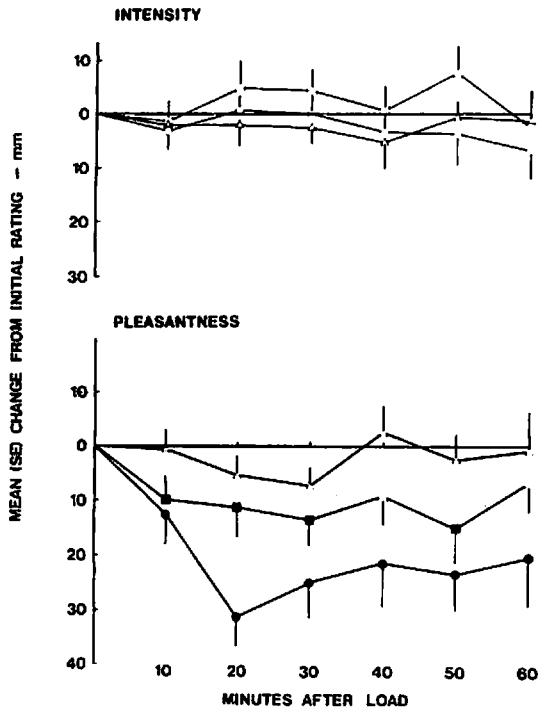
PARADOXICAL EFFECTS OF AN INTENSE SWEETENER (ASPARTAME) ON APPETITE

SIR,—The mechanisms involved in the control of appetite[1] include the monitoring of calories or energy flux.[2] In anticipating intake, animals, including man, make use of relations between the taste of foods and their metabolic consequences.[3] Artificial intense sweeteners have a dual function: they increase the palatability of food and drinks and so promote ingestion whilst not adding to calorie intake. However, these sweeteners uncouple the sensory dimension (sweet taste) of foods from their calorific properties and so may distort the information used by the regulatory mechanisms involved in the control of intake. Moreover, aspartame, a dipeptide of phenylalanine and aspartic acid, may have other effects on appetite mechanisms. Phenylalanine releases cholecystokinin,[4] which is an endogenous anorectic agent;[5,6] and, as a precursor of catecholamine neurotransmitters,[7] phenylalanine may facilitate intake via hypothalamic adrenoreceptors implicated in central appetite control mechanisms.[8]

We have investigated the effects of aspartame on some measures involved in appetite control in 95 male and female volunteers aged 18–22. The term "alliesthesia"[9] refers to the decline in perceived pleasantness of food during and after ingestion. In the laboratory changes in perceived pleasantness (hedonic ratings) of sucrose solutions are measured after a glucose (50 g in 200 ml) load. We have compared the effect of glucose with an aspartame load (162 mg in

Aspartame
Weight-gain



Effect of consuming glucose (circles), aspartame (squares), or water (triangles) on perceived intensity and pleasantness of sucrose.

Closed symbols indicate significant change from baseline (smallest $t_{16}=2\cdot136$, $p<0\cdot05$).

200 ml) of equivalent sweetness. We have also monitored changes in measures of appetite motivation (visual analogue rating scales), which are sensitive to nutritional manipulations[10] and which correlate well with food intake.[11]

For volunteers tested shortly after eating the aspartame load (energy value 3 kcal) produced a clear and significant negative alliesthesia (depression of hedonic ratings for the 10 ml samples of 20% sucrose).

The figure indicates that this effect was about half as potent as that induced by the glucose load (188 kcal). Neither load affected ratings of intensity, showing that it is perceived pleasantness which is modulated and not overall sensory acuity. In contrast to their similar directional effects on alliesthesia, these two compounds showed divergent actions on the measures of motivation (hunger, desire to eat, fullness, and estimated consumption). As expected, the calorie-containing glucose caused a decline in rated motivation to eat and an increase in ratings of fullness. On the other hand, aspartame increased rated motivation to eat and decreased ratings of fullness. The ratings, made every 10 min for an hour, revealed that after aspartame appetite ratings were not suppressed and, on certain occasions in the second half of the test period, increased (significant difference from baseline; $t_{16}=2\cdot478$, $p<0\cdot05$). After the control water load appetite ratings did not differ from baseline.

One crucial question is—did the volunteers who consumed aspartame get hungrier than those who took water? We found significant differences in motivational ratings in aspartame and water loaded volunteers 40–60 min after ingestion of the loads ($t_{31}=2\cdot161$; $p<0\cdot05$). These effects however, are not apparent when testing is done on volunteers fasted for 4 hours.

Taken as a whole, these data indicate that aspartame, in some circumstances, has appetite-stimulating properties in comparison with the ingestion of water. Moreover, under all conditions glucose loads suppressed motivational ratings, in contrast with aspartame. After ingestion of aspartame the volunteers were left with a "residual hunger" compared with what they reported after glucose. In other studies on calorie-reduced foods we have shown that this residual hunger is functional—ie, it leads to increased food consumption. Since there is a widely held belief that artificial sweeteners provide all the psychological manifestations (sensory pleasure, satisfaction of hunger) of sugars without the calories, it seems important to point out that this is not *invariably* true.

These findings are paradoxical. There appears to be a contrast between the effects of aspartame on alliesthesia (suggesting a suppression of appetite) and the effects on motivation to eat (suggesting a facilitation of appetite or absence of suppression). Consequently, individuals may receive ambiguous signals important for the control of appetite and ingestion. This confusion of psychobiological information may lead to a loss of control over appetite, particularly in vulnerable individuals of normal weight who are dieting and who may be consuming large amounts of dietary aids for weight control. In turn, this may contribute to disordered patterns of eating prevalent among certain groups of normal weight individuals.[12]

Biopsychology Laboratories,
Department of Psychology,
Leeds University,
Leeds LS2 9JT

J. E. BLUNDELL
A. J. HILL

1. Morley JE, Levine AS. The central control of appetite. *Lancet* 1983; i: 398–401.
2. Booth DA. Acquired behaviour controlling energy intake and output. In: Stunkard AJ, ed. Obesity. Philadelphia: Saunders, 1980: 101–43.
3. Le Magnen J. Sensory stimuli initiating food intake: their role in overeating. In: Kroeze JHA, ed. Preference behaviour and chemoreception. London: Information Retrieval, 1979: 175–88.
4. Gibbs J, Falasco JD, McHugh PR. Cholecystokinin-decreased food intake in rhesus monkeys. *Am J Physiol* 1976; 230: 15–18.
5. Smith GP, Gibbs J. Brain-gut peptides and the control of food intake. In: Martin JB, Reichlin S, Bick KL, eds. Neurosecretion and brain peptides. New York: Raven, 1981: 389–95.
6. Kissileff HR, Pi-Sunyer FX, Thornton J, Smith GP. C-terminal octapeptide of cholecystokinin decreases food intake in man. *Am J Clin Nutr* 1981; 34: 154–60.
7. Wurtman RJ, Hefti F, Melamed E. Precursor control of neurotransmitter synthesis. *Pharmacol Rev* 1981; 32: 315–35.
8. Leibowitz SF. Neurochemical systems of the hypothalamus—control of feeding and drinking behaviour and water-electrolyte excretion. In: Morgane PJ, Panksepp J, eds. Handbook of the hypothalamus. New York: Marcel Dekker, 1980: 299–343.
9. Cabanac M. The physiological role of pleasure. *Science* 1971; 173: 1103–07.
10. Blundell JE, Hill AJ. Analysis of hunger: inter-relationships with palatability, nutrient composition and eating. In: Hirsch J, Van Itallie TB, eds. Recent advances in obesity research, vol IV. London: Libey, 1985: 118–29.
11. Hill AJ, Blundell JE. Macronutrients and satiety: the effects of a high protein or high carbohydrate meal on subjective motivation to eat and food preferences. *Nutr Behav* (in press).
12. Fairburn CG, Cooper PJ. Self-induced vomiting and bulimia nervosa: an undetected problem. *Br Med J* 1982; 284: 1153–55.

anhedonia

Of the 24 other common causes of death, only bronchitis, stomach cancer, and rheumatic heart disease were similarly related to infant mortality. Those diseases are associated with poor living conditions, and mortality from them is declining. Ischemic heart disease is strongly correlated with both neonatal and postneonatal mortality.

Starvation diarrhea: Metabolic basis. The terminal diarrhea of kwashiorkor or marasmus may be due largely to malnutrition of the intestinal epithelium. Experimental data suggest that the first days of treatment should be devoted to restoration of epithelial function, to prevent worsening of diarrhea by osmotic food loads. Those who devise refeeding regimens should take into account that the small intestine requires glutamine and the colon mucosa requires macromolecules, such as complex polysaccharides and dietary fiber, for bacterial fermentation and production of short-chain fatty acids. Glucose given in oral rehydration fluids may be fermented in the colon, but glucose has a high osmotic pressure, causing fluid to be retained in the colon. This proves detrimental to bacterial proliferation and further fermentation. Nutrition of the small bowel mucosa is promoted by an increase in the vascular supply of amino acids. Approximately 5 to 7 days should be allowed for the starved intestinal epithelium to return to reasonably functional capacity.

Appetite and artificial sweeteners. Artificial intense sweeteners not only increase the palatability of food and drink and reduce caloric intake, but also uncouple the sensory dimension (i.e., sweet taste) of foods from their calorific properties. Thus, the information used by the regulatory mechanisms involved in the control of intake may be distorted. Aspartame may have other effects on appetite mechanisms. One of its components, phenylalanine, releases cholecystokinin, an endogenous anorectic agent. Also, as a precursor of catecholamine neurotransmitters, phenylalanine may facilitate uptake via hypothalamic adrenoreceptors implicated in central appetite control mechanisms. Effects of aspartame on some measures of appetite control were measured in 95 men and women. Observations were made on the decline in perceived pleasantness of food during and after ingestion (alliesthesia). Hedonic ratings were obtained when participants ingested sucrose solutions after a glucose load or an aspartame load of equivalent sweetness. For those tested shortly after eating the aspartame load, a significant negative alliesthesia (i.e., depression of hedonic ratings) occurred. This effect was about half as potent as that induced by the glucose load. Neither load affected ratings of intensity, showing that overall sensory acuity is not modulated, whereas pleasantness is. Glucose and aspartame showed divergent actions on the measures of motivation (hunger, desire to eat, fullness, and estimated consumption). The calorie-containing glucose caused a decline in rated motivation to eat and an increase in ratings of fullness. Aspartame increased motivation to eat and decreased feelings of fullness. In general, the data indicate that aspartame, in some circumstances, has appetite-stimulating properties in comparison with ingestion of water. Under all conditions, glucose loads suppressed motivational rating. Aspartame left subjects with a "residual hunger," leading to increased food consumption. Thus, individuals may receive ambiguous signals important for the control of appetite and ingestion. This confusion of psychobiological information may lead to a loss of control over appetite, particularly in vulnerable persons of normal weight who are dieting and may be consuming large amounts of dietary aids for weight control.

THE LANCET

Vol. I. May 10, 1986

*Infant mortality, childhood nutrition, and ischaemic heart disease in England and Wales. D.J.P. Barker and C. Osmond.—p. 1077.

*Metabolic basis of starvation diarrhoea: Implications for treatment. W.E.W. Roediger.—p. 1082.

Hypercarotenaemia and vitamin A overdosage from proprietary baby food. H.F. Stirling, S.C. Laing, and D.G.D. Barr.—p. 1089.

*Paradoxical effects of an intense sweetener (aspartame on appetite. J.E. Blundell and A.J. Hill.—p. 1092.

Sodium, blood pressure, and calcium antagonists. J.C. Kingswood and F.D. Thompson.—p. 1102.

Childhood nutrition and ischemic heart disease. Poor nutrition in early life appears to increase susceptibility to the effects of an affluent diet. This conclusion is based on a geographical comparison of infant mortality between 1921 and 1925 and death in adults from ischemic heart disease and other leading causes in 1968 and 1978. England and Wales were divided into 212 local authority areas. A strong geographical relationship was found between ischemic heart disease mortality in adults and infant mortality.