Hyperkinesis and Sensitivity to the Aniline Food Dyes

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Introduction

In the past several years there has been a progressive increase in the number of hyperkinetic children seen in American schools. This disorder is much more common in children in the United States than in Scandinavian countries. It is proposed that the reason for the marked difference in frequency can be partly accounted for by the extensive use of food dyes and additives in "quick energy" processed American foods.

A convenient and simple method for determination of sensitivity to the food dyes has been developed (Hawley and Buckley, 1974). A concentrate of these coloring agents can be purchased in any supermarket. These colors are mixtures of standard FD and C dyes which have been approved for use by the F.D.A. (See Table 1.) A series of one to five dilutions is made and one drop is placed under the tongue, and the child is simply observed for 15 minutes to determine his response. If the child becomes hyperactive he should be placed on the salicylate-free diet. The food dye testing is of value to encourage the parents to be willing to continue the diet for the two-week period necessary in order to see if the child's behavior will improve. If the child does improve, the salicylate-containing fruits and vegetables can be used in special challenge tests to see whether they provoke any symptoms. Foods which contain the aniline dyes, such as luncheon meats, hot dogs, soft drinks, and ice cream must be avoided indefinitely. An improvement may occur in psychotic children so that they are not so disturbed, even though the psychiatric disorder remains.

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The Hyperkinetic State

The state of hyperkinesis is one of increased motor activity, impulsiveness, distractibility, and impaired motor coordination. These children often have a decreased pain threshold so that they tend to ignore punishment. They also have a paradoxical response to stimulants which allow more effective con-

TABLE 1

FD&C Dyes in Liquid Food Color

Food Color	% Dye	Milligrams/100cc	FD&C Dye
Red Red #2	2.5	25	Yellow #6
Yellow Yellow #6	4.0	40	Yellow #5
Blue Red #2	1.5	15	Blue#1
Green Blue#1	2:5	25	Yellow #5

The use of Red #2 is now prohibited. A blend of Red #40, Blue #1, and Red #3 is currently **used** in liquid red food color. It is used at the same percentage of the formula.

centration with less distractibility in performance (Buckley, 1972). There are proposals that hyperkinetic children have deficits in catecholamine production, especially in the dopaminergic pathways. Arnold and associates (1973) have found a differential response of the symptoms of aggressivity and hyperactivity to I-amphetamine and d-amphetamine. This may well indicate that increased aggressiveness is associated with dopamine deficits while hyperactive distractibility may be due to norepinephrine responses.

The diagnosis of "minimum brain dysfunction" developed as a label for several kinds of cognitive, learning, and behavior disorders. C. K. Conners has separated several subgroups of hyperkinetic behavior (1973). As these children mature they develop a high incidence of emotional disorders. As children they have a lowered threshold for activation of the sympathetic division of the autonomic system. This can lead to an unstable autonomic balance which is present in many kinds of adult psychiatric disorders.

Allergic Response Patterns

There is an increased frequency of allergic responses in behaviorally upset children. They often have a history of a sensitivity to cow's milk as small infants. One quite common reaction has been called the allergic tension-fatigue syndrome (Speer, 1970). Behaviorally disturbed children often have sallow, pale skin and dark rings under their eyes. There is a frequent history of seasonal allergy to dust and molds which affects the respiratory tract. The findings that the central nervous system can also be a "shock organ" for allergy and chemical sensitivity (Speer, 1970) have been ignored by most psychiatrists and by physicians in general.

Food allergy responses change as the infant develops. It is infrequent to find a fixed food allergy which occurs each time a particular food is eaten. The foods to which patients are sensitive are often favorite foods which they consume each day. They develop a craving when these foods have been withheld for a week. The presence of a food allergy cannot be effectively determined by conventional scratch skin testing. The most efficient method is to impose a total fast from all foods, medications, and beverages for a period of four to five days. The foods are then carefully introduced in such a way as to be able to identify postprandial responses as being the result of sensitivity to one particular food. During the first two days of the fasting period the person characteristically is irritable and has a strong craving for foods to which he has an allergy-addiction.

SENSITIVITY TO FOOD DYES

SALICYLATE-FREE DIET

(These Foods and Products Should Be Avoided)

I. FOODS

Almonds
Apples
Apricots
Blackberries
Boysenberries
Cherries
Currants
Dewberries
Gooseberries
Grapes or raisins
Nectarines
Oranges
Peaches
Plums or prunes
Raspberries
Strawberries
Cucumbers and pickles
Tomatoes

II. FLAVORINGS (Omit artificially flavored foods and drinks, particularly those that contain FD &C Dye No. 5, Tartrazine).

Ice Cream
Oleomargarine
Gin and all distilled beverages (except vodka)
Cake Mixes
Bakery goods (except plain bread)
Jello
Candies
Gum
Frankfurters
Cloves
Oil of Wintergreen
Toothpaste and toothpowder

Mint Flavors
Lozenges
Mouthwash
Jam or jelly
Lunch meats (salami, bologna, etc.)

III. BEVERAGES

Cider and cider vinegars
Wine and wine vinegars
Kool Aid and similar beverages
Soda pop (all soft drinks)
Gin and all distilled drinks (except vodka)
All tea
Beer
Diet drinks and supplements
Birch beer

IV. DRUGS

1. All medicines containing aspirin, such as Bufferin, Anacin, Excedrin, Alka-Seltzer, Empirin, Darvon compound, etc., all medications that contain salicylates.

2. Perfumes.

NOTE: Check all labels of prepared foods or drugs for artificial flavoring.

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It is also possible to study food sensitivity by the sublingual or the intracutaneous administration of various dilutions of extracts of the foods. The sublingual method is usually estimated to be about 75 percent effective compared with the fasting method. The intracutaneous method is more effective than sublingual testing.

The usual hyperkinetic and distractible child seen in practice does not have these kinds of typical food allergy responses as the basis for the disorder. There is a much higher rate of sensitivity to the aniline coal tar derivative food dyes than to natural foods. An excellent and cautious method of testing for sensitivity to these dyes has been developed by Lockey (1973) and is presented as an appendix to this paper. A pertinent presentation of food allergy responses affecting the behavior

of very young children has been made by Weiss and Kaufman (1971). They found a group of small children with a history of colic, chronic irritability, sleep disturbance, and recurrent temper tantrums. They all had a family history of allergy and glucose metabolic disorder. They were often dealt with as if the mother was somehow responsible for the disorder. The children were placed on the diet for atopic dermatitis which eliminates milk, chocolate, eggs, citrus, nuts, grape, fish, and whole wheat. They had considerable improvement when kept on the diet for two to six weeks. It also relieved the mothers of some of their guilt feelings about the child's behavior. It is characteristic in our culture that mothers are blamed for all of the behavior problems of their children. These findings indicate that the major cause of the behavior problem for these children was a food allergy.

It appears that food sensitivity and food dye sensitivity can have quite similar CNS excitant effects. This response need not be caused by the same neurophysiologic mechanisms in order to cause a release of a similar "final common pathway" for disturbed behavior.

The Sublingual Dye Test

We have found a simple method for performing the sublingual food dye sensitivity test. A bottle of the basic food colors, red, blue, and yellow, can be purchased at a local supermarket. See Table 1 for identification of the food dyes which are present in the standard food colors sold in grocery stores. These dyes are the ones which are extensively used in the processed foods. The bottles of color are considered to be the "concentrate solution." Two cc of this solution is diluted with 8 *cc* of distilled water, and this is solution #1. After it is prepared, 2 cc of it can be mixed with 8 cc distilled water, and this is solution #2. This is repeated four more times so that we have six dilutions of each food dye.

The child's resting pulse is determined, and a drop of solution #4 is placed under the tongue. The child must wait for five seconds before he swallows. If no reaction occurs in 15 minutes, the test can be repeated with one drop of #3 solution. It often happens that the activity level has increased gradually but undramatically when dilution #3 has been used. One of the paradoxical findings seen in this variety of sublingual testings can often be seen in this group of patients. Placing one sublingual drop of more concentrated solution #1 will occasionally cause a dramatic decrease in activity. If no response occurs when dilution #3 is used, then dilution #1 can be used.

When the sublingual sensitivity test is used to determine food allergy, an increase in the pulse rate in the following 15 minutes is very common. The sublingual test for aniline food dyes is seldom followed by an increase in pulse rate, however. The most frequent finding is a gradual and progressive increase in activity which usually lasts for several hours.

It is likely that the mechanism for sensitivity to food dyes is different from the immunochemical response involved in food allergy per se. The parents must be told of the possibility of delayed reactions which can occur after they have brought the child home. Because of the possibility of an intense reaction, these studies should not be casually used by nonprofessionals. The commercial dyes purchased in the grocery store are mixtures FD and C aniline dyes. We need only determine that a sensitivity to such dyes exists. A sensitivity to one dye indicates that all of them must be avoided.

The "Cave Man" Diet

It is quite useful to have this test confirm the sensitivity since it is now necessary to avoid all foods containing salicylates and food additives for two weeks. In particular this specifies that soft drinks, ice cream, malted milk, hot dogs, hamburgers, puddings, cakes, and pies must not be eaten. The food limitations are often better accepted

when the children are told they are on a "cave man diet." A diet restricting foods which are high in salicylates in addition to these food additives should be followed. With a significant improvement in two weeks, the foods which have been avoided should then be evaluated by provocative food testing. Occasionally a child sensitive to the aniline dyes is also sensitive to citrus or apples which have been withheld because of the salicylate content. When the improved child has a lunch of soft drinks and a hot dog, an afternoon of disturbed behavior will usually occur.

Case Report #1

Billy is a physically healthy five-year-old boy who was referred for evaluation of his response to Ritalin. While his behavior was improved by the medication, he remained both distractible and disruptive. Past history reveals that he was a large baby who had a paralysis of his right arm for five weeks following a difficult delivery. He was consistently hyperactive and physically awkward or clumsy. His I.Q. was 124 with no impairment of special skills.

When first seen he was a pleasant but inattentive boy whose flow of speech gradually accelerated as he became familiar with the office. When the food dyes were tested he was in a state of constant movement and speech. He had a paradoxical response to the sublingual administration of the food dyes. One drop of the #1 dilution of the yellow dye resulted in dramatic decrease in speech and activity. He sat down and read a children's book when told to do so. His mother was amazed by the response. When one drop of the #3 dilution of yellow dye was placed beneath his tongue, his activity gradually accelerated and his pulse rate increased from 96 to 112. It was explained to his mother that the response to the dyes indicated that he should be placed on the special diet. Analysis of his hair for trace minerals revealed a very low level of manganese, and drops of zinc-manganese solution were prescribed.

Within a week his behavior was considerably improved, and the amount of Ritalin could be gradually reduced. After a month it was found that 10 mg of Ritalin in the morning was still needed, but that his behavior was now much more acceptable. Evaluation of food allergy by the intradermal test method revealed only a borderline sensitivity to wheat, corn, and yeast. Treatment with subdermal injections was begun after he had been on the diet for one month, but no significant changes in activity levels were noticed as a result of two months of therapy. Three months after going on the "cave man" diet it was found that Ritalin could be discontinued entirely.

Case Report #2

Richard is a tall, thin 18-year-old "boy" who appears to be younger than he actually is. He has a sparse blond beard, braces on his teeth, and an effeminate manner. When he came in he announced "I do not have anything mentally wrong. My trouble is physical and chemical."

His mother is a professional woman who reports that he has improved considerably in the past five years since he was found to have reactive hypoglycemia. At that time he was placed on nutritional management with an emphasis upon organic foods. They believed that he was sensitive to food additives so he had been withdrawn from soft drinks, frankfurters, bakery goods, and "quick energy" foods. He was taking large amounts of the B-complex vitamins and C and E.

The history is consistent with childhood schizophrenic reaction and has many features of autism. Hair for analysis of trace minerals was obtained, and the sublingual food dye test was explained. One drop of dilution #4 of the blue dye was placed under his tongue. About five minutes later he began pacing about the room with abrupt, angry movements. He would stare at the door, and then walk over to a bookshelf. He said "I am a snorting bull," but would not elaborate upon this. In five or 10 minutes he was

calm again and said he no longer felt upset. This behavior resembled his activity several years previously before the diet and food dye restriction. His mother found this to be a dramatic validation of her suspicion that the food dyes could precipitate psychotic episodes.

Discussion

We have found that 40 percent of over 100 hyperkinetic school children have had positive responses to the sublingual sensitivity test. Their mothers have noticed behavior changes in which symptoms return when the children cheat on the diet. A study was done in Santa Cruz, California, under the direction of Dr. Ben Feingold. They studied 25 hyperkinetic school children who were placed on the aniline dye-and salicylate-free diet. This Department of Education study found that 12 of the 25 children were reported to be significantly improved by both their parents and school teachers.

The hyperkinetic child has a constitutionally low threshold for activation of the sympathetic division of the autonomic system. This can be influenced by nutritional, metabolic, and allergic mechanisms as well as by psychologic or social stress. Even if stimulants have been found to be useful, evaluation of nutritional status with the five-hour glucose-tolerance test can be of value. When a hypoglycemic response is associated with symptoms, a high-protein, low-starch hypoglycemia diet will often lead to significant behavior improvements. Acute hypoglycemic episodes have an inhibitory effect upon a negative feedback center in the central hypothalamic area. This will release the sympathetic system for increased activity (Buckley, 1969). Wunderlich (1973) reports that glucose-tolerance tests were done in a juvenile detention center in Florida. Of 50 children tested, 40 percent were found to be symptomatic during the test. Most of them had a flat glucose-tolerance curve. The hypoglycemic disturbance of glucose metabolism can alter limbic system activity and cause the sympathetic autonomic division to have increased activity. This lowered activation threshold will cause the child to be consistently on the verge of "fight or flight" behavior. Such children are often helped by the use of large amounts of the water-soluble vitamins (Cott, 1971).

Hypoglycemia reactions quite frequently occur to people who have central nervous system allergic responses. It is possible for hypoglycemic episodes to result from a simple overload of refined sugar or starch. Hypoglycemia can also occur as part of an allergic response to foods. The foods most likely to do so are wheat and eggs.

The child who is allergically sensitive to food is almost certain to have significant inhalant allergies as well. They should be evaluated for inhalant antigens, particularly the non-seasonal dusts and molds. The food allergy can become symptomatic when the grass or trees are pollinating, and these children will be seasonally hyperactive.

Aniline Dye Sensitivity

The sensitivity of adults to aniline food dyes was first reported by Stephen Lockey in 1948. By 1960 he and other allergists had published reports upon dermatologic and respiratory system responses to both the yellow and the red aniline food dyes. During this time a sensitivity of patients to salicylate and to foods containing salicylates had been discovered. This diet was often successful for treating patients with complicated disorders. Lockey eventually advised withdrawal from the aniline food dyes as part of this salicylate-free diet. When it was clinically successful the patient would then do a series of provocative feeding tests to find whether foods containing natural salicylates could provoke symptoms.

As a result of these findings concerning aspirin sensitivity and food dyes, Dr. Ben Feingold of the Kaiser Foundation Allergy Clinics in San Francisco began to use such a diet for patients who had gotten

little help from more conventional therapy. This diet was also ordered for many children at the clinic. This is how the sensitivity of hyperkinetic children to food dyes was discovered. These findings by Feingold led the senior author (Dr. Hawley) to develop a sublingual method of food dye testing with dyes purchased in local supermarkets.

Adult patients are more sensitive to these aniline dyes, and so the first solution used should be #6. This is because the reaction in adults and some adolescents can be a severe headache. Progressively greater concentrations can then be used just as when the hyperkinetic child is tested. We begin the child's testing with solution #3, to be followed by dilution #1 in 20 minutes. When one drop of solution #4 or #3 has caused a prompt increase in activity, a drop of #1 can be the relieving dosage which causes a prompt decrease in activity. Some children have curled up and actually fallen asleep when a more concentrated solution was used. This is another example of the paradoxical nature of hyperkinesis.

It is useful to refer parents to Dr. Feingold's book, **Why Your Child is Hyperactive** (1975). This is a book written for the layman public which presents some case histories and excellent reasons for use of the salicylate-and food dye-free diet. This is presented as a therapeutic trial to be used as a simple withdrawal test. Regrettably, his instructions do not include the avoidance of refined starches and sugars except as too often used in soft drinks and sweet rolls.

There is a possible synergism of food additives which we can now consider. In some excellent studies at the Institute for Nutritional Studies, Ershoff and associates have found that food additives have an increased toxic response when food fibers are removed from the diet. These findings have pertinence when we recall that the typical diet of both Americans and Europeans is also deficient in food fiber.
Ershoff (Ershoff and Marshall, 1975;
Ershoff and Thurston, 1974) has shown that when growing rats have been deprived of food fibers on an otherwise nutritious diet they can have a sensitivity to several of the food additives. These include the aniline dye FD and C red #2, sodium cyclamate, and polyoxyethylene sorbitan monostearate ("Tween 60"). When food fibers alone were added to the diet the toxic response to these food additives disappeared. This indicates that a similar physiologic mechanism is influencing the toxic responses to these different chemicals. Ershoff (to be published) has recently shown that when smaller amounts of these chemicals are given to the same animal they will be synergistic with each other in causing toxic reactions.

Conclusion

The aniline coal tar derivative food dyes can cause hypersensitivity responses in both adults and children. Adults often have headaches while children often become distractible and hyperactive. It appears that tartrazine, FD and C yellow #5, is the most frequently offending dye. Other food additives in addition to the dyes can have toxic effects, and when a sensitivity response occurs all food additives must be avoided. For this reason testing with the mixtures of aniline dyes purchased at food stores is clinically warranted. The instructions to all sensitive patients is to use the salicylate-free diet. When an improvement occurs, the foods which have been withdrawn can be used for one meal as a provocative feeding test. If no response occurs it can be used indefinitely on a rotation basis every four days. Some of these foods could cause difficulty if used every day for a week.

We have found that about 40 percent of hyperkinetic children have responses to these dyes when tested by sublingual drops. These are the children who should be placed on the salicylate-free diet. We find that it is useful to supplement the diet with large amounts of vitamin C, vitamin B6, and niacinamide. Supplemental vitamins or medication should

never be of the "chewable" variety which contain food additives.

A sensitivity to these compounds is not uncommon in psychotically disturbed children. This is not to state that their psychosis is the result of this sensitivity **per se.** This is to confirm that a sensitivity can occur in these children, and when it does it will complicate the disorder. The removal of such potential toxins from the diet of disturbed children should be one treatment proposal which no group would oppose.

In the course of evolution no mammal had opportunity to adapt to these kinds of hydrocarbon compounds. Dubos emphasizes that man will probably never be able to adapt himself to "the toxic effects of chemical pollution and of certain synthetic products, to the physiological and mental difficulties caused by lack of physical effort, to the mechanization of life, and to the presence of a wide variety of artificial stimulants."

APPENDIX

Food dye preparations as used by Dr. Stephen Lockey. Physicians can obtain small water-soluble samples of 10 food dyes, from the Division of Specialty Chemicals, Allied Chemical Corp., as described in his paper. These are the FD and C Blue 1, 2, Green 3, Red 2, 3, 4, 40, Violet 1, and Yellow 5 and 6. **Method:** dilute 2 g of the food color with 98 ml of triple distilled water. This solution will contain 20 mg of the particular dye per milliliter. This is dilution #1. A further dilution should be prepared, using 1 ml of dilution #1 and 9 ml of triple distilled water, so that 1 ml will contain 2 mg of the FD and C certified food color. This is the dilution for testing the patient. **Testing Method:** 1 ml of dilution #2 is placed sublingually, and patient is observed for 20 minutes for possible bronchospasm, dermatitis, edema, headache, or other reaction. If no sensitivity occurs, the test can be repeated with dilution #1.

TABLE 2

F.D. & C. Colors
(Feingold, 1968)

Blue #1 (Brilliant Blue)	Bottled Soft Drinks
Green #3	Mint Flavored Jelly
Red #2	Breakfast Cereal Imitation Jellies Bottled Soft Drinks
Red #3 (Erythrosine)	Canned Fruit Cocktail Fruit Salad Cherry Pie Mix
Yellow #5 (Tartrazine)	Imitation Strawberry Jelly Bottled Soft Drinks Drugs
Yellow #6	Bottled Soft Drinks

TABLE 3

Classification of Intentional Additives
(Feingold, 1968)

1. Preservatives	33
2. Antioxidants	28
3. Sequestrants	45
Chelating Agents	
Metal Scavengers	
Emulsifiers	
Stabilizing Agents	
4. Surface Active Agents	111
5. Stabilizers, Thickeners	39
6. Bleaching and Maturing Agents	24
7. Buffers, Acids, Alkalies	60
8. Food Colors	34
9. Non-nutritive and Special Dietary Sweeteners	4
10. Nutritive Supplement	117
11. Flavorings - Synthetic	1610
12. Flavorings - Natural	502
13. Miscellaneous	157
Yeast Foods	
Texturizers	
Firming Agents	
Binders	
Anti-caking Agents	
Enzymes	
Total Number of Additives	2764

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