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Editorial

Worldwide, there are now more overweight and obese people than those who are hungry and under-nourished. We all know that people become obese because their energy expenditure in physical activity is lower than their dietary energy intake. Lean people assume that the answer is simple – increase physical activity and reduce food intake. As the plethora of slimming regimes and diet programmes on offer suggests, it is not so simple. Abete *et al.* (2006) discuss the relative merits of different macronutrient composition in energy-reduced diets for weight reduction. High-fat, high-protein, low-carbohydrate diets, which were the fashionable regime last year, are effective, although their long-term safety is unclear. The authors suggest that fat and protein may have greater satiety value than carbohydrate, so that total energy intake is reduced. Alternative explanations for their effectiveness are that there will be a need for gluconeogenesis from amino acids to maintain plasma glucose (an energy expensive process) and as Robinson *et al.* (1990) have shown, there is a considerable increase in protein turnover, and hence energy expenditure, in response to a high-protein meal. Low-carbohydrate, high-protein diets, while effective, may also pose long-term hazards; Ingenbleek & Young (2004) discussed the potential hazards of a high protein intake in view of our evolutionary adaptation to conserve the sulphur amino acids, and there is growing evidence that excessively high habitual protein intakes are associated with a variety of problems. The alternative approach, which is one that will be instinctively supported by most nutritionists since it corresponds with the general advice on a prudent diet, and is not associated with any (known) long-term hazards, is a low-fat diet, high-carbohydrate diet. Abete *et al.* (2006) note that it should be complex carbohydrate, not sugars; presumably the carbohydrate should also have a low glycaemic index – certainly that is the current fashion.

In a previous issue of this journal (Bender, 2005) we noted that while glycaemic index is a simple concept to explain to students, Brouns *et al.* (2005) required twenty pages to discuss the methods used to measure it. In this issue Fardet *et al.* (2006) consider the factors involved in determining the widely varying glycaemic index of different types of bread, ranging from close to that of glucose for the traditional French baguette to very low for bread including whole grains; the nutritional and health benefits of whole grain cereals were reviewed by Slavin (2004). Fardet *et al.* (2006) note that both the raw materials and the baking process affect the glycaemic index, and they suggest a number of ways in which processes can be modified in order to produce bread with a low glycaemic index. These include: addition of maize flour, with a high proportion of amylose, which is more resistant to digestion; use of monoacylglycerols as antistaling agents, which complex some of the starch and slow its hydrolysis (traditionally the baguette does not contain antistaling additives, which is why it is bought fresh for each meal); addition of soluble non-starch polysaccharides to increase the viscosity of the intestinal contents and so slow absorption; and changes to the baking process to increase the proportion of resistant starch. All very laudable, and much to the benefit of diabetics and the obese, but a freshly baked (highly glycaemic) baguette is a delight, at least as an occasional nutritional sin.

α-Linolenic acid is a dietary essential; the textbooks tell us that its main function is as a precursor of the long-chain *n*-3 polyunsaturated fatty acids (PUFA) that are important in cell membrane phospholipids and as substrates for synthesis of prostaglandins and other eicosanoids. This has led to use of oils rich in α-linolenic acid for manufacture of spreads, and widespread consumption of supplements of flaxseed (linseed) oil (in which α-linolenic acid accounts for more than half the total fatty acid content) as a way of increasing (beneficial) *n*-3 long-chain PUFA. Burdge & Calder (2006) review the metabolism of α-linolenic acid; surprisingly, despite being a dietary essential, it is also a substrate for β-oxidation, with some of the resultant acetyl CoA undergoing complete oxidation to carbon dioxide, and some being used for synthesis of saturated fatty acids. There is a marked difference between men and women in the proportion of α-linolenic acid undergoing oxidation, and they suggest that β-oxidation represents a mechanism to control its availability for the synthesis of long-chain *n*-3 PUFA. Stable isotope studies suggest that only a small proportion of (supplements of) α-linolenic acid undergo elongation and desaturation. Reflecting the greater proportion of α-linolenic acid undergoing β-oxidation in men than in women, women form considerably more long chain *n*-3 PUFA from α-linolenic acid than do men. Intervention studies with α-linolenic acid show that it has significantly less effect on cardiovascular disease risk factors and markers of inflammation than would be expected, and the authors conclude that increased consumption may be of little benefit in improving long-chain *n*-3 PUFA status.

If α-linolenic acid is a poor precursor of long-chain *n*-3 PUFA, then presumably we should consume oily fish (and perhaps take fish oil supplements) to reduce the risk of cardiovascular disease and cancer, and alleviate inflammation. This is certainly the received wisdom, and there is ample epidemiological evidence of the beneficial effects of consuming oily fish (Baracos *et al.* 2004). Turner *et al.* (2006) note that randomised controlled trials of fish oil supplements have shown mixed results, with less benefit than expected. They suggest that this is because long-chain PUFA are very susceptible to oxidation, and although fish oil is a high (economic) value nutritional supplement, it is

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essentially a by-product of the manufacture of fish meal for use as a fertiliser and feedstuff in aquaculture, and the quality of much fish oil on the market is relatively poor, with varying proportions of lipid oxidation products. These have a number of adverse effects, including increasing whole body oxidative stress, and inflammation, as well as increasing the susceptibility of plasma lipoproteins to further oxidation, increasing uptake by macrophages and so atherogenesis. The authors conclude that future studies of fish oil supplements must report the degree of lipid oxidation in the supplements used, and what antioxidants were present.

Previous reviews in this journal have investigated the interaction between prebiotics and intestinal bacteria (Gibson *et al.* 2004; Van Loo, 2004) and the effects of diet on intestinal bacterial metabolism, and hence odour production, in pigs (Phung *et al.* 2005). In this issue Bauer *et al.* (2006) review the dietary and other factors that influence the development of the intestinal microflora in human beings and other monogastric animals. The neonate has a germ-free intestinal tract; in the adult, intestinal bacteria outnumber the cells of the human body by at least an order of magnitude. Some 400 species have been identified by traditional culture methods, but this may be a gross underestimate, since molecular genetic techniques suggest that there are many more species that cannot readily be cultured. Some of these may be introduced accidentally from the environment, but breast milk provides a large number of micro-organisms which colonise the gastro-intestinal tract and may well inhibit the growth of pathogens. The main dietary factor affecting the development of intestinal flora is carbohydrate – resistant starch, non-starch polysaccharides and fermentable oligosaccharides all provide an abundant substrate for bacterial fermentation and growth, generally promoting the development of desirable species. By contrast, a number of pathogenic organisms are protein fermenters, and their growth is enhanced by an excessive amount of protein in the intestinal lumen. Dietary fat may affect intestinal bacterial populations, either directly or as a result of increased bile salt secretion. Short- and medium-chain fatty acids have an antibacterial action, and, as Decuypere & Dierick (2003) suggested, a combination of triacylglycerols containing medium-chain fatty acids and lipase incorporated into animal feed may well provide an alternative to antibiotic use.

Adams (2006) continues the theme of promoting the health of farm animals by dietary manipulation. He notes that many of the pharmaceutical products that have been used to control disease in poultry have now been banned in the European Union and elsewhere, and vaccination (where effective vaccines are available) is not always practicable or effective. Echoing some of the conclusions of Bauer *et al.* (2006), he cites evidence that low-protein diets, with a high fibre content, reduce the severity of some infections in pigs, an effect that is nullified by increasing the protein content of the diet. Formic, fumaric, lactic and propionic acids added to animal feed have a significant antibacterial action, and have been used in piglets and poultry to alleviate intestinal infections; the mechanism of action is unclear. Other dietary manipulations may modify the virulence of pathogenic organisms, enhance the host's immune system function and maintain gastro-intestinal integrity. An exciting approach to vaccination is the potential use of edible vaccines raised in transgenic plants, which stimulate antibody production by the enteric immune system. Once the genetic modification of the plants has been achieved, the vaccines can readily and inexpensively be administered by incorporating the plants in the animal feedstuff.

While non-starch polysaccharides may have some beneficial effects in animal diets, they are also potentially a source of useable carbohydrate. Cowieson *et al.* (2006) discuss the use of enzymes added to wheat and barley based diets for poultry, to hydrolyse oligosaccharides that are resistant to the birds' digestive enzymes. The enzymes have a greater effect than simply releasing useable carbohydrate; by hydrolysing the oligosaccharides they reduce the viscosity of the intestinal contents, so enhancing absorption – the opposite of the effect discussed above of adding soluble non-starch polysaccharides to bread to lower its glycaemic index. The enzymes may also lyse some bacterial cell wall components, so modifying intestinal flora, and releasing the bacterial contents for absorption by the host. Suitable combinations of enzymes will lyse cell walls in non-cereal ingredients of poultry feed, so enhancing digestibility and increasing the nutritional value of the feedstuff.

Chickens also feature in a review of the nutritional regulation of protein synthesis by Tesseraud *et al.* (2006). Most of our knowledge of the role of amino acids and insulin in controlling protein synthesis comes from mammals. Activation of the insulin receptor initiates two sets of intracellular responses: the classical rapid metabolic effects which involve modulation of the activity of existing enzyme proteins, and the slower effects (mediated by mitogen-activated protein kinase) which involve increased protein synthesis by activation of mRNA translation. Broiler chickens (which have been bred specifically for their rapid rate of growth, have a very high rate of muscle protein synthesis; they reach a weight of 2·5 kg in less than 6 weeks) seem to be relatively insensitive to insulin, and there are a number of differences between mammals and chickens in the details of insulin receptor action. Further work in this area may have direct relevance for human beings. In the metabolic syndrome and early type II diabetes mellitus, tissue resistance to the rapid metabolic effects of insulin leads to hyperinsulinaemia which, in turn, has adverse effects, since the mitogenic actions of insulin seem to be unimpaired.

In one of the heroic self-experiments to study nutritional deficiency, Herbert (1962) deprived himself of folic acid, and, with characteristic attention to detail recorded not only haematological and metabolic changes, but also mood changes. He reported the development of a depressive psychosis as he became deficient. Folate is central to the metabolism of one-carbon units, and hence to the methylation reactions involved in synthesis and inactivation of several neurotransmitters. Intermittently over the last half century, aberrant methylation has been suggested as a factor in schizophrenia, depression and bipolar manic-depressive illness. Sugden (2006) reviews the evidence that folate

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nutritional status and one-carbon metabolism are indeed important in psychiatric illness, in the metabolism of both neurotransmitters and membrane phospholipids (which in turn will affect responsiveness to neurotransmitters). In addition to short-term metabolic effects, there is also evidence that the development of psychiatric illness may be the result of epigenetic effects – early folate deficiency may lead to changes in DNA methylation, and hence long-term changes in gene expression. Conversely, children programmed *in utero* by high maternal folate status may be more likely to develop autism and schizophrenia during the critical periods of selective neuronal apoptosis at age 2–3 years and in adolescence – she suggests that the price of reducing neural tube defects may be an increase in psychiatric illness.

There is ample evidence that the polyphenols in red wine (Cooper *et al.* 2004), olive oil (Tripoli *et al.* 2005) and other foods are nutritionally useful antioxidants, and by extrapolation it has been assumed that anthocyanins in berries are similarly protective. Kay (2006) notes that much of the evidence for protective effects of anthocyanins is based on *in vitro* studies, and there is only a limited amount of information available concerning their absorption and metabolism. Such evidence as is available suggests that they are absorbed and transported in the bloodstream mainly as metabolites; there is obviously a great deal of work yet to be done in this area.

Whether we like it or not, many athletes, sportspersons and bodybuilders take nutritional supplements. Some are simple mixtures of vitamins and minerals, some are perceived ergogenic aids such as creatine or carnitine (although there is only limited evidence of efficacy), others are high protein supplements (especially favoured by bodybuilders, despite the evidence that protein intake above normal requirements has little or no effect on muscle growth). In the USA the definition of nutritional supplements (which are therefore freely available) includes herbs and botanicals (and extracts thereof), many of which have prohormone, androgenic, anabolic, stimulant or narcotic actions. This means that compounds that may well have adverse health effects, and would lead to an athlete failing a drugs test, are freely available. Van Thuyne *et al.* (2006) review the use of nutritional supplements, especially by athletes, and also the presence in these supplements of substances banned by the World Anti-Doping Agency. Sometimes analysis of the supplements shows that there is very much less of the active ingredients than is claimed on the label; more worryingly for the consumer, banned substances may be present, but not declared on the label (or declared as simply an extract of a herb, not naming the presumed active ingredients).

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