Modern Nutrition in Health and Disease

Sixth Edition

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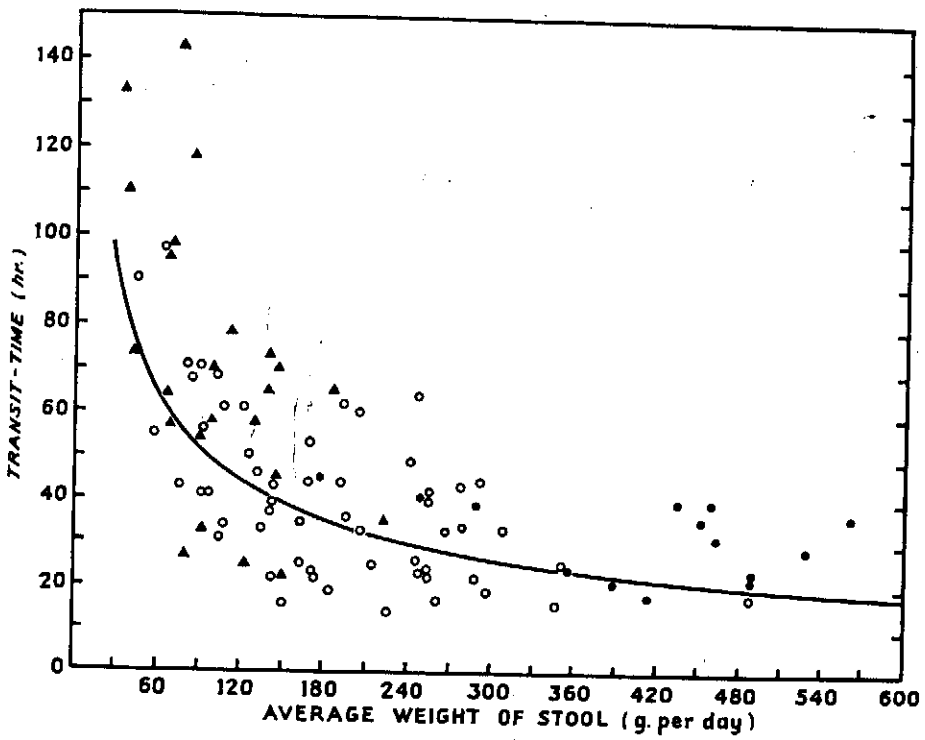

Fig. 4–4. Relationship between stool weight and oral-to-anal transit time for individuals on diets of varying fiber content. O = vegetarians, vegans and African boarding-school (mixed) diet; o = African villagers (high-residue) diet; ▲ = English boarding-school and British Navy (low-residue) diet. Transit time of radioactive plastic pellets included with the meal was detected by exposure of stools to x-ray film. (From Burkitt, Walker and Painter.[30])

high-fiber group. Thus, the colonic effects of the high-fiber diet occurred but were not accompanied by lowering of cholesterol levels. This lack of effect was found whether the subjects ate high-cholesterol or cholesterol-free diets. Although the serum cholesterol may be reduced by a single type of dietary fiber such as pectin or guar, further experiments on the effect of high quantities of specific fiber on cholesterol lowering are indicated. It is unlikely, however, that the ingestion of these substances would be as beneficial as the ion exchange resin, cholestyramine, presently used to reduce cholesterol. The decrease in coronary artery disease and the lower cholesterol levels in the rural African population is more probably caused by the low animal-fat diet and high physical activity than by a high-fiber diet.

Dietary Fiber and Diabetes. In recent years, pectin has been shown to slow the gastric release of ingested food, especially sugars. Thus, postprandial blood sugar might rise more slowly with a resultant lower insulin response. In fact, recent studies have confirmed that fiber-free substances such as apple juice produce higher postprandial insulin levels than do equicaloric quantities of intact apples.[33] Other studies in diabetics have demonstrated lower blood sugar levels after meals containing pectin.[34] Theoretically, pectin may improve diabetic control by reducing the absorption rate of sugar. It is not clear, however, whether this pharmacologic ef-

and children may complain of abdominal distress, and occasionally the genital and urinary tracts as well as the cardiovascular system may be involved. The allergic response of individuals is evaluated by skin tests. This is accomplished by subcutaneous injection or patch testing of extracts of the suspected materials; if the individual is sensitive, a response is elicited after a specific period of time.

The Graminaceae family is comprised of a group of foods that commonly produce allergenic responses in people. These staple foods include barley, corn, oats, rice, rye and wheat; of this group, wheat is the most common offender. Vegetables comprise a large group of allergenic foods that vary considerably in importance. Legumes are the most important, and the soybean has also been described in some cases as an allergen when used as a milk substitute.[131] Fruits, particularly strawberries, are allergenic to some people; bananas and pineapples are allergenic but considerably less so than strawberries.[132] Additional miscellaneous food allergens are found in chocolate, coffee, tea, carbonated beverages, beer, alcoholic distillates, condiments and flavors, yeast and molds.

One of the better understood forms of food allergies is so-called celiac disease or gluten enteropathy, an adverse response by certain individuals to certain fractions of wheat gluten. This disease has many of the symptoms seen in patients with idiopathic and tropical sprue.[133] A number of early investigators reported that the elimination of wheat from the diet produced an improvement in the condition of celiac patients. Even the so-called banana diet, as originally proposed by Haas,[134] was one that completely eliminated wheat.[135] The dramatic response observed by the Dutch investigators with one of their pediatric patients when wheat gluten was added to or removed from the diet was enough to establish this protein as the dietary factor associated with the characteristic symptoms.[136,137] When wheat gluten is removed from the diet improvement occurs in all aspects of the disease, but it may require as long as a year before the individual is completely restored to normal functioning.[138]

A description of the clinical aspects of gluten enteropathy and its dietary treatment are given in Chapter 31B. Much attention has been focused on the constituents of gluten and their relation to the intestinal changes,[138–143] but the exact composition of the deleterious gluten fraction is still uncertain.

Saponins

The saponins have been identified in at least four hundred different species belonging to more than eighty different plant families. These toxins, which occur as glycosides, have a bitter taste and characteristically hemolyze red blood cells. Although saponins have been studied from the point of view of hemolytic activity and, in some cases, for their therapeutic properties those occurring in foods and feeds have been studied very little. The nutritional significance of soybeans and alfalfas in which saponins occur makes this area one of potential significance to human populations.

Alfalfa saponins are comprised of at least three different types, and soybean saponins have been separated into five fractions which differ in their activity.[144,145] The two major classes of saponins, according to structural formulas, are the triterpenoids found in sugar beets and the steroid saponins represented by dioscin. Saponins are also present in spinach, asparagus and horse chestnut.[146] In addition, they are widely used in soft drinks, beers, confections and other food products because of their ability to stabilize aqueous solutions and suspensions of oil or powders. Saponins, particularly those in several species of Dioscorea, are major sources of starting material for the commercial synthesis of progesterone and other steroid products.[147]

seem to exert a sparing effect on PUFA in the plasma and liver of rats.[224] Although the optimum requirement of EFA for the male rat is approximately 1.3 per cent of calories, that for female rats is approximately 0.5 per cent.[223] Similar differences in EFA requirement have been observed in other animal species as well.[225,226]

EFA deficiency results in alterations in cell membranes. It is probable that the change in the fatty acid composition of phospholipids of the membrane is the primary lesion of EFA deficiency.[227] One of the biochemical criteria for EFA deficiency is the effect on mitochondrial permeability;[228] liver mitochondria prepared from EFA-deficient rats evidently have altered permeability, since they swell rapidly in vitro and possibly in vivo as well, under conditions that preserve the shape and size of normal mitochondria.[229] It has been shown that mitochondria prepared from livers of EFA-deficient rats oxidize substrates of the citric acid cycle more rapidly than do normal mitochondria. At the same time less high-energy phosphate is formed.[230] This uncoupled phosphorylation might explain the increased metabolic rate, the high endogenous respiration and the elevated cytochrome oxidase activity[212] in the EFA-deficient animal.

It is difficult to deplete adult animals of essential fatty acids because of their large reservoir of linoleate in adipose tissue. Even prolonged feeding of a deficient diet may not produce deficiency symptoms, although Collins and Sinclair[230] have produced an EFA deficiency in patients through parenteral feeding of saturated fat. In infants receiving fat-free total parenteral nutrition (TPN) for many weeks, scaly skin lesions, thrombocytopenia and poor wound healing were accompanied by low levels of linoleic and arachidonic acid in plasma and a high concentration of 5,8,11-eicosatrienoic acid (the trienoic acid characteristic of EFA deficiency).[231] More recently, reports of an EFA deficiency syndrome in adult patients during TPN, oral fat-free feeding or in those with lesions of the GI tract have appeared.[232–235] Essential fatty acid deficiency symptoms have been produced in adult rats by feeding a fat-free diet in restricted amounts until they weighed one-half of their original weight, and then by feeding the fat-free diet ad libitum.[236] It is in young growing animals that essential fatty acid deficiency is produced in the shortest length of time.[237] It is now established that essential fatty acids are required by the human infant. The requirement appears to be 0.5 per cent of calories.[238] Collins et al.[239] concluded that the adult man requires at least 7.5 gm per day of linoleic acid, an amount equal to approximately 2 per cent of the total caloric intake of an adult man consuming a 3000-cal diet. There are some indications that atherosclerosis is accompanied by some derangements of EFA metabolism.[240]

Even though EFA deficiency symptoms have been corrected in some cases by topical application of EFA-rich oils,[241,242] a recent report has shown that this method is not universally effective.[243]

'An excessive intake of EFA (and polyunsaturated fatty acids in general) may have some adverse effects. First of all, the antioxidant capability of the body is challenged. Cholesteryl linoleate hydroperoxides have been isolated from atheromatous plaques and they appeared to be similar to those produced by autooxidation.[244] However, most of the natural dietary sources of PUFA are also excellent sources of active forms of vitamin E. The need for vitamin E is related to the amount of PUFA in the diet and in tissues, and this must be considered when the nutritive adequacy of diets high in PUFA is being evaluated.[212] It has been reported[245] that a high PUFA diet did not cause a decrease in serum vitamin E levels in humans. However, supplemental vitamin E may be advisable for an extended period if a high PUFA intake is discontinued.

It has been suggested that a high polyunsaturated to saturated (P/S) fatty

acid ratio promotes gallstone formation.[246] Hofman et al.[247] pointed out that this may be due in part to a stimulation of cholesterol biosynthesis. Also, cholesterol secretion into the bile may be increased, causing elevated lithogenicity of the bile.[248]

Similarly there have been suggestions that high PUFA intakes may result in the formation of more bile salts, which can be degraded by carcinogen-producing bacteria, thus increasing the risk of colon cancer.[249]

Further recognition of the importance of essential fatty acids in nutrition has recently been demonstrated by the fact that EFA are precursors for the hormone-like substances called prostaglandins.[250,251]

PROSTAGLANDINS (PG)

About 40 years ago, Goldblatt[252] and von Euler[253] independently discovered that seminal fluid and extracts of vesicular glands contained a lipid fraction with potent vasodepressor activity and able to stimulate smooth muscle. In 1960 Bergström and Sjövall[254] crystallized from many kilograms of sheep vesicular glands an active principle which they named prostaglandin E_1 (PGE_1). Three years later, Bergström and co-workers[255] established the structure of PGE_1 and also of a series of structurally related compounds.

To date, dozens of different, naturally occurring prostaglandins have been isolated, all of which are derivatives of prostanoic acid (C20-cyclopentanoic acid) and which appear to be widely distributed in animal tissues.[256] Four series of natural prostaglandins have been described, designated by the letters E, F, A and B, corresponding to differences in the ring structure and variations in degree of unsaturation of the side chain.

In 1964, two groups of investigators, Van Dorp et al.[257] and Bergström et al.,[258] reported that prostaglandins could be synthesized from polyunsaturated fatty acids. The conversion involved a ring closure (Fig. 5–1). In the synthesis of prostaglandins from dihomo-γ-linolenic acid and arachidonic acid, prostaglandin endoperoxides and tromboxanes are among the intermediates and metabolites.[259,260] A competition between unsaturated fatty acids was observed in PG formation, i.e. linolenic acid was found to compete irreversibly with arachidonic acid for PG synthetase.[261] Although prostaglandins can be formed from a variety of polyunsaturated fatty acids, Van Dorp and co-workers[273,278] found that biologically active prostaglandins are formed only from those unsaturated fatty acids which have appreciable EFA activity; therefore, these workers postulated that the sole essential function of the EFA was as precursors for prostaglandin formation. However, attempts to cure EFA deficiency in rats by oral or intravenous administration of prostaglandins have been unsuccessful. It is possible, of course, that the administered prostaglandins did not reach the location where they were needed, and it is also possible that there is a difference between administered prostaglandins and prostaglandins formed in situ. However, this is the first time since the discovery of essential fatty acids that the role of EFA as precursors for other physiologically active metabolites has been studied. Recent reports indicate that an increase in dietary linoleic acid intake directly influences prostaglandin biosynthesis.[262] Such findings give support to the hypothesis postulated by Thomasson[263] that the beneficial effects of dietary linoleic acid can be explained by an increased prostaglandin synthesis.

The functions of prostaglandins in animal metabolism are many and varied. Since the highest concentrations of prostaglandin activity are found in accessory reproductive tissues and in semen, it was originally proposed that prostaglandins played a role in reproduction by causing vasodilation, by facilitating ejaculation or by contributing to sperm viability and transport.[264] It has been proposed that, in

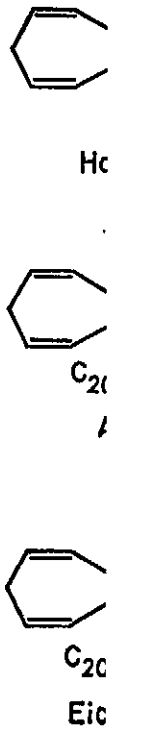

Fig. 5–1. Formati

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