advertising, dissemination of public information on the hazards of smoking, aid to persons who want to quit, taxation and other economic disincentives, and planning aimed at shifting the emphasis of Southern agriculture away from tobacco growing and cigarette manufacturing and toward food production and other socially useful activities.

The epidemiologists have done a fine job of elucidating the health hazards of smoking and have documented the magnitude of the current smoking-induced cancer epidemic. The counting of deaths has been accomplished with precision and care. Can the health profession and the public generate as much enthusiasm for, and interest in, the task of reducing cigarette smoking as they have for the development of the artificial heart? Only time will tell.

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NEUROCHEMICAL CHANGES FOLLOWING HIGH-DOSE ASPARTAME WITH DIETARY CARBOHYDRATES

To the Editor: Two years ago, the Food and Drug Administration approved the use of the artificial sweetener aspartame (L-methyl N-(alpha-aspartyl)-L-phenylalanine) as a tabletop sugar substitute and additive in dry foods and beverage bases. At the time, I supported that decision. Now the FDA has approved expanding the sweetener's use by allowing its inclusion in soft drinks. My laboratory has undertaken pilot studies suggesting that such an increase in aspartame's use may cause neurochemical changes that could have functional or behavioral consequences, particularly in people with certain underlying diseases. Our data also show that if aspartame-containing beverages are consumed along with dietary carbohydrates (e.g., a sandwich, cake, or cookies) the sweetener's effect on brain composition is potentiated. Because the carbohydrates cause an insulin-mediated fall in plasma concentrations of the branched-chain amino acids that compete with phenylalanine and tyrosine for transport across the blood–brain barrier,[1,2]

We have completed two experiments on rats receiving aspartame plus sufficient carbohydrate to lower plasma branched-chain amino acid levels. Data from one experiment, presented below, show that aspartame alone almost doubled rat brain phenylalanine levels, and this effect was again doubled if the animals concurrently consumed carbohydrate (Table 1). The aspartame–carbohydrate combination also raised the brain tyrosine level to 311 per cent (that in control rats), and suppressed by about half the physiologic increase[3] in brain tryptophan that follows consumption of a carbohydrate-rich meal. The sweetener also completely blocked the normal increases in brain serotonin and 5-hydroxyindoleacetic acid[4] produced by the carbohydrate meal.

Table Effects of Aspartame and Glucose on Rat Brain Amino Acids and Serotonin.*

	Water Only	Glucose and Water	Glucose and Aspartame	Water and Aspartame
Tyrosine	54.4 ± 2.7	73.1 ± 3.3	187.1 ± 9.5 †‡	139.7 ± 8.4 †
Phenylalanine	39.3 ± 0.9	56.4 ± 1.4	109.3 ± 2.4 †	75.5 ± 2.3 †
Tryptophan	20.8 ± 0.4	30.2 ± 0.5	25.5 ± 0.7 †	20.3 ± 0.6
Serotonin	485 ± 16	548 ± 16	473 ± 15	484 ± 15
5-HIAA	361 ± 15	569 ± 35	314 ± 29	372 ± 43
Total	846 ± 17	1,118 ± 38	784 ± 28	855 ± 42

*Groups of eight rats were killed two hours after receiving glucose (1 g per kilogram), aspartame (200 mg per kilogram), or both by stomach tube. Data are given as means ± S.E.M. nanomoles per gram (amino acids) or nanograms per gram (serotonin and 5-hydroxyindoleacetic acid [5-HIAA]).

†Significantly different from comparable group not receiving aspartame ($P<0.01$).

The dose of aspartame used in these studies was consistent with the amount that an eight-year-old child might consume during a hot afternoon, if the sweetener was added to soft drinks at the level currently used in Canada (about 300 mg per liter): three cans of diet soft drink (about 1 liter) provide 500 mg, which, with an anticipated additional 100 mg from other foods, yields 20 mg per kilogram of body weight. If the child also eats a sandwich or other carbohydrate-containing foods, the rise in brain phenylalanine is doubled (Table 1), becoming equivalent to a dose of 40 mg per kilogram without the carbohydrate, for human beings, or 200 mg per kilogram for rats (Young V: personal communication). If the child is one of the more than 3 million Americans heterozygous for phenylketonuria, the effect of the three cans of soda on brain phenylalanine is probably further doubled.[5] Unfortunately, there is no way for the child or his parents to know that he is a phenylketonuria heterozygote unless and until — some years later — his wife gives birth to a homozygote with clinically manifest disease.

Catecholamine release from frequently firing neurons may be amplified by the additional tyrosine[1,6] or suppressed by the phenylalanine. At a certain, unknown level the phenylalanine could also become directly toxic to the brain, as happens in phenylketonuria. (The normal range for brain phenylalanine in animals consuming diets containing 0 to 10 per cent protein is 33 to 68 nmol per gram[6]; unlike aspartame, protein provides the bloodstream with both phenylalanine and branched-chain amino acids that compete with it for brain uptake.[1]) The tyrosine and phenylalanine could also affect neurotransmission through their products, phenylethylamine and tyramine.

People most likely to have behavioral[7] or functional changes after high doses of aspartame are those with conditions such as hypertension, Parkinson's disease, insomnia, or hyperkinesis, or those taking drugs that interact with plasma phenylalanine or tyrosine (levodopa or monoamine oxidase inhibitors). The clinical implications of any such effects of aspartame remain to be determined, but in the meantime physicians should be alert to the possibilities.

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RECURRENT MENINGOCOCCEMIA ASSOCIATED WITH IgG$_2$-SUBCLASS DEFICIENCY

To the Editor: We recently encountered a child who had repeated episodes of meningococcal infection at 6 and 14 months of age. He was first seen in January 1982 because of fever and rash. Examination revealed an infant with an apparent severe infection, a rectal temperature of 38.33°C (101°F), and a diffuse macular morbilliform exanthem with a few scattered petechiae. The patient was admitted for treatment and evaluation of suspected meningitis, which was subsequently determined by culture to be *Neisseria meningitidis*, untypable. He responded promptly to parenteral antibiotic therapy and had an uneventful recovery. The family was treated with rifampin.

Approximately eight months after discharge, the patient was evaluated for another febrile episode (38.9°C [102°F]), which was thought to be caused by otitis media. Blood cultures were obtained, and the child was treated with oral amoxicillin on an outpatient basis. Three days later the blood culture was reported to be positive for *N. meningitidis*. The family was immediately contacted, and the patient returned to the emergency room; he was extremely lethargic and had nuchal rigidity. Laboratory examination included a complete blood count (white-cell count, 10,600; neutrophils, 30 per cent; band cells, 6 per cent; monocytes, 9 per cent; and lymphocytes, 51 per cent) and spinal tap (white-cell count, 770; neutrophils, 94 per cent; protein, 76 mg per deciliter; and glucose, 45 mg per deciliter). Blood sugar was 94 mg per deciliter. The diagnosis of partially treated meningitis was made, and therapy with intravenous ampicillin and chloramphenicol was initiated. The cerebrospinal-fluid culture grew *Staphylococcus epidermidis*, which was thought to be a contaminant. A computed tomography scan was negative. The hospital course was complicated by diarrhea due to *Campylobacter fetus jejuni* (treated with erythromycin) and oral candidiasis (treated with nystatin). Evaluation for immunodeficiency showed a serum IgG of 550 mg per deciliter, a serum IgM of 84 mg per deciliter, a serum IgA of 31 mg per deciliter, and the presence of salivary IgA. A candida skin test was nonreactive. The patient was referred to the Children's Hospital Medical Center in Boston, where further testing demonstrated a normal hemolytic complement, normal late-acting complement components, and an IgG$_2$-subclass level of 36 mg per deciliter (normal, 68 mg per deciliter), and the diagnosis of IgG$_2$-subclass deficiency was made. The patient was given gamma globulin (0.6 ml per kilogram of body weight, to be administered monthly) and has done well since.

A review of the medical literature for the past decade (1970–1983) revealed 15 previous case reports of recurrent meningococcal infection.[1-11] Only two could be documented in children under 6 years of age. Thirteen patients had an underlying cause predisposing to infection, including 10 with complement deficiencies.[11] The three unexplained cases were not reported to have been investigated for either complement or IgG$_2$-subclass deficiency. Selective deficiencies of the gamma-G-globulin subclass have been reported in the past to be the cause of recurrent pyogenic infections,[12] including those with *Hemophilus influenzae*, *Staphylococcus aureus*, and *Streptococcus pyogenes*. We have not, however, been able to find previous case of recurrent meningococcemia attributable to this problem.

In conclusion, every child who presents with recurrent meningococcemia should have a thorough investigation for immunodeficiency, including a search for complement deficiencies as well as IgG$_2$-subclass deficiency. Gamma globulin may be of benefit to those with IgG$_2$-subclass deficiency. In any case, precise diagnosis is important for proper evaluation and management of intercurrent febrile illnesses.

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NURSE SURGEONS: A NEW ROLE FOR NURSES

To the Editor: The search for reduction in the cost of health services should soon proceed to its next logical step: the introduction of a new kind of nurse specialist, the certified registered nurse surgeon (CRNS). Specially trained nurses would be allowed to provide and bill for surgical procedures on the written order of a licensed physician. Costly anesthesia services are often provided by certified reg-