cerebellar disease, chronic encephalitis, and dementia (all mainly associated with toluene).⁹ Dose-response relations are not clear, but the tenth of experimental sniffers who become chronic abusers are most at risk. Neuropsychological impairment is unlikely in volatile substance abuse as practised by schoolchildren.¹⁰ Perioral eczema and chronic upper respiratory tract inflammation may result from repeated contact, especially with adhesives, and those who inhale petrol may in addition develop lead poisoning.¹¹ Solvent abuse in late pregnancy may result in neonatal depression, and solvents may possibly be teratogenic.¹²⁻¹³ A degree of tolerance develops with daily use, and symptoms similar to alcohol withdrawal have been described in people who stop abruptly.¹⁴ Organic solvents have a dependence potential, and (like other drugs that are abused) have reinforcing properties in animals.¹⁵

The treatment of acute solvent toxicity consists of standard measures, with cardiorespiratory resuscitation when necessary, conventional treatment of arrhythmias, and intensive supportive treatment.⁴ The management of long term abusers is difficult: a combination of counselling and psychotherapeutic techniques is often needed.⁴⁻¹⁶ Prevention is clearly a better strategy, but that is easier said than done. Voluntary guidelines issued by manufacturers in 1984 and the Intoxicating Substances (Supply) Act of 1985 placed some restrictions on the sales of solvents to people under 18, though solvent abuse is not illegal.¹⁷ Most observers believe that the best approach is through education in public health with the provision of family and community counselling, residential care, and alternative recreational facilities.¹⁸⁻¹⁹ Such measures are also applicable to smoking, alcohol, and other drug

abuse—but they have done little yet to reduce the use of or the mortality from any of these drugs.

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- 1 Ramsey J, Anderson HR, Bloor K, Flanagan RJ. An introduction to the practice, prevalence and chemical toxicology of volatile substance abuse. *Hum Toxicol* 1989;8:261-9.
- 2 Edeh J. Volatile substance abuse in relation to alcohol and illicit drugs: psychosocial perspectives. *Hum Toxicol* 1989;8:313-7.
- 3 King MD, Day RE, Oliver JS, Lush M, Watson JM. Solvent encephalopathy. *Br Med J* 1981;283:663-5.
- 4 Richardson H. Volatile substance abuse: evaluation and treatment. *Hum Toxicol* 1989;8:319-22.
- 5 Davies B, Thorley A, O'Connor D. Progression of addiction careers in young adult solvent misusers. *Br Med J* 1985;290:109-10.
- 6 Black D. Misuse of solvents. *Health Trends* 1982;14:27-8.
- 7 Shepherd RT. Mechanism of sudden death associated with volatile substance abuse. *Hum Toxicol* 1989;8:287-92.
- 8 Marjot R, McLeod AA. Chronic non-neurological toxicity from volatile substance abuse. *Hum Toxicol* 1989;8:301-6.
- 9 Lolin Y. Chronic neurological toxicity associated with exposure to volatile substances. *Hum Toxicol* 1989;8:293-300.
- 10 Chadwick O, Anderson R, Bland M, Ramsay J. Neuropsychological consequences of volatile substance abuse: a population based study of secondary school pupils. *Br Med J* 1989;298:1679-84.
- 11 Meredith TJ, Ruprah M, Liddle A, Flanagan RJ. Diagnosis and treatment of acute poisoning with volatile substances. *Hum Toxicol* 1989;8:227-86.
- 12 Tourant C, Lippman S. Fetal solvents syndrome. *Lancet* 1979;ii:1356.
- 13 Holmberg PC. Central nervous system defects in children born to mothers exposed to organic solvents during pregnancy. *Lancet* 1979;ii:177.
- 14 Glaser HH, Massengale OH. Glue-sniffing in children: deliberate inhalation of vaporized plastic cement. *JAMA* 1962;181:300-3.
- 15 Woods JH. Behavioral pharmacology of drug self-administration. In: Lipton MA, DiMascio A, Killam KF, eds. *Psychopharmacology: a generation of progress*. New York: Raven Press, 1978: 595-607.
- 16 O'Connor D. The use of suggestion techniques with adolescents in the treatment of glue sniffing and solvent abuse. *Hum Toxicol* 1982;1:313-20.
- 17 Liss BI. Government, trade and industry and other preventative responses to volatile substance abuse. *Hum Toxicol* 1989;8:327-30.
- 18 Billington AC. Volatile substance abuse: the role of agencies in the community in prevention and counselling. *Hum Toxicol* 1989;8:323-5.
- 19 Lee JT. Volatile substance abuse within a health education context. *Hum Toxicol* 1989;8:331-4.

Nibblers, gorgers, snackers, and grazers

Eating little and (very) often is beneficial to health

The belief that one should eat three "proper" meals a day and not between meals is deeply ingrained in the British public's mind¹ despite the evidence from studies of eating patterns that the traditional way is rapidly disappearing in favour of eating many times a day. Indeed, some people nowadays eat virtually continuously in a meal pattern that the marketing men have labelled "grazing."

Late last year a study was published showing that increasing meal frequency may have some important and potentially beneficial effects.² Professor David Jenkins and his colleagues have spent years (first in Oxford and now in Toronto) describing the metabolic effects of the rate of entry into the blood of absorbed carbohydrates and have argued for the benefits of slow release (*lente*) carbohydrates for patients with diabetes.³

Their recent paper may be seen as an extension of this concept; but instead of attenuating digestion and absorption by the choice of foods, the changes were made to the eating process itself.² In the study the effects of consuming a standardised 2500 kcal (10.46 MJ) diet in three meals were compared with those of the same intake divided into 17 portions of roughly equal size and composition eaten hourly throughout the day. Seven men took part in a randomised crossover design with each pattern being followed for two weeks. On the penultimate day of each regimen venous blood was taken while the men were fasting

and further specimens taken at two hourly intervals for 12 hours for measurement of concentrations of hormones and other metabolic markers. On the final day of the diet a glucose tolerance test was carried out, and on the day after that the metabolic responses to a standardised breakfast were measured. The analyses were designed to examine the effects of the eating patterns on glucose, cholesterol, and lipid metabolism.

The result that attracted most attention was the fall in total serum cholesterol concentration with the 17 portions a day regimen, which was greater than that with the more conventional meal pattern. This fall was also accompanied by a significant decrease in low density lipoprotein cholesterol and apolipoprotein B concentrations. Serum insulin concentrations in the three meals a day period showed a pronounced cyclical pattern, whereas those for the 17 portion period rose a little from the overnight fasting value and remained virtually constant through the day. Similar differences were seen with the patterns of C peptide and free fatty acid concentrations in serum.

The authors think that the lower serum cholesterol concentrations in the 17 portion period may be due to the lower insulin concentrations in this period compared with the period for the conventional meal pattern. This resulted in reduced hepatic synthesis, which in turn is compatible with an increase in the number of low density lipoprotein

receptors. They further argue that the 17 meal regimen, "nibbling," would have contributed to reduced risk of coronary heart disease.

This interesting and important series of observations is consistent with the earlier observations that the frequency of meals is related to the experience of coronary heart disease in middle aged men⁴ and to obesity in children.⁵ The design was such that with the "nibbling" regimen there was virtually a continuous absorptive state for over 17 hours—an extreme "lente" carbohydrate diet. Whether the title of the paper—nibbling versus gorging—is justified is another issue: it may be stretching the English language somewhat to describe three meals of between 750 and 1000 kcal (3.14 and 4.18 MJ) as "gorging," especially when the men did not gain weight. Conversely, eating 17 portions of about 150 kcal (0.63 MJ) is not nibbling in the way that is common in free living people: the energy intake was closely controlled and the composition of the meal portions was unusual.

The diet studied was a good example of a "prudent" diet: a third of the energy came from fats and over half from carbohydrates, mainly complex, while the dietary fibre intake was about 37 g a day. So the diet was such that the decrease in

serum cholesterol concentrations was predictable.

What the results do achieve is to raise some intriguing questions about the biochemical effects of changes in the nutrient flux into the body, and the authors' use of provocative labels should not detract from an original experimental approach. The lesson for the man in the street is that he can stay healthy if he chooses to adopt a "grazing" pattern of eating—provided that he also chooses to eat a low fat, high complex carbohydrate diet and to control his energy intake.

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- 1 British Nutrition Foundation. *Eating behaviour and attitudes to food, nutrition and health*. London: British Nutrition Foundation, 1982.
- 2 Jenkins DJA, Wolever TMS, Vuksan V, et al. Nibbling versus gorging: metabolic advantages of increased meal frequency. *N Engl J Med* 1989;321:929-34.
- 3 Jenkins DJA. Lente carbohydrate: a newer approach to the dietary management of diabetes. *Diabetes Care* 1982;5:634-41.
- 4 Fabry P, Tepperman J. Meal frequency—a possible risk factor in human pathology. *Am J Clin Nutr* 1970;23:1059-68.
- 5 Young CM, Frankel DL, Scanlan SS, et al. Frequency of feeding, weight reduction and nutrient utilisation. *J Am Diet Assoc* 1971;59:473-80.

Rabies in Britain

Britain remains vigilant and safe

Rabies is widely and correctly perceived as a horrible disease that causes intense distress to patients and those around them and that the most intensive modern treatment cannot cure. Happily it is very rare in both animals and humans in Britain, though we are reminded of its dangers by posters at every seaport and airport. Last week reports of a dog infected in France brought the disease back into the public eye. Occasional cases are still seen in people who contract the infection abroad. The spectre of a future epidemic in Britain has now been raised, however, because the Channel tunnel will soon be completed and efforts are being made to reduce border controls between countries of the European Community in 1992.

The virus is undoubtedly present in Continental Europe and is causing cases of rabies—almost entirely in animals. But it is held in check in Britain by stringent quarantine regulations. In recent years, however, real advances have been made in our understanding of the molecular biology of the virus and the spread of the disease in wildlife, and several new vaccines have been developed. Though it is too big a subject to treat comprehensively in a short editorial, we will address the questions, What does a rational analysis show? and What should Britain plan to do in the future?

Rabies was eradicated from Britain at the beginning of the century. We maintain a cordon sanitaire by quarantining and vaccinating all imported mammals and maintaining a watch for illicit importations at ports of entry. On the continent of Europe, in North America, and in many other parts of the world rabies is controlled. In these countries rabies persists in wildlife, though its impact and the species affected vary. The spread of infection to domestic animals and humans is limited by licensing controls, by prophylactic vaccination of dogs and other animals, and by vaccination after exposure of humans bitten by known or possibly rabid animals. In combination these measures have proved effective, largely protecting the animals with which humans live and ensuring that possible breaches of the protected zone are rendered harmless by

vaccination after exposure. With the modern highly purified vaccines this is now simple and harmless.^{1,2} Deaths from rabies are very rare in developed countries; in the United States they are fewer than one a year. Nevertheless, the system increases the complexity and cost of human and veterinary medicine. In less developed countries in Asia, Africa, and Latin America, where rabies is inadequately controlled, thousands of cases in animals and humans occur each year.

Vaccination against rabies is not recommended as a routine prophylactic measure to travellers from Britain going overseas, though it is recommended and may be given (without any fee) to "persons at occupational risk at home and abroad."³ Other travellers may receive vaccine on payment. The United States phrasing is that vaccination should be considered for "persons planning to be in countries or areas of countries for more than a month where rabies is a constant threat."⁴

In Europe the main risk lies in spread from naturally infected foxes. Infection is carefully monitored—for example, in Germany and France—and the data collected have been subjected to extensive analysis. Mathematical models of the features of rabies have shown that the virus spreads across country in which foxes can move—but it may be held up at natural barriers such as wide rivers. If the population density falls too low—say, below one animal per square kilometre—the infection cannot propagate; and as there is no alternative host and long term carriage of rabies does not occur the disease dies out.⁵ This may occur naturally or be achieved (with difficulty) by killing foxes with poisons. The virus would also die out if a substantial proportion of animals was made resistant by vaccination. This sounds impossible but was done successfully in areas of Switzerland and Germany by feeding bait containing a live attenuated rabies virus that infects by the oral route and prevents infection and disease by the wild type of virus.⁶ Work is continuing, and a recent study showed that techniques such as dropping vaccine infected pellets or chicken heads from a helicopter can vaccinate