SUGAR AND THE HYPERACTIVE CHILD

ALTHOUGH scientific opinion favors a genetic origin for most cases of attention deficit–hyperactivity disorder, this explanation does not necessarily exclude alternative causes or precipitating factors, such as common dietary components to which some persons are thought to be abnormally sensitive. The current interest in environmental and lifestyle factors as causes of disease establishes a favorable climate for hypotheses about the adverse effects of diet on behavior. Such dietary hypotheses are mainly prompted, however, by parents' reports that their children become restless, irritable, and intractable in reaction to certain foods or additives. Feingold's sweeping indictment of commercial additives to foods[1] was endorsed by many parents who thought they could directly observe the harmful effects of dyes, flavors, and preservatives on their children. Open clinical studies were somewhat supportive, but controlled studies were not. Any adverse effects of additives were demonstrable only in one group of children (preschool),[2] only with the use of unusually large amounts of food dyes,[3] or only in a small minority of allegedly sensitive children.[4]

The interest in additives has waned, but one earlier hypothesis has had more staying power: the view that sugar "sets some children off." Parents cite cane sugar as the most frequent trigger of hyperactive behavior.[5] In response, many primary care physicians recommend restricting sugar for their hyperactive patients.[6]

The sugar hypothesis has been investigated energetically. As with the research on additives, open studies that are vulnerable to placebo effects have had the more encouraging outcomes.[5,7] The outcomes of controlled studies have been complex and discrepant. In a study of hyperactive children, Prinz et al.[8] found significant correlations between sugar ingestion and blind ratings of destructive, aggressive, or restless behavior in the playroom, but not between sugar ingestion and activity level. They found the opposite pattern of correlations in a normal group of children. These results raise the possibility that sugar affects behavior both in normal children and in those with attention deficit–hyperactivity disorder, but in different ways. However, when Milich and Pelham[9] gave 16 hyperactive boys challenges of sucrose and aspartame, none of 25 dependent measures revealed any differential effects. Would a sample based on parents' reports of sugar sensitivity yield more convincing results? Behar et al.[10] challenged 21 "sugar-reactive" boys with glucose, sucrose, and saccharin. The only significant change was the opposite of that expected: less motor activity when sugar was given. Sexual differences complicate the issue. Rosen et al.[11] found that a sugar challenge impaired the cognitive performance of girls but improved that of boys. Even expected outcomes can be equivocal. Wolraich et al.[12] used sugar and aspartame challenges in normal boys and in those with attention deficit–hyperactivity disorder. Although most of the 37 measures yielded insignificant correlations, the activity level and number of shifts in attention did significantly increase with an increased sugar intake. These limited correlations could indicate a causal relation in either direction: greater consumption of sugar may result in more disordered behavior or more disinhibited behavior may result in greater sugar consumption.

Whereas a positive outcome can be decisive, a negative outcome usually prompts suggestions about how the study might have been better designed. In the study reported in this issue of the *Journal*,[13] Wolraich et al. have taken pains to meet previous objections with respect to the choice of the study population, the dependent variables, and the maintenance of blinded conditions. They worked with two groups of children in whom, according to previous claims, any adverse response to sugar should have been relatively easy to detect: normal preschoolers and grade-school children whose parents consider them sensitive to sugar. The children spent three weeks each on diets containing sugar, aspartame, and saccharin. The transitions between diets were well disguised by dummy diets. Thirty-nine relevant measures were used, including ratings and observations of behavior and performance on tests. Overall, comparisons among the three diets were resoundingly negative, as were analyses of individual measures.

Evidently, these children did not react adversely to sugar, and certainly not to an extent commensurate with parents' reports. This perplexing result is similar to the findings of studies of additives. The parents' reports of substances in the diet causing disordered behavior were not confirmed. Of course, it is possible that some children are sensitive to sugar, but that no such children were represented in these samples. In one report, 9 of 55 hyperactive children on diets that excluded sugar had an adverse response when sugar was reintroduced.[14] But sugar ranked only 18th among the many dietary components incriminated in this report.

Given the largely negative findings and the failure of the occasional significant outcome to be confirmed in subsequent studies, it appears that any adverse effect of sugar is by no means as severe or as prevalent as uncontrolled observation and opinion would suggest. Specifically, there is no evidence that sugar alone can turn a child with normal attention into a hyperactive child. The same applies to aspartame, which has also been suspected of causing behavior disorders in some children.[15] Several studies reveal no systematic differences in blood glucose levels after ingestion of sucrose in children with attention deficit–hyperactivity disorder or in those reported to be sensitive to sugar. This is not to say that children with attention deficit–hyperactivity disorder necessarily metabolize sugar normally. In well-controlled studies, Conners et al.[16] have demonstrated an abnormal relation between the effect of a sugar challenge and the nutritional composition of the previous meal. Normal children challenged with sucrose had more problems with attention after a high-carbohydrate breakfast than after a high-protein breakfast, but the reverse was true for children

with attention deficit–hyperactivity disorder. This finding deserves further study, but it is the opposite of that predicted by the hypothesis about sugar and hyperactivity. Given the high quality of recent negative studies, further investigation of this hypothesis may yield diminishing returns.

Why are placebo effects so powerful in studies of nutrition and behavior? Why do people so readily perceive a relation between food and hyperactive behavior that can rarely be confirmed and is at best subtle? The answers may be related to the current tendency to incriminate external factors when the pathogenesis of a disorder is not totally clear or in preference to genetic factors. This attributional bias poses a problem for clinical research. Extrinsic factors that may be harmful must be detected, and lay reports of apparent ill effects are a valuable guide to what may be worth studying. However, these reports occur in such profusion about so many substances, and studying them calls for such exacting protocols, that it is necessary to choose which ones to study, and there may not be sufficient resources to study them all. The choice may have to be made on impressionistic grounds that are not persuasive to everyone. Worse, studies with negative outcomes fail to prove hypotheses but do not disprove them. It remains unclear how many negative findings are needed to close a particular line of investigation, so that resources can be redirected to the next apparent culprit. There are no objective guidelines on such decisions.

Sugar clearly does not induce psychopathology where there was none before, but it may on occasion aggravate an existing behavior disorder. Sugar-free diets can be burdensome and socially inhibiting, and they should not be endorsed purely on the basis of anecdotal evidence. The potential usefulness of such a diet for a particular child should first be determined by putting the child on a temporary elimination diet and acquiring behavior ratings from several observers.

Tufts University
Medford, MA 02155 MARCEL KINSBOURNE, M.D.

REFERENCES

1. Feingold BF. Hyperkinesis and learning disabilities linked to artificial food flavors and colors. Am J Nurs 1975;75:797-803.
2. Harley JP, Ray RS, Tomasi L, et al. Hyperkinesis and food additives: testing the Feingold hypothesis. Pediatrics 1978;61:818-28.
3. Swanson JM, Kinsbourne M. Food dyes impair performance of hyperactive children on a laboratory learning test. Science 1980;207:1485-7.
4. Weiss B, Williams JH, Margen S, et al. Behavioral responses to artificial food colors. Science 1980;207:1487-9.
5. Crook WG. Food allergy — the great masquerader. Pediatr Clin North Am 1975;22:227-38.
6. Bennett FC, Sherman R. Management of childhood "hyperactivity" by primary care physicians. J Dev Behav Pediatr 1983;4:88-93.
7. Rapp DJ. Does diet affect hyperactivity? J Learn Disabil 1978;11:383-9.
8. Prinz RJ, Roberts WA, Hantman E. Dietary correlates of hyperactive behavior in children. J Consult Clin Psychol 1980;48:760-9.
9. Milich R, Pelham WE. Effects of sugar ingestion on the classroom and playground behavior of attention deficit disordered boys. J Consult Clin Psychol 1986;54:714-8.
10. Behar D, Rapoport JL, Adams AJ, Berg CJ, Cornblath M. Sugar challenge testing with children considered behaviorally "sugar reactive." Nutr Behav 1984;1:277-88.
11. Rosen LA, Booth SR, Bender ME, McGrath ML, Sorrell S, Drabman RS. Effects of sugar (sucrose) on children's behavior. J Consult Clin Psychol 1988;56:583-9.
12. Wolraich M, Milich R, Stumbo P, Schultz F. Effects of sucrose ingestion on the behavior of hyperactive boys. J Pediatr 1985;106:675-82.
13. Wolraich ML, Lindgren SD, Stumbo PJ, Stegink LD, Appelbaum MI, Kiritsy MC. Effects of diets high in sucrose or aspartame on the behavior and cognitive performance of children. N Engl J Med 1994;330:301-7.
14. Egger J, Carter CM, Graham PJ, Gumley D, Soothill JF. Controlled trial of oligoantigenic treatment in the hyperkinetic syndrome. Lancet 1985;1:540-5.
15. Wurtman RJ. Neurochemical changes following high-dose aspartame with dietary carbohydrates. N Engl J Med 1983;309:429-30.
16. Conners CK, Caldwell JA, Caldwell JL. Effects of breakfast and sweetener on the cognitive performance of children. Psychophysiology 1985;22:573. abstract.

SOUNDING BOARD

U.S. DRUG LAWS — AN INTRODUCTION

The two Sounding Board articles that follow address substance abuse. The first, by Lester Grinspoon and James Bakalar, argues for relaxing the laws against drug use; the second, by Herbert Kleber, favors retaining them. Because these laws are confusing and may not be widely understood by our readers, Rachel Hart, research assistant at the Journal, *prepared the following summary.*

Drug-control laws, which are established by both federal and state statutes, generally regulate three activities: the manufacture, distribution, and possession of drugs. Other illegal drug-related activities, such as possessing drug-related paraphernalia, laundering money, and driving while intoxicated, are regulated by a variety of other state and federal statutes. Narcotics offenders may be prosecuted under state or federal laws.

The federal government divides controlled substances into five categories, or schedules, with schedule I drugs — those with the highest potential for abuse and no accepted medical use — being the most strictly controlled. Examples of schedule I drugs include heroin, lysergic acid diethylamide (LSD), and "designer drugs" (unnamed chemical substances designed to mimic the pharmacologic effects of scheduled drugs). Schedule II drugs, which include morphine, cocaine, and codeine, have a high potential for abuse but also have limited accepted medical uses. Schedule III, IV, and V drugs all have accepted medical uses and are considered by federal authorities to have a progressively lower potential for abuse — the higher the schedule number, the lower the potential.

State schedules are usually similar but not identical to the federal schedules. Marijuana, for instance, is classified by the federal government's Controlled Substances Act as a schedule I drug, whereas many states either create a separate category for it or leave it on the schedule of the most strictly controlled drugs but specify less severe penalties for its possession. The severity of penalties also varies from state to state. Possession of 2 oz of marijuana, for example, may be a misdemeanor in one state and a felony in another.