“Skimming” of insured patients, “dumping” of emergency patients who cannot afford to pay, and promoting profitable lines of service to the exclusion of those that are unprofitable are simply not appropriate practices for our voluntary hospitals and will surely lead to changes in the way they are treated by governmental taxing authorities.

In a fascinating account of his hospital’s recent successful struggle to avoid property taxation by the city of Burlington, James H. Taylor, president of the Medical Center Hospital of Vermont, warns voluntary hospital managers and their boards of trustees that a “hospital’s charitable heritage should not be put aside in a zeal to demonstrate businesslike management.” He says, “An organization that has not retained the spirit of charity, the sense of service, compassion for the sick and injured, and leadership in addressing community needs will not be successful in holding itself out to be charitable.” He is absolutely right.

Of course, his beleaguered colleagues on voluntary hospital boards in most places around the country agree with him, but will wonder how the charitable traditions of their hospital can be preserved in today’s increasingly commercial and competitive health care environment, in which private enterprise is fostered and price seems more important than service. They may well ask, If society wants us to continue to serve the needs of all the sick, why is there no adequate public support for the poor? Why, indeed?

ARNOLD S. RELMAN, M.D.

REFERENCES


CORRESPONDENCE

ASPARTAME AND HEADACHE

To the Editor: In their meticulous study in 40 volunteers, Schiffman et al. (Nov. 5 issue) found that the incidence of headache after the administration of aspartame was not significantly different from the incidence of headache after the administration of placebo. Although this result seems to refute the role of aspartame as a headache trigger, we propose an alternative interpretation.

Spontaneous consumer complaints suggest that aspartame triggers headache. We surveyed 171 patients consecutively evaluated at the Montefiore Headache Unit with regard to dietary factors and headaches and found that aspartame was reported to be a headache precipitant in 8.2 percent — significantly more frequently than carbohydrates, a food item used as a negative control (P<0.05), but less frequently than alcohol, the positive control item (P<0.001).

Thus, consumer complaints and survey data support the role of aspartame as a dietary trigger of headaches, whereas a double-blind, placebo-controlled trial does not. This pattern of findings has previously been noted for such classic dietary triggers of headache as tyramine and chocolate. In several studies, the incidence of headache associated with these agents and the incidence associated with placebo were equivalent (Table 1).

Despite these findings, both tyramine and chocolate are still widely reported to be headache triggers and considered as such by headache specialists. Counseling about these dietary factors remains a standard part of treatment in many headache centers.

Table 1 shows that in 20 to 44 percent of patients, placebo trigger headaches, indicating that these agents are potent headache triggers, at least in the context of the double-blind trials listed. Since anxiety and stress are widely known to precipitate headaches, this is not a startling finding.

If placebos are effective headache triggers, double-blind trials may be an insensitive method of identifying dietary factors in headache. The double-blind design heightens the subjects’ expectation that a headache may develop and may therefore increase the incidence of headaches associated with placebo. As a design alternative, subjects volunteering for a placebo-controlled trial could be told that they had been randomly assigned to the placebo arm of the study. Under such circumstances, the headaches associated with placebo may diminish, whereas those associated with an active agent may still occur.

Schiffman et al. conclude that aspartame is no more likely than placebo to trigger headaches. This cautious conclusion is indubitable in the light of their careful study. However, the methodological considerations discussed above, the experience with chocolate and tyramine, and the anecdotal7 and survey reports of aspartame-triggered headaches suggest that aspartame may still be an important dietary trigger of headache in some people.

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voluntary hospitals, or at least to demand evidence of sufficient charitable community services as a condition of continued tax exemptions. There has even been talk in Congress about making revenues from patient care in voluntary hospitals subject to federal income tax (business income unrelated to patient care has, of course, always been taxable).

Is it true that the voluntary and for-profit hospitals are carrying the same relative burden of charitable care for the 35 to 40 million Americans who have no insurance? If so, the tax-exempt status of the voluntary hospitals would indeed be hard to justify.

The answer to this question is complicated by the fact that hospital financial reports usually do not distinguish between charity care and bad debts. Both are usually lumped together and reported as "unreimbursed care." Furthermore, reports are usually based on revenues or charges rather than on actual costs, thus making it difficult to compare hospitals with different prices directly. Nevertheless, several studies over the past few years have compared unreimbursed care in different types of hospitals. The results have shown, as expected, that publicly owned hospitals provide proportionately more unreimbursed care than either voluntary or for-profit private hospitals. For example, a 1983 study by the American Hospital Association showed that although tax-supported public institutions accounted for only 18 percent of all the charges made by nonprofit short-term hospitals, they contributed 35 percent of all unreimbursed care. The remaining 65 percent of the country's unreimbursed hospital care is provided in private institutions, approximately 3200 of which are not-for-profit and therefore tax-exempt, and approximately 800 of which are for-profit and therefore taxed.

Viewed nationally, there did not seem to be much difference in this study between the two types of private hospitals. The American Hospital Association survey found that the voluntary hospitals provided unreimbursed care valued at 4.2 percent of their charges, whereas the corresponding figure for the for-profit hospitals was 3.1 percent. It was estimated that true charity care accounted for 1.2 percent of the charges in the voluntary hospitals and 0.1 percent of those in the for-profit hospitals.

This survey has been criticized because of a relatively low rate of response from the private sector, particularly from investor-owned hospitals. However, other national studies have found smaller differences or no difference in the amount of unreimbursed care between voluntary and investor-owned hospitals, thus seeming to support the troubling conclusion that tax-exempt hospitals are not clearly more committed to charitable service than their tax-paying competitors.

However, some observers have pointed out that national surveys are misleading because they include states with and without investor-owned hospitals and states with various amounts of publicly funded health insurance. After all, states with no investor-owned hospitals or with substantial public support for hospital care of the indigent would be expected to have relatively small average contributions by voluntary hospitals for unreimbursed care. If investor-owned hospitals do contribute relatively less unreimbursed care than voluntary hospitals, the difference would be most apparent in states with relatively little public support for the poor and relatively large proportions of investor-owned hospitals. Furthermore, since investor-owned hospitals are known to charge more on the average than voluntary hospitals, any differences between the two would be more apparent if costs rather than charges were compared.

A Special Report in this issue of the *Journal* summarizes the results of an important new study that examines the question of unreimbursed care from this more sophisticated perspective. Lewin and Associates, a respected health care consulting firm, was commissioned by the Volunteer Trustees of Not-for-Profit Hospitals and supported by a coalition of voluntary hospitals, health care associations, and the Commonwealth Fund to compare the amount of unreimbursed care in voluntary hospitals with that in investor-owned hospitals. Five states were selected for individual study; in all five there were substantial numbers of investor-owned hospitals, and state agencies could provide adequate and reliable data. Calculated costs rather than charges were used as the basis of comparison.

The results are illuminating and persuasive. In four states (Florida, North Carolina, Tennessee, and Virginia), the burden of unreimbursed care borne by the voluntary hospitals in 1984 or 1985 was 50 percent to more than 100 percent greater than that borne by the investor-owned hospitals. In those states the average contribution of the voluntary hospitals ranged from 6.7 to 10.5 percent of total costs; that of the investor-owned hospitals from 3.7 to 4.9 percent. In California, where the extensive availability of publicly financed hospital care leaves little need for free care in the nonprofit hospitals, both voluntary and investor-owned hospitals had relatively small burdens of unreimbursed care, but even there the contribution of the voluntary hospitals was 15 percent higher.

When one considers further that the fraction of unreimbursed care contributed by charity rather than bad debts is probably much higher in the voluntary hospitals, and that the cost of unreimbursed care to the investor-owned hospitals is reduced by lowered tax liability, these differences in unreimbursed-care burdens become even more important.

Thus, in at least one important dimension, the community service rendered by voluntary hospitals has been shown to be much greater than that provided by the tax-paying hospitals. That is the way it ought to be, if the preferential tax treatment of voluntary hospitals is to be justified. However, scrutiny of the voluntary sector should not stop there. Society needs to be assured that tax-exempt hospitals are continuing to pursue the goals that first defined their social mission.
To the Editor: Schiffman et al. reported that aspartame is not more likely than placebo to produce headaches. For the past few years in our headache clinic, we have systemically inquired about aspar- tate usage. We have been impressed by the number of cases in which an observer (not necessarily the patient) detected a clear aggra- vation of symptoms at the time of introduction of aspartame into the diet.

We believe that the study of Schiffman et al. had some serious flaws and did not reflect the realities of migraine due to dietary factors. Migraine is a hereditary disease of vasoregulatory instability,1 and affected patients are exquisitely sensitive to a number of stimuli, including dietary substances such as tyramine,2 phenyleth- ylamine, and histamine. The group studied was selected on the basis of patients' claims of alleged adverse reactions. By limiting a prospective study to a well-defined group of persons susceptible to migraine headaches, the investigators would have had a homogene- ously constructed with a high sensitivity to food triggers. This would have more clearly separated reactors from nonreactors.

The patients' symptoms were evaluated on the day either as- partame or placebo was administered. It is well known that delayed reactions can occur up to 72 hours after ingestion.3 In the study of Schiffman et al., the blinded challenges were separated by only 48 hours, making it impossible to draw any conclusions. Moreover, we think that this single challenge is insufficient to confirm nonimmunologic adverse effects, since these may occur only after a certain threshold or cumulative level is reached. In addition, while these patients were in the hospital, did they eat a diet free of other vasoactive substances (a "headache diet"), or were they allowed to eat foods that may trigger headaches? We think it is premature to exonerate aspartame from being a cause of vascular headaches. Persons susceptible to migraine and other vascular headaches should continue to be warned of the possible aggravating role of aspartame, and this substance should remain on the list of items to be excluded from the diets of these patients until further studies are completed.

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The above letters were referred to the authors of the article in question, who offer the following reply:

To the Editor: Although anecdotal reports of symptoms occurring after the consumption of aspartame may seem convincing, such reports are not proof of causality because of a multiplicity of confounding variables and biases.1 For example, aspartame is never consumed in its pure form. Thus, other product ingredients, as well as environmental factors and medications that may be associated with headache, cannot be controlled. The Centers for Disease Control evaluated anecdotal complaints about aspartame in 1984 and concluded that "only focused clinical studies can thoroughly evaluate whether these cases were actually due to aspartame sensitivity."2 By designing and conducting a randomized, double-blind, placebo-controlled crossover study with appropriate statistical power in persons who said they had headache within 24 hours after the consumption of products containing aspartame, we were able to eliminate methodological problems that have arisen.

The issue of potential food sensitivities other than that to as-

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Letters referring to a recent journal article must be received within six weeks of the article's publication. We are unable to provide pre-publication proofs, and unpublished material will not be returned to authors unless a stamped, self-addressed envelope is enclosed. Receipt of letters is not acknowledged, but correspondents will be notified when a decision is made.
partame, raised by Lipton et al. and Steinmetzer and Kunkel, was controlled in the study design. Subjects ate exactly the same foods on both Tuesday and Thursday, the test days, on which they were given either aspartame or a placebo. In addition, identical foods were eaten on Monday and Wednesday, the two days before the test days. Intake of foods containing tyramine or chocolate was minimal.

The absorption, pharmacokinetics, and metabolism of aspartame have been well documented by other investigators.5-4 The use of aspartame capsules in clinical studies is appropriate and necessary when double-blind conditions are essential. A recently completed study demonstrated that there was no difference in the extent of absorption of aspartame given in capsules and that administered in solution in a dose twice that used in our protocol.4 Stegink et al.5 investigated the same dosage regimen used in our study (10 mg per kilogram of body weight every two hours for three doses [the equivalent of 4 liters of a beverage sweetened with aspartame]) and found that the peak plasma levels of phenylalanine did not exceed those that occur after a normal meal. Furthermore, other groups have evaluated the effect of an "acute" dose of 10 mg of aspartame per kilogram on plasma phenylalanine levels in normal persons and carriers of phenylketonuria and concluded that the plasma phenylalanine levels reached were far below those observed in the basal state among persons who have brain damage due to phenylketonuria or even among those who have a benign form of non-phenylketonuric hyperphenylalaninemia.6

Elsas expresses concern that a "mechanistic hypothesis" was not tested. This assertion is surprising in view of our descriptions of changes in circulating catecholamines, which were consistent with previous findings in patients with migraine headache.7 The positive changes in circulating catecholamines found in our study were independent of exposure to aspartame or placebo.


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TRANSMISSION OF HUMAN IMMUNODEFICIENCY VIRUS (HIV)

To the Editor: Friedland and Klein's review of the transmission of human immunodeficiency virus (HIV) (Oct. 29 issue)1 presents a balanced view of the issues concerning heterosexual transmission. However, one misconception is perpetuated: that an equal prevalence of HIV infection in the male partners of infected women and in the female partners of infected men implies a similar efficiency of transmission in either direction. Similar prevalences of infection are seen in men and women after repeated exposure to gonorrhea, despite substantially more efficient transmission from men to women than from women to men after a single exposure.2-2 In the absence of genital ulcers or other cofactors that may be more common in central African than in North American heterosexuals, anatomical considerations suggest that the pattern of HIV transmission should be similar to that of other sexually transmitted pathogens carried in cervical and urethral secretions or in semen.

The relative inefficiency of female-to-male transmission is also supported by the fact that in the United States 1045 cases of the acquired immunodeficiency syndrome (AIDS) in women, but only 293 in men (through March 21, 1988), have been attributed to heterosexual exposure. Because of societal attitudes concerning homosexuality, a larger proportion of men than of women are likely to deny existing risk factors, so even the number cited above may overestimate the number of heterosexually acquired cases in men. Moreover, in many of these cases, exposure histories were not obtained by trained interviewers. In New York City, where there are undoubtedly more women infected with HIV than are known,4,5 the diagnosis of AIDS in women, the pattern of HIV transmission should be similar to that of other sexually transmitted pathogens carried in cervical and urethral secretions or in semen.

The relative inefficiency of female-to-male transmission is also supported by the fact that in the United States 1045 cases of the acquired immunodeficiency syndrome (AIDS) in women, but only 293 in men (through March 21, 1988), have been attributed to heterosexual exposure. Because of societal attitudes concerning homosexuality, a larger proportion of men than of women are likely to deny existing risk factors, so even the number cited above may overestimate the number of heterosexually acquired cases in men. Moreover, in many of these cases, exposure histories were not obtained by trained interviewers. In New York City, where there are undoubtedly more women infected with HIV than are known,4,5 the diagnosis of AIDS in women, the pattern of HIV transmission should be similar to that of other sexually transmitted pathogens carried in cervical and urethral secretions or in semen.

At present, sustained heterosexual transmission of HIV seems to be limited by relatively inefficient female-to-male spread. As Friedland and Klein point out, however, this situation could change, and education to modify both heterosexual and homosexual behavior remains one of the nation's highest health priorities.

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Original Articles

Detection of Human T-Cell Lymphoma/Leukemia Virus Type I DNA and Antigen in Spinal Fluid and Blood of Patients with Chronic Progressive Myelopathy

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Prevalence of Patent Foramen Ovale in Patients with Stroke

P. Lechat, J.L. Mas, G. Lascault, P. Loron, M. Theard, M. Klimczac, G. Drobinski, D. Thomas, and Y. Grosogogeat

Clonal Chromosomal Abnormalities Showing Multiple-Cell-Lineage Involvement in Acute Myeloid Leukemia

Mauri Keinänen, James D. Griffin, Clara D. Bloomfield, Joy Machnicki, and Albert de la Chapelle

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Mary Ruth Buchness, Henry W. Lim, Virgil A. Hatcher, Miguel Sanchez, and Nicholas A. Soter

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Setting the Record Straight: The Provision of Uncompensated Care by Not-for-Profit Hospitals

Lawrence S. Lewin, Timothy J. Eckels, and Linda B. Miller

Information for Authors
birth-weight infants. We do agree, however, that the outcome has improved for this select group — but at what cost? The joys of following the intact survivors are tempered with the sadness one feels when caring for children with multiple handicaps. Let us appear unduly pessimistic, we have been encouraged by the simultaneous nationwide increase in the number of intact survivors. However, as Nichols confirms, the majority of these infants weigh 700 g or more, and very few are below 600 g at birth.

We do question Dr. Nichols' assumption that the immediate airways shown in his Figure 1 are not capable of transmitting oxygen to the capillaries. Our experience has shown, surprisingly, that with positive pressure ventilation, even infants with this degree of immaturity can sometimes be adequately ventilated for extended periods. As we noted in our report, they may later die of disease-related or treatment-related complications. We would like to reiterate that simultaneously with the search for more effective means of life support for these extremely immature infants, it is important to broaden the efforts and implement plans to reduce the incidence of prematurity.

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MIGRAINE PROVOKED BY ASPARTAME

To the Editor: Aspartame (NutraSweet) is an artificial sweetener that is 150 to 200 times sweeter than sucrose and is a dipeptide composed of the methyl ester of phenylalanine and aspartic acid. It was approved for use in carbonated beverages in July 1983 and a marked rise in aspartame-related complaints to the Food and Drug Administration followed, with neurologic and behavioral symptoms (including headache) being the most common cause of complaints. Dietary substances, including phenylethylamine, tyramine, and nitrates, have been noted to have a role in migraine headache. The following case suggests the possibility that aspartame may act as such a provoking factor in migraine.

A 31-year-old white woman who had had migraine in childhood had a recurrence of migraine in August 1984 in the setting of heavy consumption of dietetic soft drinks. These vascular headaches were well controlled with propranolol therapy for approximately 18 months, until fatigue led to tapering and discontinuation of the propranolol. Within one month, the patient noted a marked increase in "throbbing" vascular headaches with associated gastrointestinal symptoms, which occurred daily within one to two hours of the ingestion of two to three 12-oz (355-ml) cans of Diet Coke. At that time, she was drinking six to eight 12-oz cans of diet soda per day, 15 aspartame tablets, and unknown quantities of aspartame in other foods (total aspartame, 1000 to 1500 mg per day). During a 10-day trial of avoidance of all dietary soft drinks and added aspartame, the patient noted a marked decrease, and then complete disappearance, of all headaches. Rechallenge with 500 mg of pure aspartame in solution (14 fluid ounces) resulted in the occurrence of an identical headache within 1½ hours. Consumption of 222 mg of saccharin and 90 g of sucrose in solution (14 fluid ounces) (adjusted to approximately equal sweetness) had no effect, and ingestion of all three solutions by a subject without migraine (D. R. J.) had no effect.

A number of adverse reactions to aspartame have now been reported, including granulomatous panniculitis, urticaria, and a possible association between aspartame and seizures. Potential mechanisms for a central nervous system effect of aspartame include an immunologic mechanism and a change in the levels of brain neurochemicals. Considering the widespread distribution of aspartame in food products and the relatively high prevalence of migraine and seizures, it is prudent to include inquiries about aspartame consumption in the evaluation of patients with these disorders. Future clinical observations of the possible role of aspartame as an inciting or provocative factor in migraine and other neurologic illnesses are obviously needed.

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The above letter was referred to the NutraSweet Company, which offers the following reply:

To the Editor: Dr. Johns has studied a patient with migraine headaches thought to result from the ingestion of aspartame. With a symptom as subjective as headache, it is important that a double-blind, randomized, crossover, placebo-controlled design be employed before one can be certain about a causal role for a particular substance.

We would offer the suggestion only that the study be repeated with the sweeteners administered in capsules, since solutions of aspartame and saccharin are easily distinguished by taste. Thus, the study of this patient was not truly blinded. A double-blind design would be preferable, and we would be pleased to supply the capsules should Dr. Johns wish to repeat these experiments using such an unequivocal design.

Aspartame is used by over 100 million people in the United States, and it is remarkable that the product has been associated with so few idiosyncratic reactions, even at the anecdotal level. Nevertheless, we endeavor to study each potential adverse reaction in well-controlled clinical studies at major medical centers. Should any physicians find patients whose clinical histories suggest a possible relation to aspartame ingestion, we hope they will contact us for referral.

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