared with the third meal tested, with only 2 g fat) without a later rebound.

Some of these observations are not entirely new. It has long been appreciated that addition of fat to a carbohydrate load slows gastric emptying and reduces the glycaemic response (Jenkins *et al.* 1981). However, this experiment adds important new information by extending the period of observation well beyond the 2 or 3 h that is standard in most studies of glycaemic responses. At that stage adverse effects of fat are seen that would be missed in shorter experiments. The effects of the different amounts of fat are also interesting, suggesting that a moderate fat content of 33 % energy (compared with the high-fat meal in which fat supplied 55 % energy) has no adverse and perhaps some beneficial effect. At a time when there is much controversy about the potential adverse effects of low-fat diets (Connor & Connor, 1997; Katan *et al.* 1997), this might add weight to arguments for inclusion of a moderate amount of fat in the diet. However, it also has to be noted that the addition of even the moderate fat content (17 g, 33 % energy) considerably increased the energy content of the meal, and presumably its energy density.

There are some interesting data in the paper by Normand *et al.* (2001) on plasma NEFA concentrations. These fell after each meal, as expected, reflecting the suppression of lipolysis by insulin. They then rose again, but with very different time-courses following the different meals. After the high-fat meal, plasma NEFA concentrations rose rapidly from the nadir at about 1 h to reach a peak at 3 h after the meal before steadily declining again. This mid-postprandial rise was coincident with the peak plasma TG concentration and the authors speculate that the high NEFA concentrations might reflect hydrolysis of dietary TG (i.e. lipoprotein lipase-mediated hydrolysis of chylomicron-TG in the circulation). This could perhaps have been verified by assessing the composition of the plasma NEFA pool, which in other experiments has been shown to change in the postprandial period to reflect dietary fat (Griffiths *et al.* 1994; Binnert *et al.* 1996; Fielding *et al.* 1996). Again, this could be seen as an adverse effect of a high fat:carbohydrate ratio since a similar rise in NEFA was not seen after the other meals. Other work clearly shows the importance of the fat:carbohydrate ratio in determining postprandial plasma NEFA concentrations (Whitley *et al.* 1997). Given the suggestions that elevated postprandial NEFA concentrations may be associated with insulin resistance and risk of cardiovascular disease (Frayn *et al.* 1996; Frayn, 1998*b*), this seems yet another argument for a more moderate or low fat intake.

Many researchers in the field of dietary fat or carbohydrate give their test meals in the form of milk shakes containing the fat, with something bland like cornflakes to provide carbohydrate. Interestingly, cultural differences seem to affect the choice of test meal for postprandial studies. The large Atherosclerosis Risk in Communities Study, administered in the US, used a test meal based on ice cream and whipping cream (Sharrett *et al.* 2001). A recent study from Newcastle-upon-Tyne, UK used pea soup (similar to the local delicacy of 'mushy peas') to provide complex carbohydrate (Robertson *et al.* 2000). In Finland subjects have drunk a cream mixture followed by pure fish oil (Ågren *et al.* 2001). Here we see the evidence of Lyon, the 'World Capital of Gastronomy' (Michelin Tyre, 1997), in that the subjects ate pasta with added sunflower oil, rather typical perhaps of a southern European diet. It is worth noting that the Lyon Diet-Heart study, in which patients who had suffered a myocardial infarction were randomised to receive either standard dietary advice, or advice to consume a Mediterranean-style diet with abundant *n*-3 polyunsaturated fatty acids, showed such enormous benefits of the Mediterranean-style diet that it was terminated after an average of 2·5 years. A later

follow-up analysis at 4 years showed that the difference in all-cause mortality between the groups remained marked (about half in the test group compared with the control group; for 'cardiac deaths' the ratio was 1:3) (de Lorgeril *et al.* 1999). We should, therefore, be ready to believe dietary studies arising from this part of the world. Equally importantly, we should remember that there could be differences between southern Europeans and northern Europeans (and perhaps north Americans might be similar to the latter). Their patterns of response to meal ingestion are very different, with a more rapid peak of lipaemia in the southern Europeans (Zampelas *et al.* 1998). Therefore it will be very interesting to see these studies repeated in other populations, to assess their generalisability.

In summary, perhaps two important messages come out of the study of Normand and colleagues (Normand *et al.* 2001). One is that the adverse effects of high-fat diets may extend beyond the matter of energy density, to include potentially adverse effects on glucose and other metabolites in plasma. The second is that we should never forget, in our experimental studies, that in daily life we eat complex mixtures of macro- and micronutrients, and that studying any of these in isolation is likely to give an incomplete picture.

Keith N Frayn
Oxford Lipid Metabolism Group
Oxford Centre for Diabetes,
Endocrinology and Metabolism
Radcliffe Infirmary
Oxford OX2 6HE
UK

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