encouraging the latter. It is wrong to recommend¹ that "Reduction of fat intake should apply particularly to saturated fats—namely, fats of animal origin—because fish are and poultry can be rich in EFA, just as vegetable fats can be rich (for example, unprocessed oils) or poor (for example, hard margarines). As pointed out in my letter on "Prescription for a better British diet" (7 April, p 952), we should be interested in the ratio of EFA to certain of the non-EFA.

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Total cardiovascular mortality in men (age adjusted 45-64 y) in seven countries, 1968-77 (in the north of Belgium it was 4.7 and in the south 6.0 per 1000 in 1976).

- ¹ Sinclair, H M, *Lancet*, 1956, 1, 381.
- ² Sinclair, H M, *Symposium of the Zoological Society of London*, 1968, 21, 275.
- ³ Kritchevsky, D, et al, *Atherosclerosis*, 1973, 17, 225.
- ⁴ Ström, A, and Jensen, R H, *Lancet*, 1951, 1, 126.
- ⁵ Dedichen, J, et al, *Transactions of 5th Conference of the Josiah Macy Junior Foundation*, NY, 1951, p 117.
- ⁶ Joint Working Party of the Royal College of Physicians of London and the British Cardiac Society, *Journal of the Royal College of Physicians of London*, 1976, 10, 219.

SIR,—Sir John McMichael (20 January, p 173) repeats statements regularly referred to by opponents of the lipid heart hypothesis. One of these, the cholesterol-thyroidectomy problem, has already been dealt with by Dr P B S Fowler (10 March, p 681). Another is the "observation" of Groen et al¹ about Trappist and Benedictine monks, which has been discussed by Dr J I Mann (17 March, p 732).

On the other hand, I agree completely with Sir John that common margarines with their high content of saturated fat and *trans* fatty acids, and oils with a high erucic acid content, are unsuitable in a prudent diet. But this cannot result in a condemnation of all vegetable oils with a low saturated fatty acid content. Many countries with a high vegetable oil, low butter consumption (the south of France, Italy, Greece, Spain) have much lower coronary and total mortality in middle age groups than in most other western countries. For example, coronary and total mortality (age adjusted 45-64) respectively were in 1975: Greece 1.6 and 8.6 per 1000, England and Wales 4.8 and 12.5 per 1000.² In Belgium about 40% of all vegetable oils are accounted for by corn oil, a product only available since 1955. Soybean oil and peanut oil are near 30% each. No visible harm resulted from this. On the contrary.

The existence of different food habits between the north and the south of Belgium has been documented³ and recently confirmed⁴⁻⁶: saturated fat and food cholesterol is higher in the south, polyunsaturated higher in the north. This goes together with a higher serum cholesterol and a higher coronary, cardiovascular, and total mortality in the south.^{3,4} Other possible confounding variables such as sugar intake, serum triglycerides, vegetable and fruit consumption, total crude fibre, meat consumption, salt intake, blood pressure, smoking habits, stomach cancer, lung cancer, and total cancer were found either equal or slightly higher in the north.^{3,4,6,7} More important, however, is that since 1968 the consumption of butter (higher in the south), the intake of common (bad) margarines (higher in the north), and the intake of salt have decreased substantially in both regions.^{5,8} Concomitantly, a decrease in coronary, total cardiovascular, and total mortality was observed in both the north and the south, resulting in a sizable decrease for Belgium as a whole. This was not as evident in neighbouring countries, including England and Wales (see accompanying figure, in which the United States has been included for comparison).

We do not conclude that those findings prove a causal relationship between saturated fat and coronary atherosclerosis, but at least they are consistent with it. Together with all the accumulated evidence in favour of the lipid-heart hypothesis it "provides a sufficient

basis for immediate and positive dietary advice," to quote Dr Ruth Kay (3 March, p 623).

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- ¹ Groen, J J, et al, *American Journal of Clinical Nutrition*, 1962, 10, 456.
- ² Joossens, J V, et al, *Lancet*, 1977, 1, 1069.
- ³ Joossens, J V, *Acta Cardiologica*, suppl, in press.
- ⁴ Vastesager, M, *Acta Cardiologica*, suppl, in press.
- ⁵ Fondou, M, *Acta Cardiologica*, suppl, in press.
- ⁶ Kesteloot, H, and Van Houste, O, *Bruxelles Médical*, 1974, 24, suppl, p 29.
- ⁷ Vastesager, M, et al, *Acta Cardiologica*, 1974, 29, 441.
- ⁸ Joossens, J V, *Het Medisch Jaar 1978*, p 2. Utrecht, Bohn, Scheltema, and Holkema, 1978.

A Welsh diet for Britain?

SIR,—Our studies of the nineteenth century Welsh diet may be of interest to those of your contributors and readers anxious to modify present-day dietary patterns (Dr R Passmore and others, 24 February, p 527, and subsequent correspondents).

Our primary sources have been the values given by Edward Smith (a careful and painstaking investigator) in his reports of surveys of the diet of Welsh agricultural workers in 1863^{1,2}; caution must, of course, be exercised in interpreting Smith's figures³ but comments by other observers of nineteenth-century Welsh dietary patterns leave little doubt that Smith's reports were in essence a valid representation of the facts. For our calculations we used the values given by Paul and Southgate⁴; in some cases (for example, cheese and buttermilk) the calculations were based on analyses of samples prepared by us in accordance with nineteenth-century practice in Wales.

The diet was an extremely simple one and, as Smith indicated, differed substantially in certain respects (for example, consumption of cheese and bread) from that of corresponding groups in England. The mean daily adult intakes of bread, potatoes, cheese, and buttermilk or skimmed milk were 903 g, 490 g, 38 g, and 348 ml respectively and these four foodstuffs alone accounted for over 80% of both the energy and the protein intakes. Eggs, fruit, and alcohol were not taken and meat (mainly bacon) and vegetables were eaten only sparingly; the daily intake of oatmeal was 50 g per adult. Despite its simple structure the diet provided energy and all the essential nutrients at levels in excess of present-day recommended dietary intakes⁵; interestingly, too, it has a remarkable resemblance to the type of diet adumbrated by Mellanby as a "target diet" for a self-sufficient Britain.⁶

Of much greater interest to those preoccupied with the dietary induction of disease is the structure

of the "Wales 1870" diet in terms of "risk determinants"—dietary factors believed to have a correlative relationship with the incidence of certain diseases of affluence. In the accompanying table the "Wales 1870" diet is compared with the "Wales 1977" diet⁷ in terms of certain commonly accepted risk determinants; the recommendation for the risk determinant is a consensus of the recommendations of 18 committees that have sought to recommend a prudent diet for the prevention of cardiovascular and other diseases associated with affluence and a rapidly developing technology.⁸

"Risk determinants" in the "Wales 1870" diet compared with the "Wales 1977" diet and recommended targets

	Recommendation ^a	"Wales 1870"	"Wales 1977" ^{7,8}
Fat (% of total energy)	No greater than 33	25	40
PUFA (% of total fat)	Increase present intake	18.5	9.1
PUFA: SFA	c 1.0	0.42	0.20
Cholesterol (mg/day)	Maximum 300	130	517
Sucrose (g/day)	Decrease present intake	26	133
Dietary fibre (g/day)	Increase present intake	65	21

PUFA = polyunsaturated fatty acids; SFA = saturated fatty acids.

The "Wales 1870" diet scores heavily as regards its risk determinants—a not entirely unexpected finding if one accepts that the emergence of such diseases is at least in part a consequence of the failure of the metabolic adaptability of the tissues to keep pace with rapidly induced changes in the diet. A partial or complete reversion to a "Wales 1870" type of dietary pattern could therefore be a most desirable change.

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- ¹ Smith, E, Report from Commissioners, 13, Public Health Act, Public Records, vol XXVIII, 1864.
- ² Report of the National Eisteddfod of Wales, Chester, 1866, Carnarvon, Rees, 1866.
- ³ Barber, T C, Oddy, D J, and Yudkin, J, *The Dietary Surveys of Dr Edward Smith, 1862-3*. London, Queen Elizabeth College (Staples Press), 1970.
- ⁴ Paul, A A, and Southgate, D A T, McCance and Widdowson's *The Composition of Foods*. HMSO, London, 1978.
- ⁵ Department of Health and Social Security, *Recommended Intakes of Nutrients for the United Kingdom*. London, HMSO, 1969.
- ⁶ Mellanby, K, *Can Britain Feed Itself?* London, Merlin Press, 1975.
- ⁷ Ministry of Agriculture, Fisheries, and Food, *Household Food Consumption and Expenditure, 1977*. London, HMSO, 1978.
- ⁸ Robbins, C J (editor), *Food, Health and Farming*. Reading, Centre for Agricultural Strategy, 1978.

Does adipocyte hypercellularity in obesity exist?

SIR,—Let us end the discussion between Dr R T Jung and others (29 July, 1978, p 319, and 7 April, p 956) and ourselves (20 January, p 197) regarding adipose hypercellularity with a summarising statement which we believe shows that the differences in opinion are not very large. Actually there is probably only a quantitative difference in evaluation.

Let us first state that we both find that fat cell weight does not increase any more after a certain elevation of body fat mass. After this point, with increasing body fat subcutaneous fat cell number therefore must increase. The only difference here is a slightly varying degree of obesity where this is occurring.

The second point is the matter of visceral fat cells. We are happy that we were reminded of the excellent, careful work by Salans *et al.*¹ These authors have as a matter of fact already studied this question very carefully. They studied the fat cell sizes at three subcutaneous and three visceral depots in fairly extensive material from obese and non-obese subjects. They then analysed their data from a number of different aspects, including calculations of fat cell number with and without visceral fat cells taken into account, and with different assumed percentages of visceral fat. Their conclusion was that "... mean adipose cell number for the obese group is always significantly greater than that for the non-obese, irrespective of the cell size used and of the assumed distribution of total body fat."

Not only the conclusions but also the results obtained are to a rather large extent different from those of Jung *et al.*, and it is a pity that the reason for this has not been analysed in their report. The study by Salans *et al.* shows conclusively that hypercellularity does exist. If we use the data of Jung *et al.*, it does not exist if there are large differences in adipocyte distribution between subcutaneous and visceral fat in obese and non-obese subjects; and this is a very unlikely situation.

Both these arguments demonstrate that the difference in opinion between our groups is actually quantitative. We believe that both groups agree on the basic point—that is, that adipose hypercellularity does exist, only its significance being evaluated differently. We do, of course, not use mean plus one SD of controls as cutting point for definition of hyperplastic obesity other than for analytical purposes.² In this report the low limit had to be set (arbitrarily, as stated in our paper) in order to get a large enough group of hypercellular patients. This again emphasises the quantitative aspects here: these are rare patients. We do, however, apparently see more such patients than Dr Jung and his colleagues, probably because we have a referring "filter," the very frequent everyday problem of slight obesity usually being taken care of outside our hospital. These severely obese subjects are, however, a considerable clinical problem although they are relatively few.

To sum up and close the discussion from our side, Dr Jung and his colleagues have brought up some important technical problems remaining in the field of adipocyte counting. We believe that we both think that adipose hypercellularity exists, although the division line is rather elusive and arbitrary, just like the definition of obesity itself. We see more of the seriousness of the hypercellularity problem than the English group does because we apparently get different patient material.

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¹ Salans, L., Cushman, S W., and Weismann, R E, *Journal of Clinical Investigation*, 1973, **52**, 929.

² Björntorp, P, *et al.*, *American Journal of Clinical Nutrition*, 1975, **28**, 445.

Long-term parenteral nutrition

SIR,—As directors of the Home Parenteral Nutrition Programme at the University of Washington, Seattle, we would like to make several comments regarding the article on home parenteral nutrition by Drs Karin Ladefoged and Stig Jarnum (22 July 1978, p 262). These comments are based on our own extensive experience over the last nine years.¹

The authors do not make any differentiation between the complication rate for the standard subclavian vein catheter and the Broviac catheter. We have exclusively used the

Broviac catheter and have a much lower complication rate in our patients than the authors have reported. Specifically, in 137 catheters used in 94 patients with a total infusion time of 1644 patient months, we have noticed only 23 episodes of associated septicaemia and five episodes of venous thrombosis.² It is noteworthy that none of our patients are on long-term anticoagulation.

The authors commented that unlike other programmes they have found it difficult to maintain a standard parenteral nutrition infusion programme. This may be due to the unusually high percentage of patients that they have with jejunostomies. However, in our patients with short-bowel syndrome and either jejunostomies or ileostomies we keep the patients on a standard total parenteral nutrition programme and supplement them with normal saline as needed to replace excessive gastrointestinal loss. We have been able to instruct our home patients to use a two-channel infusion system—one channel for nutrients is connected by a "Y" to the other channel, which handles the normal saline.

Although some of our patients have been on home parenteral nutrition for over five years, we have seen vertebral compression fractures only in patients who have been on steroids. We have never seen significant osteomalacia with spontaneous bone fractures. However, we give patients 400 units of vitamin D daily, while the authors in this study gave them only 1200 units weekly. Perhaps their patients are therefore deficient in vitamin D.

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¹ Rault, R M J, and Scribner, B H, *Progress in Gastroenterology*, 1977, **3**, 545.

² Miller, D G, *et al.*, *Surgery, Gynecology and Obstetrics*, in press.

Nutrition and cancer

SIR,—Your leading article on malnutrition and cancer (7 April, p 912) reminds us that the cachexia of cancer is wrongly compared with the state of starvation. Starvation is a hypometabolic state in which there is a reduction in the turnover of carbohydrate, fat, and protein stores.¹ Ketone bodies appear to play a major regulatory role.² On the other hand, cancer cachexia is a hypermetabolic state³ with increases in glycolysis, gluconeogenesis, lipolysis, and protein catabolism.^{4,5} Moreover, ketosis is an uncommon phenomenon in cancer patients (personal observations).

Using intravenous lipid solutions, we induced ketosis for eight days in a patient who had advanced hepatic cancer and peritoneal metastases. During that time she received only 56% of her usual calorie intake. However, she did not experience any change in her body weight, abdominal girth, or general well-being. Furthermore, she felt sated for the first time in months. Her serum albumin concentration gradually increased and her urinary and serum urea concentrations decreased, suggesting a reduction in endogenous protein catabolism. Neither hypoglycaemia nor lactic acidosis was observed.

Ketone bodies have been shown to reduce the growth, in culture, of transformed

lymphoblasts from Burkitt's lymphoma and this effect is reversible, non-toxic, and proportional to the concentration of the ketone body up to 20mM.⁶ Normal cells are also known to have reduced cell growth rates in starvation.^{7,8} In leukaemia patients it has been shown that elevations in the proportion of immature cells in the bloodstream can be correlated with elevations in the basal metabolic rate.⁹

Surely these experimental findings raise the question: are forced feeding regimens for the treatment of advanced cancer metabolically sound? We have commenced a clinical trial to evaluate the role of hypometabolic (that is, ketotic) states in cancer therapy.

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¹ Cahill, G F, *Clinical Endocrinology and Metabolism*, 1976, **5**, 397.

² Newsholme, E A, *Clinical Endocrinology and Metabolism*, 1976, **5**, 543.

³ Tannenbaum, A, and Silverstone, H, *Advances in Cancer Research*, 1953, **1**, 452.

⁴ Waterhouse, C, *Annals of the New York Academy of Sciences*, 1974, **230**, 86.

⁵ Gold, J, *Annals of the New York Academy of Sciences*, 1974, **230**, 103.

⁶ Magee, B, *et al.*, in *Proceedings of Australian Symposium on Nutrition and Cancer*, 1978, p 25.

⁷ Aldewachi, *et al.*, *Journal of Anatomy*, 1975, **119**, 105.

⁸ Stragand, J J, and Hagemann, R F, *American Journal of Clinical Nutrition*, 1977, **30**, 918.

⁹ Gunderson, A H, *Boston Medical and Surgical Journal*, 1921, **185**, 785.

Cancer after cardiac transplantation

SIR,—Your leading article "Cancer after cardiac transplantation" (24 February, p 509) remarks: "The striking increase in the incidence of lymphoid neoplasms in patients who have transplants is intriguing but unexplained." It may therefore, be pertinent to draw attention to some animal models in which high incidences of malignant lymphoma were the long-term clinical result of a variety of experimental situations.

Armstrong *et al.*¹ trace the development of lymphomas associated with chronic allogeneic disease in mice as a "continuous transition from an immunological disorder, allogeneic disease, to a malignant growth... initiated by the transplantation of foreign lymphoid cells." Chronic antigenic stimulation of host tissues by allogeneic histocompatibility antigens resulted in neoplasia in this instance.

Another murine system excludes major histocompatibility by using syngeneic recipients.² In this system malignant lymphoma has also been the sequel to syngeneic transplantations without immunosuppression. A high incidence of lymphoma (60-70%) was the neoplastic outcome in syngeneic recipients of mammary gland and lymph node tissue,³ irrespective of the different treatments of the grafts before transplantation. Von Boehmer *et al.*⁴ reported that a syngeneic mixed lymphocyte reaction in mice between thymus cells and peripheral lymphocytes indicates the presence of antigenic differences between syngeneic lymphocytes even without a difference at a major histocompatibility locus. These authors postulate the presence of an antigen on peripheral lymphocytes not coded for by the major histocompatibility complex. Chronic stimulation of host lymphoid tissue by this antigen may play a part in the development of lymphoma in syngeneic graft recipients.

Even in autologous hosts it was possible to induce malignant lymphoma⁵ by first exposing the