Food Systems: The Relationship between Health and Food Science/Technology

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Changes in our understanding of diet and health drive changes in the way foods are processed. Conversely, what is available on the shelf will have an impact on the choices consumers make, thereby affecting their health. Historical examples of industrial manipulation of the diet include fortification and enrichment of cereal grains with vitamins; increased production of unsaturated vegetable oils and margarine as substitutes for hydrogenated fat, lard, and butter; lowered cholesterol content foods; reduced sugar content foods; lower sodium foods; decreased portion sizes or caloric density in prepackaged foods for use in weight loss or maintenance; and increased calcium levels to prevent osteoporosis. However, degenerative diseases such as cancer, atherosclerosis, bone disease, arthritis, and dementia will continue to be prevalent in the future. Whether or not the food systems available on the shelf can influence all of these disease states is not clear; however, studies have indicated that nutritional factors do contribute to the development of some of these diseases. Patterns in food consumption have changed and will continue to change as recommendations such as decreased consumption of saturated fats, salt, and cholesterol continue to be made. Increased ingestion of fish and/or fish oil is one recommendation that has been suggested because of the effect of omega-3 fatty acids on platelet aggregability and circulating levels of lipids. Wildly speculating from preliminary studies, fish oil has also been recommended for disease states including arthritis, cancer, and diseases of the immune system. A variety of investigators have demonstrated that nutrition can influence the central nervous system in some fashion and this has been extrapolated to mean that nutrients affect the way that we feel and behave. Future recommendations may include changes in the type of food ingested that will alter neurotransmitter status and perhaps be useful as adjuvant therapy to drug therapy. In addition to known nutrient effects of foods, our future understanding will involve the recognition of more and more nonnutritive substances. Some of these substances, such as the indoles, have been recognized as potential anticarcinogens. Regulatory substances including serotonin, estrogens, and releasing factors of hormones have been identified in various foods. Because of agricultural (i.e., genetic manipulation) and process technological changes, the future could bring a more varied diet to the population, but with less of the components we ate in the past. Historically, we have learned that a varied diet is beneficial. Each time we have administered a very defined diet to either animals or to humans, we have discovered new nutritional deficiency diseases. As our understanding of the impact of nutrients on health evolves, we can be assured that scientists and the consuming public will force changes in our food systems and the way in which we preserve and prepare food.

Introduction

Food preparation and processing is an ever-changing arena for the creative mind. Consumer needs eventually result in changes in the way food is processed, and the food industry is constantly attempting to predict what the consumer wants through market research. Such predictions have resulted in the search for tasty, convenient, and if possible low-caloric foods at a competitive price. Predicting the future and the needs of a population is a dangerous pursuit, which was indicated by the predictions more than three decades ago by a group of American business, government, and academic leaders (1). They suggested that by the end of the 1980s cancer would be cured, that the national debt would be slashed, that transcontinental mail would be delivered by guided missile, that a great surfeit of oil would be present unless chemists would work out a means of making plastics and synthetic fiber from oil, and that energy would be virtually free. Obviously, their predictions were not precise, although we still have ½ years for their thoughts to become realities. In this brief review we will discuss some of the nutritional research that will undoubtedly lead to changes in the processed foods that will be available and will result in changes in the way we eat.

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Our knowledge and understanding of nutritional science has resulted in changes in the way we process our foods. For example, we have fortified and enriched cereal grains with vitamins and minerals, increased the production of vegetable oils and margarine as substitutes for lard and butter, have offered more products with lower sodium content, and decreased the portion sizes in prepackaged foods. None of these changes have occurred without significant debate and discussion among consumer groups as well as experts in food science and nutrition. During the past three decades we have focused on nutrition and degenerative disease, since the number of individuals with vitamin and mineral deficiencies has decreased and infectious disease has been controlled because of antibiotic therapy. Therefore, the emphasis has been placed on the major killer diseases including heart disease and cancer. In the 1980s we are coming full circle, with infectious disease due to acquired immune deficiency syndrome (AIDS) occupying much of our attention. Therefore, we must ask the question, “What new knowledge about nutrition during recent times will drive changes in the way food is supplied to the consumer during the twenty-first century?”

Nutrition and Behavior

Many people believe that what we eat affects the way we feel and behave. However, many scientists feel that dietary treatments for behavioral problems represent shamanism. Nevertheless, if one searches the literature, there are many references to the involvement of food in migraine headaches, hyperactivity in young boys, screaming and laughing in autistic children, anorexia, aggressive behavior, and regulation of sleep [for review see (2,3)]. It would be gratifying for individuals in the twelfth century who believed that some foods acted as aphrodisiacs to find that eight centuries later we still are discussing the role of food in behavior.

There is little dispute that undernutrition can result in a series of behavioral changes in people. The well-publicized starvation studies conducted at the University of Minnesota by Keys on conscientious objectors during World War II demonstrated that young healthy men who were deprived of significant calories showed apathy and decreased interest in many activities including sex (4). Similar results were noted in concentration camp victims during World War II (5). Malnutrition is associated with poor social and intellectual skills in children. Studies in rats indicate that very early malnutrition can result in permanent brain damage, with fewer and smaller neurons present in the brain (6). Also, it is known that various vitamin and mineral deficiencies result in alterations in the nervous system. For example, in severe niacin deficiency, people are known to become demented, delirious, and manic (7). Zinc deficiency results in lethargy, apathy, decreased sexual drive, and decreased taste perception for various flavors.

Unfortunately, our understanding of how nutrition affects behavior in the well-nourished individual is not as clear. We do know that various nutrients serve as precursors for neurotransmitters, suggesting that what we eat may affect the proportion of neurotransmitters present in the central nervous system. Tryptophan is a precursor for serotonin, tyrosine for catecholamines, choline for acetylcholine, and histidine for histamine. One might predict that ingesting large quantities of tryptophan or protein causes behavioral changes, knowing that serotonin affects sleep, aggression, food intake, and pain. However, feeding a diet high in protein does not increase the amount of serotonin present in the blood and brain (8). Instead, eating a high carbohydrate diet increases the circulating serotonin and serotonin present in the brain. This paradox is explained by the fact that insulin is released after a high-carbohydrate meal, which results in the uptake of large neutral amino acids other than tryptophan. Thus, there is a lower concentration of other circulating large neutral amino acids and less competition for the transport of tryptophan across the blood/brain barrier. Also, tryptophan is present in relatively small amounts in high protein foods, compared to other large neutral amino acids.

Several studies have indicated that L-tryptophan or high carbohydrate diets may increase sleep time or result in decreased alertness (9). Tryptophan (2 g/day) has also elevated pain thresholds in healthy pain-free subjects (10). However, other studies in animals suggest that dietary tryptophan may not result in functionally active serotonin; that is, although serotonin is synthesized it may be catabolized prior to becoming active (11).

Food additives have been implicated as a causal factor in attention deficit disorder (ADD), also known as hyperactivity. Dr. Benjamin Feingold, an allergist, felt that certain low-molecular weight chemicals in foods resulted in hyperactivity (12). He suggested that a diet that eliminated all foods containing artificial food colorings or flavorings would aid children with ADD. Feingold and his followers believed that the behaviors improved in half of hyperactive children strictly adhering to his diet. A large series of studies to test the Feingold hypothesis, either of a challenge type or a control-versus-experimental protocol, were conducted by scientists. At least 14 studies were conducted on more than 200 children, and in almost all cases no differences in the behavior of the children were noted, except at times by the parents (13).

In 1985, Egger and colleagues (14) studied 76 hyperactive children who were placed on a strict diet for 4 weeks containing only two meats, two starches, one vegetable, and two fruits, plus vitamin and mineral supplements. Specific foods were then introduced, one at a time. Eighty-two percent of the children improved during the open-challenge period. Behavior decayed when certain challenge foods were presented. The most aggravating foods included yellow dye no. 5 (tartrazine) and sodium benzoate, a preservative. Some children had problems following the ingestion of milk, chocolate, eggs, wheat, corn, oats, and fish.

Sugar has been a substance about which anecdotal
tales concerning behavioral changes abound. Prinz et al. (15) reported that boys with a high sucrose intake scored lower on a behavioral test that evaluated attention span. He also stated that sucrose intake correlated directly with aggression, restlessness, and destructive behavior in hyperactive children. In double-blind studies, however, sucrose has been reported to actually have a calming effect in children (16).

Diet has been implicated in migraine headaches since the time of Hippocrates. Sufferers of migraines have been told to avoid milk and other dairy products. A study by Hanington (17) indicated that in 500 migraine sufferers the headaches were associated with ingestion of chocolate and cheese. Tyramine, which is present in cheese is known to precipitate migraine attacks in some individuals. β-phenylethylamine, a compound found in chocolate, can also precipitate migraine attacks in sufferers. This amine is also found in a variety of fermented foods. Today controversy exists over whether a major artificial sweetener, aspartame, is a cause of headaches and other neurological disorders.

In 1982 Morley (18) suggested that hormone-like substances present in foods may affect our physiology. Alfalfa contains thyrotropin-releasing hormone, oat contains a peptide similar to luteinizing-releasing hormone, and milk and wheat contain peptides similar to opioids. In fact, opioid compounds found in wheat have demonstrated alterations in gastrointestinal transit time and the concentration in blood somatostatin (19). Such compounds may affect us by a) working in the lumen of the gastrointestinal tract, b) being absorbed intact and altering peripheral sites, and c) being absorbed and crossing the blood/brain barrier.

The effects of food on behavior have been discussed since the recording of history. Recent data suggest that food may indeed be involved in altered nervous system activity. However, the temptation to extrapolate such data has resulted in the public being taught a variety of misconceptions such as that eating a high carbohydrate meal will result in a calming effect and that eating specific mixes of macronutrients will alter symptoms of premenstrual syndrome. Interpretation of the data from studies on nutrition and behavior needs to be conducted extremely carefully. Nonetheless, one might speculate that in the twenty-first century, foods may be compounded in an attempt to change the way we feel. Certain extra-nutritional factors may be left out of foods and others added to achieve this result.

Nutrition and Heart Disease

For many years the consumer has been aware that diet plays a role in atherosclerosis. Atherosclerosis is a multifactorial disease, as is true for most disease states in which nutrition is involved. It is influenced by genetics, alcohol consumption and tobacco use, stress, exercise, and nutrition. Thus, the consumer is confused. They may know individuals who, for years, have eaten eggs for breakfast or steak and potatoes daily and have no heart disease. However, it is clear that the ingestion of certain saturated fatty acids can increase the risk of heart disease via an alteration in blood cholesterol levels. Based on the early equation of Keys et al. (20), dietary cholesterol is not the major nutritional factor that alters serum cholesterol, but rather saturated fats. Recently, Bonanome and Grundy (21) have reconfirmed older data suggesting that the serum cholesterol of subjects ingesting stearic acid (18:0) was lower when compared to cholesterol levels in subjects ingesting palmitic acid (16:0). This could potentially result in the production of foods that have a higher ratio of stearic to palmitic acid present in their fat. A committee of the National Research Council has recently published a document entitled “Designing Foods,” which addresses the way in which food products from animals can be redesigned to make them healthier (22). It would be desirable to decrease total fat without altering the palatability of beef, pork, or lamb. There is also work to either extract cholesterol out of dairy products or to insert a cholesterol-oxidizing gene in dairy starter cultures to produce cholesterol-free cheeses and yogurt.

An area of great current interest is that of the omega-3 fatty acids as related to heart disease. The public has been told to eat less fat and more carbohydrate, yet Eskimos are known to eat virtually only fat and protein. Based on the diet of the Eskimos, one might predict that they would experience a high incidence of heart disease; however, the incidence of atherosclerosis is very low in this population (23). Many investigators have attributed this decreased incidence of heart disease in the Greenlandic Eskimo to their large consumption of fatty fishes that contain a good deal of omega-3 fatty acids. This family of fatty acids contains a double bond three carbons from the terminal methyl group. The omega-3 fatty acids that are prevalent in fish are eicosapentaenoic acid (EPA, C20:5) and docosahexaenoic acid (DHA, C22:6). Fatty acids serve as precursors of the eicosanoids that alter muscle contraction, platelet aggregability, inflammatory processes, and a variety of other physiological functions. The omega-3 fatty acids are precursors for eicosanoids that may be involved in the relationship between diet and heart disease.

Many studies have been conducted evaluating the effect of EPA and/or DHA on serum triglyceride and cholesterol levels. Doses of 6 g or less of omega-3 fatty acids reduce triglyceride, but do not clearly alter serum cholesterol levels (24–27). In fact, low doses of fish oil increase the ration of LDL/HDL cholesterol in hyperlipemic patients. At the present time it is not clear that fish oils will lower serum cholesterol and be beneficial for hyperlipemic patients unless very high doses of omega-3 fatty acids are ingested (28). Fish oil, however, does have other effects that might decrease cardiovascular disease. Consumption of omega-3 fatty acids seems to reduce the synthesis of thromboxane A2 and increase the level of innocuous thromboxane A3 (29,30). Also, levels of prostacyclin are increased. These changes have been reported to decrease platelet aggregability, re-
resulting in a decreased clotting time. Based on data collected by Kromhout et al. (31), eating as little as 14 g of fish/day for 20 years might decrease coronary death rates. This effect seems not to be due to omega-3 fatty acids, since these individuals consumed very low levels of total omega-3 fatty acids (< 1 g of omega-3 fatty acids weekly). A major problem facing the food industry in this area would be the high oxidizability of the omega-3 fatty acids. It is very unlikely that palatable products can be made using the present technology.

Researchers suggest that dietary fiber is another substance that may be involved in the development of atherosclerosis [for review see (32)]. Epidemiological data indicate that in regions of the world where people consume large amounts of dietary fiber, there is a lower incidence of heart disease. After a decade or more of work, it seems that there are several reasons why consumption of high fiber diets may alter the incidence of coronary artery disease. First, when one consumes a diet naturally high in fiber, little fat is consumed and in addition, the fat is generally of the unsaturated type. Secondly, soluble dietary fiber has the ability to bind bile acids and bile salts. Cholesterol is the precursor of these emulsifiers; therefore one way to rid the body of cholesterol is to increase the excretion of bile acids. This is the basis by which the drug cholestryramine functions. Thus, ingestion of a high fiber diet may decrease serum cholesterol. However, it should be noted that simple addition of wheat bran to a Western diet is not the means of achieving the effect on blood cholesterol. We need to manufacture more foods containing soluble fiber besides the insoluble wheat bran usually added to foods. Of course, one can simply ingest fruits and vegetables that are high in soluble fiber.

The collection of such data indicates that we will probably continue to alter our eating patterns to decrease the incidence of atherosclerosis. It is likely that foods will be manufactured that will contain the best ratios of fatty acids, based on the knowledge gathered over the next few decades. There has been a steady decline in the number of deaths due to atherosclerosis during the past 20 years. This decrease could be attributed to many factors other than nutrition. Furthermore, the pharmaceutical industry has synthesized a variety of drugs that effectively lower blood cholesterol levels. Still, it is likely that our diet will continue to change towards one that seems to lower the circulating levels of cholesterol and increases the high-density lipoprotein (HDL) fraction. One major inhibiting factor to making new products will be the present preclusion by the FDA of any health claims on a food product label [21 CRF 109 (c)(1)]. Recently, the FDA was forced to propose more relaxed regulations (US Federal Register, August 4, 1987), but at the present these regulations are still in debate. Most health professional societies sent comments that were opposed to allowance of health claims because of what they felt would lead to unwarranted drug claims for products. Many food companies feel that without the allowance of label health claims they will not be able to market their products.

**Nutrition and Cancer**

Over time various dietary fads come and go. One that has been with us for a relatively long period is the influence of dietary fiber on health. As discussed above, dietary fiber is thought to be involved in the development of heart disease. Other than the well-known anti-constipating action of roughage in food, investigators have suggested that a deficiency in fiber intake is involved in colonic cancer, diabetes, varicose veins, and a variety of gastrointestinal diseases (33). Dietary fiber may decrease the risk of colon cancer by a) increasing stool volume, thus diluting carcinogens present in feces; b) shortening transit time and reducing the contact time between carcinogens and bowel mucosa; c) lowering the pH of the feces and inhibiting formation of carcinogens by bacteria; and d) reducing the concentration of mutagens present in human feces. As Dennis Burkitt (31) has indicated, "no community has yet been shown to pass large stools and to have other than a low rate of large bowel cancer."

As with heart disease, it is difficult to decide whether the epidemiological data about cancer and fiber is due to the large intake of fiber or to the low intake of fat. However, in some rural areas of Finland the intake of fat is as high as many Western countries, but diet is also very high in fiber (31 g/day). In these areas there is a low incidence of cancer of the large bowel (34).

The microbial flora of people who consume a large amount of fiber appears to be different from those individuals eating a Western type diet (35). Feces of individuals from areas with a low rate of colonic cancer contain fewer bacteroides and more streptococci. They seem to have a lower ratio of anaerobes to aerobes present in their feces. Also, the total fecal bile acid and neutral steroids are higher in people living in areas with a high prevalence of colonic cancer (36). In addition, bacterial metabolites of cholesterol are higher in feces of individuals living in areas with a high incidence of colon cancer. American vegetarians have been reported to have a lower fecal level of cholesterol metabolites compared with Americans on a so-called normal diet. The binding of bile acids and bile salts may make them less available for metabolism by bacteria resulting in carcinogens or co-carcinogens (37).

It should be noted that the controversy over health claim labeling started with an illegal claim made by Kellogg's on their All Bran fiber cereal (illegal in the sense of the Food Drug and Cosmetic Act). The claim, in fact, cited data from and was supported by the National Cancer Institute with respect to fiber ingestion and reduction of some kinds of cancer. The FDA was prevented from acting directly to seize the product although they had sufficient legal precedent based on seizure of glucomannan tablets and starch blockers for weight reduction claims. Labuza (38) has reviewed the history of this controversy.
Other nonnutritive components of foods, such as indoles present in cruciferous vegetables, also seem to act as anticarcinogens (39). Low energy intake and decreased fat also seems to decrease the promotion phase of cancer. Retinoids and other micronutrients also can protect against cancer [for review see (49)]. Thus, as we learn more about those foods that influence the development of cancer, we can formulate products that seem to decrease the incidence of cancer.

Future Impact of Health Research on Food Technology

Virtually every nutrient has at some time been associated with some type of disease. For example, calcium has been touted as a nutrient that will decrease hypertension, decrease colonic cancer, and, of course, delay the onset of osteoporosis. With all the knowledge accumulating about the impact of various nutrients on our well-being, how do we formulate foods that contain the correct ratio of nutrients and not cause an imbalance of nutrients in the diet? The food industry is very quick to jump on the bandwagon to supply the food/nutrient fad of the month, in many cases before all the data are in. Even though the FDA has issued guidelines (45 FR 6314, January 25, 1980) that suggest that fun foods not be nutrified or fortified, one can find many such foods (e.g., diet beverages with vitamin C or calcium). In fact, when the FDA seized a table sugar product fortified with 19 vitamins and minerals, the action was overturned in court (US vs Dextra Brand Sugar, 231 F Suppl 551; 1963).

This court action says to the industry that they can manipulate foods almost any way they want. Should we ingest high carbohydrate diets to calm us? Should we eat low fat and high fiber diets to prevent colon cancer and heart disease? Should we be increasing our consumption of fish? Should every woman drink calcium-fortified diet beverages? And should children reduce their consumption of salt? Furthermore, what type of product would be acceptable to the consumer? It is clear that no product will be viable in the marketplace unless the sensory quality is high, no matter how healthy that product is.

The food industry is faced with a tough series of problems (41). The consumer desires a high quality, convenient, and healthful food. Until recently, the food industry has avoided making health claims about its products as precluded by section 21 CFR 101.9(1)(1). It should be noted that health claims can be made in advertising that are under the scrutiny of the Federal Trade Commission, which has a different set of standards. It appears that when sufficient groups of scientists and government agencies are willing to develop a consensus as to the health benefit of a specific nutrient and its role in the prevention of a disease, the food industry will most likely develop new relevant products.

What are some of the new markets available to the industry for the health-conscious consumer? Genetic engineering; it is hoped, will improve some of the nutritional value of raw agricultural products such as altering the protein composition in corn, soy, or wheat. One might develop a fruit that is high in iron and calcium. The quality of fresh produce will be improved by hydroponics, which allows the manufacturing of the fruit to be closer to the area of sales. Controlled atmospheric packaging will be developed to elongate the shelf-life of fruits and vegetables, thus preserving more of the nutrients. Also the chemical control of the aging of fruits may be combined with irradiation as a means of pasteurizing the surface of fresh fruits to prevent decay and prolong shelf-life. As long as there continues to be a problem with overeating, low calorie ingredients, such as artificial sweeteners and nonabsorbable fats, will be used. Some technical problems are associated with low-calorie products. For example, to produce a low-calorie jam, one uses less sugar that reduces the shelf-life because of microbial growth. Since it has been suggested that high-sodium intake leads to hypertension, many low-sodium products have been developed. These low-sodium products also lead to technical problems including a change in water activity (which changes shelf-life) and a change in palatability, as well as a potential danger of the growth of pathogens that could cause infectious diseases. Such problems of tailored nutrition foods leads to some exciting challenges for the food scientist and indicate a risk/risk situation; the risk of eating a certain component versus the risk of getting food poisoning if it is removed from the food and no longer exerts microbial control.

Health scientists will continue to probe the role of various nutrients in the prevention and cure of disease. The philosopher and physician Maimonides stated that if an illness could be treated by diet, no other treatment should be used. In our advanced technocratic society it is unlikely that Maimonides’ suggestion will be adhered to; however, the knowledge about what we should eat will continue to occupy an importance place in the minds of the consumer. Whether nutritionally tailored foods will be produced that alter our physical and mental well-being remains to be seen. The future of such endeavors is dependent on the creativity of food scientists and the legal maneuvers that will allow the production of such foods while protecting the consumer.

This work was supported by the Veterans Administration Medical Center Research Funds.

REFERENCES

1. Harris, M. F. Priestly Medal address. Science and technology in the 1980's. Chem. Eng. News, March 31: 38 (1980).
2. Diet and Behavior: A multidisciplinary evaluation. Nutrition Reviews 44: 1–254 (1986).
3. Levine, A. S., and Krahn, D. D. Food and behavior. In: Nutritional Modulation of Neural Function. Academic Press, New York; 1988, pp. 223–247.
4. Keys, A., Brozek, J., Henschel, A., Mickelson, O., and Taylor, H. L. The Biology of Human Starvation, Vol. II. University of Minnesota Press, Minneapolis, MN, 1950.
5. Winick, M., Ed. Hunger Disease: Studies by the Jewish Physi-
cians in the Warsaw Ghetto. John Wiley and Sons, New York, 1979.
6. Winick, M. Malnutrition and Brain Development. Oxford University Press, London, 1976.
7. Dakhinamurti, K. B vitamins and nervous system function. In: Nutrition and the Brain. Vol. 1: Determinants of the Availability of Nutrients to the Brain (R. J. Wurtman and J. J. Wurtman, Eds.), Raven Press, New York, 1977, pp. 249–318.
8. Fernstrom, J. D., and Wurtman, R. J. Brain serotonin content: increase following ingestion of carbohydrate diet. Science 174: 1029–1025 (1971).
9. Harmann, E. L-Tryptophane as a hypnotic agent: a review. Waking Sleeping 1: 155–161 (1977).
10. Seltzer, S., Stoch, R., Marcus, R., and Jackson, E. Alteration of human pain thresholds by nutritional manipulation and L-tryptophan supplementation. Pain 13: 385–393 (1982).
11. Trulson, M. E. Dietary tryptophan does not alter the function of brain serotonin neurons. Life Sci. 37: 1067–1072 (1985).
12. Feingold, B. F. Why Your Child is Hyperactive. Random House, New York, 1975.
13. Wender, E. H. Diet and hyperkinesis. In: Controversies in Nutrition (L. Ellenbogen, Ed.), Churchill Livingstone, New York, 1981, pp. 125–138.
14. Egger, J., Carter, C. M., Graham, P. J., Gumley D., and Soothill, J. F. Controlled trial of oligoantigenic treatment in the hyperkinetic syndrome. Lancet i: 540–545 (1985).
15. Prinz, R. J., Roberts, W. A., and Hantman, E. Dietary correlates of hyperactive behavior in children. J. Consult. Clin. Psychol. 48: 760–769 (1980).
16. Behar, D., Rapoport, J. L., Adams, A. J., Berg, C. J., and Cornblath, M. Sugar challenge testing with children considered behaviorally “sugar reactive.” Nutr. Behav. 1: 277–288 (1984).
17. Hanington, E. Preliminary report on tyramine headache. Br. Med. J. ii: 500–501 (1967).
18. Morley, J. E. Food peptides. A new class of hormones? J. Am. Med. Assoc. 247: 2370–2380 (1982).
19. Morley, J. E., Levine, A. S., Yamada, T., Gebhard, R. L., Prigge, W. F., Shafer, R. B., Goetz, F. C., and Silvis, S. E. Effect of exorphins on gastrointestinal function, hormonal release and appetite. Gastroenterology 84: 1517–1523 (1983).
20. Keys, A., Anderson, J. T., and Grande, F. Serum cholesterol response to changes in the diet. II. The effect of cholesterol in the diet. Metabolism 14: 759–765 (1965).
21. Bonamone, A., and Grundy, S. M. Effect of dietary stearic acid on plasma cholesterol and lipoprotein levels. N. Engl. J. Med. 318: 1244–1248 (1988).
22. National Research Council. Designing Foods: Animals Product Options in the Marketplace. National Academy Press, Washington, DC, 1988.
23. Band, H. O., and Dyerberg, J. Lipid metabolism and ischemic heart disease in Greenland Eskimos. Adv. Nutr. Res. 3: 1–222 (1980).
24. Atkinson, P. M., Wheeler, M. C., Mendelsohn, D., Pienaar, N., and Chetty, N. Effects of a 4-week, fresh-water fish (trout) diet on platelet aggregation, platelet fatty acids, serum lipids and coagulation factors. Am. J. Hematol. 24: 143–149 (1987).
25. Barcelli, U. P., Glas-Greenwald, P., and Pollak, E. E. Enhancing effect of dietary supplements with ω-3 fatty acids on plasma fibrinolysis in normal subjects. Thromb. Res. 39: 307–312 (1985).
26. Bronsgeest-Schoute, H. C., van Gent, C. M., Luten, J. B., and Ruiter, A. The effects of various intakes of ω-3 fatty acids on the blood lipid composition in healthy human subjects. Am. J. Clin. Nutr. 34: 1752–1757 (1981).
27. Ryanance, P. B., Gordo, M. P., Sawnor, R., Passey, V., and Weston, M. J. Fish oil modifies lipids and reduces platelet aggregability in hemodialysis patients. Nephron 43: 196–202 (1986).
28. Phillipson, B. E., Rothrock, D. R., Connor, W. E., Harris, W. S., and Illingworth, D. R. Reductions of plasma lipids, lipoproteins and apoproteins by dietary fish oils in patients with hypertriglyceridemia. N. Engl. J. Med. 312: 1210–1216 (1985).
29. Willis, A. L. Nutritional and pharmacological factors in ecosystem biology. Nutr. Rev. 39: 289–301 (1981).
30. Adam, O., Wolfram, G., and Zollner, N. Effects of linoleic alpha-linolenic acid in the human diet on linoleic acid metabolism and prostaglandin biosynthesis. J. Lipid Res. 27: 421–428 (1986).
31. Kromhout, D., Boschieter, E. B., and Coulnerd, C. L. The inverse relation between fish consumption and 90-year mortality from coronary heart disease. N. Engl. J. Med. 312: 1205–1209 (1985).
32. Kritchevsky, D. Fiber and lipids. In: Dietary Fiber in Health and Disease (G. V. Vahouny and D. Kritchevsky, Eds.), Plenum Press, New York, 1982, pp. 187–192.
33. Burkitt, D. P., Walker, A. R. P., and Painter, N. S. Effect of dietary fiber on stools and transit times and its role in the causation of disease. Lancet ii: 1408–1412 (1972).
34. Burkitt, D. P. Etiology and prevention of colorectal cancer. Hospital Practice [February]: 67–77 (1984).
35. Hill, M. J., Hill, M. K., Drwar, B. S., Aries, V., Crowther, J. S., Hawkesworth, G., and Williams, R. E. O. Bacterial and the aetiology of cancer of the large bowel. Lancet ii: 95–100 (1971).
36. Hill, M. J., and Aries, V. C. Facial steroid composition and its relationship to cancer of the large bowel. J. Pathol. 104: 129–139 (1971).
37. Antonis, A., and Berensohn, I. The influence of diet on fecal lipids in South African white and Bantu prisoners. Am. J. Clin. Nutr. 11: 142–155 (1962).
38. Labuza, T. P. A perspective on health claims in food labeling. Cereal Foods World 32: 256–267 (1987).
39. Wattenberg, L. W., and Loub, D. W. Inhibition of polycyclic hydrocarbon-induced neoplasia by naturally occurring indoles. Cancer Res. 38: 1410–1413 (1978).
40. National Research Council. Diet, Nutrition and Cancer. National Academy Press, Washington, DC, 1982.
41. Labuza, T. P. Industry’s role in designing new products for health and diet: Scientific and regulatory constraints. Cereal Foods World 30: 827–830 (1985).