GUEST EDITORIAL

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Lipids: from intractable grease to oil for the wheels of life

When the *British Journal of Nutrition* was born in 1947 I was 8 years old and my knowledge of dietary lipids was restricted to the butter and somewhat unpleasant tasting margarine that people then spread on their rather uninteresting bread. My professional interest in lipid metabolism started in 1960 and so has spanned a considerable proportion of *BJN*'s lifetime. Recent papers in *BJN* and reviews in *Nutrition Research Reviews* give a flavour of what currently excites and interests people working in 'nutritional lipidology'. For example, the *BJN* that has just arrived on my desk carries a paper (Sakr *et al.* 1997) that examines how the fatty acid composition of the (human) diet influences the size of chylomicrons and how this in turn is related to the metabolism of HDL. In a recent *NRR*, Salter & White (1996) discuss the influence of dietary fatty acids on blood lipid concentrations and metabolism and then relate these observations to the activities of enzymes of lipid metabolism, changes in which may occur by mechanisms involving altered gene expression. The 1950s *BJN* reader would have been in tune with the discussion of how dietary fatty acids influence blood cholesterol but would probably not yet have been familiar with the concept of lipoprotein fractions. The techniques by which the knowledge that fatty acids may influence gene expression has been gained were quite unknown to 1950s readers.

In and around 1947, Hilditch was involved in his epic work separating, laboriously and meticulously, components of natural fats by techniques (fractional crystallization, countercurrent distribution etc.) of which today's students have only a hazy, if any, appreciation (Hilditch, 1949). Others were developing centrifugation techniques that would

later enable plasma lipoproteins to be separated, paving the way for detailed work on the role of dietary lipids in health and disease. Fulton (1952), in a *BJN* paper concerned with diet and heart disease, referred to important recent work by Gofman (a physicist) on lipoprotein separations and prophesied its later impact. Hilditch published the second edition of his famous work on *The Chemical Constitution of Natural Fats* in the year of *BJN*'s birth and volume 3 of *BJN* for 1949 contained a paper by him on this topic. The same issue also carried an article by Frazer (who first kindled my interest in lipids and in nutrition and who was later to become the first Director-General of the British Nutrition Foundation) on the mechanism of fat absorption (Frazer *et al.* 1949). This subject was one of great (and often strident!) controversy in the 1950s and whereas much progress has undoubtedly been made, a recent review (Lehner & Kuksis, 1996) reveals some still unresolved problems such as how fat digestion products migrate from the intraluminal micelles to sites of triacylglycerol resynthesis in the enterocyte: an important topic for further research.

BJN's first issue carried reports of a meeting on *Fats as Food* with the following topics:

- The world supply of fats
- Marine animals as a source of fat
- The fat required for good cooking and to make food palatable
- The nutritive value of fats with special reference to butter and margarine
- Heated fats as possible sources of carcinogens

None of these would look out of place in a contemporary symposium, although the treatment of them would differ considerably.

Many readers may not appreciate the role played by *BJN* in the publication of early work in three areas of lipid nutrition that are still of great interest today: essential fatty acids, influence of dietary fatty acids on blood lipids, and vitamin A.

Essential fatty acids had been discovered in 1929 (Burr & Burr, 1929). Publications in *BJN* reflected the enormous interest in these substances that continued through the 1950s. Volume 5 included an abstract by one Hugh Sinclair on the pathological effects of essential fatty acid deficiency some 44 years before the establishment of a Chair of Human Nutrition at Reading University that bears his name (Ramalingaswami & Sinclair, 1951). Even so, Smith (1948–9) dismissed concerns about essential fatty acid adequacy of diets as unlikely to be important in view of their widespread occurrence and the small quantities that are required. Research in the intervening period has illustrated the importance of metabolic competition between the different essential fatty acid families, and between essential and non-essential fatty acids such that absolute quantities in the diet may not be a sound guide to the essential fatty acid sufficiency of the diet.

Two Danish nutritionists who made huge contributions to essential fatty acid and fat-soluble vitamin research, E. Aaes-Jorgensen and H. Dam, published no fewer than eighteen papers on essential fatty acids in *BJN* between 1954 (volume 8) and 1962 (volume 16). These give a fascinating insight into how such research was done without the aid of many modern conveniences. Yet the five papers in volume 8, although clearly important contributions by giants in the field, might not now be regarded as 'satisfactory' by referees: there are absolutely no data on fatty acid composition!

Another lipid topic espoused by *BJN* in the early days was the metabolism of vitamin A and provitamin A. S. K. Kon (who was then editor-in-chief) and colleagues at Shinfield published a landmark paper in volume 3 demonstrating that the small intestine is a major site for the conversion of dietary *beta*-carotene into vitamin A and that the lymphatic

system is the route for transporting the vitamin A so formed (Thompson *et al.* 1949). The *BJN* continued to carry many papers on vitamin A by this and other research groups throughout the 1950s and 1960s, and later Sivakumar & Reddy (1972) published an important paper on the absorption of labelled vitamin A in children during infection. Today, the role of nutrient-binding proteins is of particular interest and a recent *BJN* carries a paper describing reduced concentrations of retinol-binding protein in diabetic rats (Tuitoek *et al.* 1996). Now that there is much concern about the apparent poor bioavailability of *beta*-carotene from some vegetables used traditionally in countries where vitamin A deficiency occurs (de Pee *et al.* 1995), it would seem appropriate that *BJN* publishes new exciting work on the topic of bioavailability.

Major buzz-phrases in nutrition now are 'antioxidant nutrients' and 'nutritional importance of fruit and vegetables'. There is much overlap but not complete identity between these areas of interest. *BJN* was prominent in publishing new exciting work on vitamin E first from Henryk Dam's group in Copenhagen (e.g. see Granados *et al.* 1949) and then a veritable explosion of activity from Bunyan, Green, Diplock and colleagues in the UK. From 1961 to 1971 about thirty papers were published by this group on diverse aspects of vitamin E metabolism, providing a solid background for understanding the newly-appreciated importance of dietary antioxidants in health in the 1980s and 1990s.

To many people, the main area of interest in lipid nutrition concerns the role of dietary fatty acids in regulating blood lipoprotein concentrations because of the interest in the role of the latter as a risk factor for cardiovascular diseases. The most cited original papers are probably those of Keys *et al.* (1957) and later Hegsted *et al.* (1965). Few people may realize that in volume 8 of *BJN*, Keys & Keys (1954) published their findings on 'Serum cholesterol and diet in clinically healthy men at Slough near London'. It seems that it was not only John Betjeman who had a morbid fascination for Slough! They found that Slough men had similar plasma total cholesterol concentrations to those in Minnesota despite a somewhat lower fat intake; that there was no correlation between dietary cholesterol and plasma cholesterol; and that whereas in middle aged men higher fat intakes were associated with higher plasma cholesterols, in younger men plasma cholesterol was independent of diet. In volume 15, Karvonen and colleagues (1961) described the effects of diet on the plasma total cholesterol of Finnish lumberjacks. These men consumed 237 g fat/d (45 % energy), compared with 105 g/d in the general population, 60 % of which was dairy fat and 30 % from meat. Their plasma cholesterol concentrations were no higher than those in the general population despite the high total fat and saturated fatty acid contents of the diet. Later, in volume 39, Murray *et al.* (1978) reported on serum cholesterol, triacylglycerols and coronary heart disease in nomadic and sedentary tribesmen in eastern Niger consuming high- (73 % energy) and low-fat (7 % energy) diets. There were no differences in plasma cholesterol; the only CHD cases were found in the sedentary men.

These publications, rarely cited, argue for a more important effect of physical activity and age on blood lipoproteins than is usually acknowledged, a topic that has been intelligently analysed by Macnair in *NRR* (Macnair, 1994).

These topics have been highly selective – geriatric editors were given free rein in these editorials! – but serve to illustrate several points. Nutrition science progresses very slowly and jerkily. It is highly dependent on the availability of methods and much reinvention of wheels occurs. Without rapid lipid separation techniques like GLC, TLC, HPLC and ultracentrifugation, progress would have been slow indeed. However, the development of today's highly automated techniques is not without its dangers. For the student, or even many established research workers, the GLC is a black box: a sample containing a complex mixture goes in one end and a detailed printout of many components is received at the

other. Little thought may be given to whether the components are correctly identified. That a certain component is arachidonic acid (20:4, or more specifically all-*cis*-5,8,11,14-eicosatetraenoic acid) may never be questioned: the computer told us what it in its turn was programmed to tell us. How many students would now attempt an unequivocal identification of a component by oxidizing the fatty acid and analysing the degradation products to confirm double bond positions before firmly asserting on paper, and with utter confidence, its identity? Yet many high-flown theories may be based on the casual structural assignment from a simple GLC printout. There is also a distressing trend to assume that diet has influenced the activity of a certain biosynthetic pathway simply on the basis of changes in tissue fatty acid composition determined by GLC, when the measurement of enzyme activities or the flow of label through a pathway may be the minimum requirement for such a deduction.

Reading *BJN* lipid papers charts the whole of this progression from the breathtaking chemical meticulousness of the 1940s to the often casual approach of the 1990s into which we are lured by the availability of sophisticated technologies and into which we are forced by the relentless need to publish, publish, publish and be funded, funded, funded...

Lest my younger readers should now be regarding me as a hopeless reactionary, the availability of these techniques has had at least one great benefit to lipid nutrition and biochemistry: it has enabled the subject to rise from one that was shunned by students before, say, the 1970s as involving uninteresting compounds that did not have the decency to dissolve in water and merely crudded up the glassware (the intractable grease of my title) to one of the most fashionable areas of biochemistry and nutrition, involving receptors, cell signalling, gene transcription and metabolic control. Key issues to which I hope *BJN* will contribute at the turn of the millenium are the immediate post-prandial metabolism of fats and its consequences, the effects of consuming foods with low or zero fat energy and our ability, or otherwise, subsequently to compensate for that energy deficit, and the absolute and relative requirements for the primary essential fatty acids and their long-chain products. In what circumstances are the long-chain polyunsaturated fatty acids conditionally essential nutrients and what are the effects of competition between the different families?

I hope that *BJN* in its newly evolving form will be prominent among nutrition journals in contributing to this sense of excitement and play a major part in disseminating new knowledge in lipid nutrition. I wish it well!

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