

## Toxicities of Natural Foods in Man: A Survey

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Foods are considered to be substances that nourish cells and enable them to grow, multiply and repair themselves. Many foods may produce bodily harm, however, by some intrinsic toxicity or by excess consumption, contamination, preparation, inherited inability to process them, hypersensitivity of the individual, or other.

The literature is scattered and voluminous and the early reports are untrustworthy. In the present discussion, man rather than animals is emphasized as well as food toxicity encountered chiefly in the United States. We have not included any commentary on federal policies of increasing toleration of food practices dangerously leading to toxicities (see Marshall, 1982).

### FOODS CONTAINING CARCINOGENS

#### Saccharin

Saccharin is the most widely used sugar substitute. In large doses it incites bladder tumors in laboratory animals and the FDA has placed it on a regulated list.

#### Tea

The black teas from Ceylon and India contain considerable *tannin* and *gallic acid*. These are controversially suspect as causative factors in esophageal cancer (Lewis and Elvin-Lewis, 1977, p. 119).

### CONTAMINANTS FAVORING CARCINOGENICITY

#### Fungus Contaminants (Mycotoxins)

Some strains of *Aspergillus*, a mold, produce *aflatoxins*. The one found most often in food is aflatoxin B<sub>1</sub>. It inhibits protein synthesis, causing the death of liver cells particularly. B<sub>1</sub> is one of the most potent hepatocarcinogens known. It is found chiefly in figs, peanuts and other nuts, and cereals (Osborne, 1982).

There is a toxic substance called *patulin* which can occur in apple juice due to contamination by molds. The substance is suspected of being carcinogenic (Crosby, 1979).

Toxins can be present in food that is not visibly moldy and they can persist even if the food is cooked or otherwise processed.

### Polycyclic Aromatic Hydrocarbons (PCHs)

PCHs are an important class of carcinogens because they are being widely dispersed in the atmosphere, soil and water from the smoke and smog of industrial cities and some have tumorigenic potency. Dangerous levels of PCHs are now detected in many foods, particularly leafy vegetables (Harvey, 1982).

## CONTAMINATION OF DRINKING WATER

Water is a food. Contamination by industrial wastes possibly leading to carcinogenicity is a huge problem and will not be considered here. There is atmospheric contamination of an incidental nature, however, nitrates posing a problem. It is contended that a high nitrate concentration in water supplies provides a risk of gastric cancer (Walters and Smith, 1981).

A concern about nitrates in water peripheral to the cancer issue centers on their reduction to nitrites by bacteria which can live in an infant's stomach due to low acidity therein. Hemoglobin, especially the persisting fetal type in the infant, is susceptible to oxidation by nitrites and methemoglobin is formed. Oxygen delivery is impaired. Cyanosis in infants who are given water from wells is a manifestation of nitrate toxicity (Gleason et al., 1969, p. 100).

Water per se can produce ill effects. Massive overdrinking (which has been used in torture) produces the syndrome of "water intoxication". Cerebral edema, convulsions and coma can follow.

Water causes gastric distress in many persons because it can excessively stimulate gastric juice, which irritates the stomach lining. That is why "club soda", which contains sodium bicarbonate, may produce no such symptoms.

## FOODS DEVELOPING CARCINOGENIC PROPERTIES BECAUSE OF PREPARATION

Charcoal broiling can result in the formation of carcinogenic hydrocarbons. Smoke imparts a flavor derived from phenolic materials produced when wood is burned in conditions of oxygen deficiency. While the phenolic flavors are formed, polynuclear aromatic hydrocarbons are also produced. Some of these, especially 3, 4-benzpyrene and benzanthracene, are carcinogenic. These occur in smoked fish, caramelized sugar and roasted coffee (Crosby, 1979). Benzpyrene is the ubiquitous carcinogen in city smog. Its metabolites, particularly *epoxides*, are active in producing malignancy in animals and possibly in man.

Fats and oils subjected to prolonged overheating by frying are controversially thought to produce carcinogens. The toxicity is claimed to increase if an oil is used repeatedly and if a shallow pan allowing oxidation is used.

Yannai (1980) presents a succinct review of toxicity induced by food processing. Thus, a cured meat such as bacon contains trace amounts of *N-nitrosodimethylamine* (NDMA) and on frying bacon *N-nitrosopyrrolidine* is formed. Both substances are claimed to be carcinogenic (Gough et al., 1976). Fortunately, both nitrosamines get lost to a considerable degree in the vapor during cooking, although some remain in the rasher and in the cooked-out fat (Holmes and Woodburn, 1981). Wasserman et al. (1978) state that frying bacon at low or medium

heat for less than 10 minutes can result in the least nitrosamine levels, although Pensabene et al. (1974) report that N-nitrosamine formation is dependent on temperature and not time.

The nitrite in bacon processing imparts flavor and color and prevents growth of *Clostridium botulinum*. Since the nitrites react with amines in the body to produce nitrosamines which are inconclusively implicated in cancer of laboratory animals (Pierson and Smoot, 1982), there are proposed substitutes or sparing agents (Widdus and Busta, 1982).

In 1978 it became known that NDMA was present in domestic and imported beers and that barley malt was the source (Havery et al., 1981). FDA regulations to modify the malting process have reduced the present nitrosamine levels markedly.

## FOODS CONTAINING MUTAGENS

Mutagens are agents that produce genetic mutations and they have a wide distribution in the diet. There are *mutagenic flavonoids* in many vegetables and mutagenic activity is said to exist in extracts from coffee and tea (Maugh, 1982). There are controversial opinions as to whether mutagens in foods contribute markedly to the risk of cancer (Committee, 1982).

### A. Caffeine

Although there is no evidence that caffeine is involved in carcinogenesis, there is a claim that it induces chromatid breakage (genetic damage) in human cells *in vitro* and that it could prove to be a dangerous mutagen (Kahlmann et al., 1968).

### B. Charring of Meat and Fish

Charred meat and fish can develop mutagenic potential. Tryptophan, serine and glutamic acid may produce mutagens at high temperature pyrolysis. Difficult decisions arise. Although cooking of meat and fish may produce mutagens, it also destroys pathogenic organisms. Further, some vegetables that contain mutagens have a high nutritive value.

## FOODS CONTAINING TOXICANTS (MAINLY CYANOGENIC GLYCOSIDES)

### A. Fruits

#### Apple (*Malus* spp.)

There is a toxic part of apples, mainly in the seeds. Lewis and Elvin-Lewis (1977) cite a case where one cup of seeds was eaten and caused death, from cyanide poisoning.

The amino acid phenylalanine in the seed converts to the cyanogenic glycoside *amygdalin*. This hydrolyzes on digestion to hydrocyanic acid. The cyanide poisons oxygen carriage by cytochrome oxidase. Victims may die within minutes of exposure. The lesson here is (1) that all parts of a food are not harmless, and (2) that children, especially, must learn this early.

#### Apricot (*Prunus armeniaca*)

Apricot plants contain amygdalin in the seeds, bark and leaves and ingestion should be avoided (Lewis and Elvin-Lewis, 1977, p. 41). Laetrile, legal in Mexico as a cancer cure, is an extract of apricot pits. The theory is that the extract yields

cyanide which preferentially attacks tumor cells. Cyanide is released by beta-glucuronidase common to tumor cells.

#### Elderberry (*Sambucus* spp.)

The fresh leaves, stems and roots contain a poisonous alkaloid, and a cyanogenic glycoside called *sambunigrin* causing cyanide poisoning. Red elderberries are very toxic.

The fully ripe fruit is harmless and is used in pies, wine, jelly and pancakes. Other parts of the plant are used as drugs.

Children using peashooters made of elderberry stems have been poisoned (Lewis and Elvin-Lewis, 1977, p. 50).

#### Cherries (*Prunus* spp.)

Seeds and leaves contain the cyanogenic glycoside *amygdalin*. The seeds are the most toxic. The fleshy part of sweet and of sour cherries is edible. That of the laurel cherry (*P. laurocerasus*) contains amygdalin.

#### Pear (*Pyrus communis*)

Pear seeds contain amygdalin and are potential poisons.

#### Peach (*Prunus persica*)

All parts of the peach contain amygdalin, concentrated mainly in the bark, leaves and seeds. Poisoning has followed ingestion of peach kernels (Liener, 1980, p. 152).

#### Plum (common is *Prunus domestica*; wild is *P. americana*)

The plum is the least toxic member of the genus *Prunus*, but the leaves and seeds contain cyanogenic glycosides that convert to hydrocyanic acid.

#### Prune (*Prunus domestica*)

The prune is the partially dried fruit of a plum. The laxative effect of prunes is well known. Prunes contain derivatives of *hydroxyphenylisatin* which acts as a gastrointestinal irritant.

#### Almond (*Prunus amygdalus*)

Almonds are the fruit of the almond tree. The seeds of the sweet variety are edible. It is difficult to separate the edible sweet almond from the bitter almond (*Prunus amygdalus* var. *amara*). The seeds of the bitter plant contain high yields of amygdalin (Abrol, 1967). Lewis and Elvin-Lewis (1977, p.41) state that 50 to 70 bitter almond nuts are fatal for adults and 7 to 10 for children.

## FOODS CONTAINING TOXICANTS

### B. Vegetables

#### Onion (*Allium cepa*)

A toxic principle thought to be an alkaloid may cause an anemia in man if onions are eaten in "large" amounts for one or more weeks (Schmutz et al., 1979, p. 155). The bulb contains the toxic material. Other related suspected foods are chives, garlic, leeks and shallots.

Onions and other plants in the genus *Allium* contain sulfur compounds called *glucosinolates*. These give rise to thiocyanates, isothiocyanates, nitriles, goitrin and progoitrin. Glucosinolates substitute for or displace iodine, preventing its uptake or accumulation in the thyroid gland. Heat reduces the direct action of these substances. Normal patterns of consumption cause no harm.

### *Eggplant (Solanum melongena)*

Eggplant is a fruit eaten as a vegetable. Botanically, it is a berry. Its leaves, stems and fruit contain solanaceous alkaloids that are claimed, without solid evidence, to be poisonous. The plant belongs to a nightshade family long suspected as being potentially toxic. Glycosides of *solasodine* are common in eggplant and solasodine is teratogenic in hamster fetuses (Kingham, 1979, p. 75).

### *Fava Bean (Vicia faba)*

Fava (broad) beans may produce acute febrile hemolytic anemia. The condition is called favism. Crises due to dry or cooked beans are of moderate intensity but severe attacks follow ingestion of fresh, raw fava seeds.

Sensitivity is hereditary and involves a deficiency of glucose-6-phosphate dehydrogenase. Causative toxic substances may be *divicine* and *isouramil* (Liener, 1980, p. 283).

The plant is widely cultivated in parts of the United States. Most cases result from eating fresh beans and thus peak incidence occurs at harvest.

### *Lima Beans (Phaseolus lunatus)*

Lima beans contain a lectin (protein hemagglutinin) called *phaseolunatin* or *linamarin* (Lewis and Elvin-Lewis, 1977, p. 44). This hydrolyzes in part to hydrocyanic acid. Thorough cooking reduces the danger of poisoning, but may not fully destroy the toxic principle. Preliminary soaking before cooking helps eliminate the toxic lectin.

### *Kidney (Navy) Beans (Phaseolus vulgaris)*

The kidney bean contains lectins (hemagglutinins) associated with human gastrointestinal disturbances. The toxin is completely destroyed by boiling (Bender and Reaidi, 1982). Of interest, the bean also contains inhibitors of alpha-amylase from the saliva and pancreas. The active inhibitor, called *phaseolamin*, when taken orally blocks starch digestion and this is the principle behind starch-blockers for weight control (Bo-Linn et al., 1982). The FDA is now in litigation as to whether these agents are drugs or foods.

### *Wheat (Triticum aestivum)*

Wheat also contains the alpha-amylase inhibitor. This may persist through bread baking and infants or adults having impaired digestive enzymes may not destroy the inhibitor. A similar problem also arises in some wheat-based breakfast cereals (Liener, 1980, p. 450).

Bread cannot be made without the gluten of wheat and some uncertain fraction in the gluten exacerbates the symptoms of patients with celiac disease (Goodhart and Shils, 1973, p. 423). Wheat is also a very common food allergen, due in part to albumin and gliadin.

### *Spinach (Spinacia oleracea)*

The leaves of spinach contain salts of *oxalic acid* that could become precursors of calcium oxalate crystals. Excesses have been controversially claimed to cause precipitates in the kidney. Spinach also lowers blood sugar (Lewis and Elvin-Lewis, 1977, p. 218). The concentrations of oxalates or hypoglycemic factors are not ordinarily toxic.

Between 1959 and 1965 in Germany, 15 cases of *nitrite* poisoning followed ingestion of spinach by babies (Simon, 1966). Poisoning occurs only if spinach contains much nitrate, which bacteria of the stomach convert to nitrite. Infants less than three months of age should not be given spinach because of bacterial action.

Arena (1979, p. 718) cites the death of a five-year old girl who ate a large number of raw spinach leaves. Epstein (1969) states that vegetables in highly fertilized soil contain 1,000 to 5,000 ppm of sodium nitrate, well exceeding the maximum permissible amount in foods.

Nitrates can convert to nitrite in cans and the nitrite reacts with the metal to produce nitrogen which swells the can. Metal cans have caused toxicity for other reasons, essentially because of dissolved tin or the lead solder used and, for that matter, even plastic containers contain toxic polymers (Liener, 1980, p. 417).

#### Potato (*Solanum tuberosum*)

The "Irish" potato is edible so long as it is not very green. Since it is a modified stem, a potato exposed to light for a period of time becomes green and it may accumulate toxic amounts of a glycoside alkaloid called *solanine*. The toxic parts of the potato include green areas under the potato skin and the sprouts. The skin is harmless when eaten in normal quantities. A concentration of 20 mg solanine/100g fresh weight is thought to be the maximum safe level for market potatoes, to prevent gastrointestinal and neurologic disorders. Fatalities are rare because sprouted potatoes are peeled. Also, solanine in boiling is leached out into the water (Koelling, 1982), although cooking does not destroy it. Solanine is a cholinesterase inhibitor.

#### Rhubarb (*Rheum rhabarbarum*)

The leaves and edible stalks of rhubarb contains rather high quantities of oxalic acid. This was once thought to be the cause of vomiting and enlargement of the liver that follows ingestion of raw leaves and stems. It is much more likely that the toxicity is due to *anthraquinone glycosides*. These are present in leaves, especially in early summer. About 10 to 20 grams of fresh leaves are highly irritating (Fairbairn, 1976, p.15). Death has sometimes followed ingestion of rhubarb (Leiner, 1980, p. 453).

#### Mushroom (*Amanita* spp)

Mushrooms are unpredictable. Some species are only occasionally poisonous. Some are poisonous only if eaten raw; others if eaten in certain seasons or stages of maturity. Cooking does not destroy all the toxins.

Some people become ill if they drink alcoholic beverages when eating mushrooms. Use of certain drugs may make a harmless mushroom toxic for some people.

The most common poisoning in the United States is from *Amanita verna* and *A. brunnescens*. Poisoning by these and the more rare *A. phalloides* is due to thermostable toxins that destroy cells. Toxins are cyclopeptides which include *phalloin*, *phalloidin*, and *amanitins*. Poisoning by *A. muscaria* is due to *ibotenic acid* and *muscimol* (Kinghorn, 1979, p. 25). There are other mushrooms that contain *psilocybin* and *psilocin* which produce hallucinations. Additional toxicants have been extracted from still other species.

#### Yams (*Dioscorea* spp.)

Yams are among compounds suspected of causing teratogenesis in man and other animals (Lewis and Elvin-Lewis, 1977, p. 95). Certain yams (*D. hirsuta*) contain an alkaloid, *dioscorine*, which produces paralysis of the central nervous system (Clasby, 1975, p. 490).

#### Sweet Potato (*Ipomoea batatas*)

Sweet potatoes produce metabolites called *phytoalexins* in response to stress (Salunkhe and Wu, 1977). An abundant metabolite is *ipomeamarone*. This is a

hepatotoxin in mice and a suspected toxin in man. It is not eliminated by baking or boiling and it is best to avoid potatoes with blemishes or discolorations.

### C. Food Colors; Spices

Nearly 65 synthetic colors are known to be in use around the world. Khanna and his co-workers (1980) review these substances and they deplore the fact that some appear to be highly toxic and nevertheless are insufficiently regulated. In the United States there are about eight color additives and the FDA certifies them.

#### Monosodium Glutamate

This is the responsible agent for the digestive upset known as the "Chinese restaurant syndrome." It is especially dangerous in baby foods because of reported damage to the brain in newborn animals (Grollman and Grollman, 1970).

#### Hot Peppers (*Capsicum* spp.)

Red chili peppers (*C. annuum*) can irritate the entire gastrointestinal tract. The symptoms are more severe with the tobacco pepper (*C. frutescens*) which is considered to be a hepatocarcinogen in rats.

#### Nutmeg (*Myristica fragrans*)

Nutmeg is the ripe seed of *M. fragrans*. It is a powerful hallucinogen. This is due to a combination of volatile oils, *myristicin*, *elemicin* and the weak carcinogen *safrole*. Ingestion of large quantities of nutmeg causes stupor and death (Merck Index, 1960, p. 700).

#### Sage (*Salvia officinalis*)

Sage represents the dried leaves of the plant. Large doses may cause nausea, vomiting and constipation (Merck Index, 1960, p. 918).

### D. Milk

Bovine milk is the main source of *orotic acid* in the human diet. Levels in cow's milk increase from 21 to 84 ppm from days 2 to 45 of lactation. Because only 10 ppm may affect liver metabolism and cause liver necrosis in rats, there is need to evaluate its possible toxicity in milk powders used in humans (Okonkwo and Kinsella, 1969). Robinson (1980) does not think that orotic acid poses a serious problem in man, but believes that research is needed on this point.

## FOODS CONTAMINATED BY TOXICANTS

### Milk

There is considerable concern about the level of pesticide residues in both bovine and human milk. Dillon et al. (1981) present a survey of this problem. Lee and Lorenz (1979) note other hazards of milk, i.e., in the cardiac-prone hypercholesterolemic person, in the lactose-intolerant person, and in the allergic person. Infants with hereditary disturbance of galactose metabolism develop serious symptoms with ingestion of milk. Such galactosemia demands rigid exclusion of lactose and galactose from the diet. Speckmann et al. (1981) claim that intolerance to lactose in an 8-ounce serving of milk is rare.

#### Rye (*Secale cereale*)

Ergot is the toxic chemical constituent of the sclerotium (branching filaments; hyphae) of *Claviceps purpurea*, a fungus that parasitizes kernels of rye (and wheat) chiefly. Ergot contains *ergonovine*, an alkaloid causing human ergotism. This is

highly controlled today, but it killed millions of people in the Middle Ages. There are burning sensations and gangrene in the extremities, and also abortion and convulsions. Epidemics in the Middle Ages were referred to as "St. Anthony's Fire" because gangrenous limbs looked as though they were burned.

#### Fish and Shellfish

Fish muscle contains histidine which can form histamine by bacterial action if left standing. Canned tuna fish has been a source of histamine poisoning (Rice et al., 1976), and the disorder called scombroid poisoning is caused chiefly by histamine.

Shellfish such as clams eat the dinoflagellates *Gonyaulax catenella* or *G. tamarensis* and thereby acquire a nitrogenous compound called *tetrodotoxin* which does not harm the shellfish, but which is often a fatal neurotoxin to man. At certain times of year the dinoflagellates so multiply as to produce a dangerous "red tide" poisonous to clams, crabs, oysters, shrimp and other marine organisms. A neurotoxin is involved called *saxitoxin* which is highly poisonous when man ingests the shellfish and this toxin is not destroyed by cooking. Fish eggs can also contain toxicants (see Liener, 1974).

#### Meat Grilled on Wooden Skewers

Wooden skewers used to hold "hot dogs" and other meat for grilling can introduce hazards. There are skewers made from the stems of an evergreen, *Nerium oleander*, which contain cardioactive glycosides that have caused deaths (Liener, 1974). The poisons are *oleandroside* and *nerioside*.

#### Beer Treated with Cobalt

At one time cobalt was added to beer to stabilize the foaming qualities. It took many years before cobalt was incriminated as the cause of severe heart attacks in heavy beer drinkers and this additive was discontinued (Alexander, 1969).

### FOODS ACTING AS TOXICANTS BECAUSE OF INHERITED DEFECTS IN THE INDIVIDUAL

For a person having severe pancreatic diabetes, where from birth insulin function may be deranged, a single ordinary meal containing cane sugar (sucrose) may set off a train of metabolic events leading to disastrous results.

Fructose occurs in many fruits and is the predominant sugar in honey. Some people are born without an enzyme, *aldolase B*, and for them fruits (and also cane sugar) have to be completely excluded to prevent gastrointestinal pain, vomiting and hypoglycemia (Cox et al., 1982). The disorder is acquired from a double dose of a recessive gene.

Persons who by gene defect lack the enzyme *lactase* fail to break down milk sugar (lactose) and they may not tolerate milk.

Fatty foods, especially french fried potatoes and onions, are anathema to most people who suffer by inheritance or otherwise from disorders of the biliary tract. This is expected since many nutrients affect the quality and amount of the bile, the movements of the gallbladder, and the tone of the sphincter of Oddi.

These so-called inborn errors of metabolism also include protein disturbances. In phenylketonuria, there is a deficiency of *phenylalanine hydroxylase* and phenylalanine intake must be sharply reduced by feeding artificial protein substitutes. In "maple syrup urine disease," the infant must ingest an artificial formula free of

valine, leucine and isoleucine. These are only examples of a class of amino acid toxicities.

## FOODS AS VITAMIN ANTAGONISTS

### A. Biotin Antagonist — Raw Eggs

Raw eggs contain a glycoprotein called *avidin*, present in the egg white up to 0.05% of the total protein content. One molecule of avidin binds four molecules of biotin (vitamin "H"). This deprives the person ingesting raw eggs of an essential growth factor (Comments, 1982-83).

### B. Thiamin Antagonists — Seafoods, Vegetables, Fruits

Fish such as carp, herring, swordfish and lake trout contain thiamin antagonists (Goodhart and Shils, 1973, p. 415). There is also anti-thiamin activity in blackberries, black currants, red beets, Brussels sprouts, red cabbage and spinach. There are antagonists for niacin in corn and millet, for pantothenic acid in yeast and for riboflavin in the akee plum.

### C. Multivitamin/Mineral Preparations

Multivitamin/mineral preparations contain analogues for B<sub>12</sub> which are claimed to be harmful to human vitamin B<sub>12</sub> metabolism (Herbert et al., 1982). It seems advisable to omit B<sub>12</sub> from vitamin/mineral preparations.

### Vitamin Poisoning — Hypervitaminosis

Only those vitamins are considered herein whose known or probable toxicities have strong documentation. Gilman (1980, p. 1553) lists recommended daily vitamin allowances for the reference man, woman and child. Quantitative values for toxic thresholds are controversial. Poisoning does not occur with ordinary daily consumption.

The recommended adult allowance for vitamin A is 5,000 I.U. Poisoning occurs after ingesting up to 100,000 units (30 mg) daily for several months. Food faddists may ingest toxic levels. Infants need about 1,500 I.U. and doses of 18,500 daily for 1 to 3 months are reported to be toxic (Goodhart and Shils, 1973, p. 153).

For vitamin D, the daily requirement for infants and adults is 400 I.U. There is a danger in giving supplements such as 4,000 I.U. in fortified foods to infants (Goodhart and Shils, 1973, p. 160). Ingestion of 50,000 units daily to children and adults should be avoided for any long periods of time.

For other vitamins, toxicities are either unknown or they occur at such repetitively high values that they may be considered relatively safe. The reports are conflicting.

## GOITROGENIC FOODS

### Soybean (*Glycine max*)

Goiters have occurred in infants fed soy milk or soy flour (Hydovitz, 1960; van Wyk et al., 1969). There are also many goitrogenic foods in the genus *Allium*, but it is only excess consumption that may be associated with toxicity.

Soybeans are toxic in other regards. One possible toxic factor, which is common to other legumes, is a *trypsin inhibitor*. Trypsin is essential in the small bowel for protein digestion. The inhibitor, present in the raw bean, is inactivated by cooking.

Soybeans are also hemagglutinins (phytoagglutinins or lectins) and this may be partly responsible for the gastrointestinal disturbances if raw soybeans are eaten.

A valid explanation is still needed to explain the growth-inhibiting action in raw soybeans (Goodhart and Shils, 1973, p. 418).

## TOXICITY OF FOOD ADDITIVES

### Preservatives and Sweeteners are Emphasized Below.

#### Preservatives

These substances extend the shelf life of foods. Shtenberg and Ignat'ev (1970) urge that sulfites and benzoates should be restricted, substituting sorbic acid. Sorbic acid and potassium sorbate are considered safe by the FDA.

Sodium nicotinate, a fresh meat color extender, has caused food poisoning, expressed particularly in edema of the extremities. This additive is not legalized in some states.

Sodium nitrite is used to prevent growth of *Clostridium botulinum* and to preserve the color of meat and fish in salting and pickling. Nitrites are potentially poisonous in several ways, one involving methemoglobin formation. Another is in formation of N-nitrosamines, formed either in processing foods or in the digestive tract by reaction with amino compounds. By similar mechanisms, nitrites react with phenolic compounds, forming aromatic nitroso substances, some of these nitrophenols being suspected of carcinogenicity (Challis, 1973).

#### Sweeteners

There are some toxic synthetic sweeteners. Cyclamates were banned in 1969 because they produced bladder cancer in rats. Saccharin is now a regulated substance with suspected carcinogenicity. Crosby (1976) reviews several sweetening agents.

Cane sugar as a natural sweetener is in a sense an additive and its local dental effects are of interest. Meals high in cane sugar favor colonization of cariogenic organisms on teeth. Restriction of cane sugar reduces bacteria such as *Streptococcus mutans* in dental plaques (Newbrun, 1982). Bibby and Mundorff (1975) blame acid candies, beverages and fruits for the highest dissolution of enamel.

## POISONING BY EXCESS MINERAL INGESTION

### A. Sodium Chloride (Table Salt)

In the United States, the daily sodium intake per person is three or more grams. An estimated safe and adequate daily intake should range from 1.1 to 3.3 grams (48 to 143 mEq.) (National Research Council, 1980). A moderate restriction is one gram. The hypertensive influence of table salt is firmly documented and the FDA proposes labelling the sodium content of processed foods.

Salt poisoning has occurred in hospitalized infants where salt was mistaken for cane sugar. Renal damage and convulsions followed. In the neonate, the repeated intake of skim milk has produced salt intoxication.

### B. Iron

The daily iron requirement is 10 to 20 mg in adult males and 8 to 15 in females (Gilman et al., 1980). Finch (1982) states that a normal person can control the accumulation of body iron despite ingestion of 5 to 10 times the normal amount. Other writers note that excesses can be dangerous because excretion hardly increases, so that iron deposits in vital organs.

Some wines of southern France contain 16 mg of iron per liter and even

American wines supply several mg daily. The Bantus of South Africa brew a beer in iron kettles and the beer contains more than 40 mg of iron per liter. A Bantu male often consumes 100 mg of iron per day in beer (Emery, 1982). A disease called secondary hemochromatosis, often fatal, occurs.

The Food and Nutrition Board of the National Academy of Sciences recommends a daily allowance of 10 mg daily for children in the first six months to supplement milk. This may be too high. Also, it is inadvisable for an adult to take vitamin/mineral preparations containing iron if iron is being ingested sufficiently from other sources.

### C. Calcium

The minimal adult requirement is 800 mg per day (Gilman, 1980, p. 1553). The predominant source is dairy products. Healthy serum contains 10 mg/dl. Levels exceeding 14 are dangerous and 18 mg/dl may cause death. Ingestion of daily quantities of calcium salts is ordinarily unlikely to cause toxicity. The so-called "milk-alkali syndrome" can be exacerbated, however, by ingestion of large quantities of milk.

### D. Fluoride

Man obtains fluoride from ingesting plants and water. Incidental sources include food additives, e.g., baking powder. Combinations of fluoridated water, toothpastes and certain foods could conceivably produce a problem especially in children. This is a developmental problem in teeth where 1.7 ppm of fluoride in water produces mottled enamel before the teeth have erupted (Gilman, 1980, p. 1547). At 4 to 6 ppm, mottling approaches 100%. Severe mottling is associated with disorders in bone mineralization. Fluoridated drinking water is restricted to 1 ppm optimally.

### E. Selenium

The estimated safe daily intake of selenium is 0.05 to 0.02 mg (Gilman, 1980, p. 1555). Where the soil and vegetation have a high selenium content, livestock develop "alkali disease" or "blind staggers." The human population in such areas is claimed, controversially, to develop gastrointestinal symptoms and liver disease from ingestion of meat, eggs, milk and vegetables (Goodhart and Shils, 1973, p. 393; Salunkhe and Wu, 1977).

## FOODS INDUCING MINERAL DEFICIENCIES

There is a large literature on *phytates* as toxins. These commonly occur in food plants and they interfere with the intestinal absorption of essential minerals by forming insoluble complexes with them. This produces the hazard of mineral deficiency in parts of the world that rely on cereal proteins (Reddy et al., 1982).

## FOODS AFFECTING CARDIOVASCULAR FUNCTION

The literature is voluminous concerning the development of atherosclerosis as influenced by dietary excess of cholesterol and low density lipids, but these will not be considered further here.

### A. The Effects of Coffee

The cardiac effects of coffee are highly controversial. Lewis and Elvin-Lewis (1977, p. 181) cite data to the effect that the risk of developing myocardial infarc-

tion is about twice as great for heavy coffee drinkers than for non-drinkers. This does not imply that caffeine is the cause since tea does not produce the same effect.

### B. Orange Oil

Orange oil is expressed from the fresh peel of the ripe fruit of the orange. *Citral* is a constituent of this oil and is thus present in marmalade, fruit juices flavored with the oil, and orange drinks made by compressing the whole fruit. There is a question whether high consumption of such foods might damage blood vessels, as seen in experimental animals (Liener, 1980, p. 442). Citral is found to greater extent in oil of lemon, which is a flavoring agent. Goodhart and Shils (1973, p. 414) discuss the controversial aspects of citral toxicity.

### C. Licorice (*Glycyrrhiza glabra*)

Hypertension associated with salt and water retention leading to edema follows licorice ingestion to excesses over time (Koster and David, 1968). Koster's patient ingested 100 grams per day. The noxious agent is a steroid-like compound called *glycyrrhetic acid*.

### D. Cheese, Drugs, Wine and Beer

Monoamine oxidase inhibitors are in widespread use to elevate the mood. *Tyramine*, present in certain brands of cheese, wine and beer, can provoke a hypertensive crisis in patients treated with monoamine oxidase inhibitors. It takes only 6 mg of tyramine to provoke hypertension in such situations (Sen, 1969), and 25 mg (which occur in many foods or alcoholic beverages) is a very dangerous level (Hutchison, 1968).

The ripening of cheese breaks down casein, one product being tyrosine. Bacteria involved convert tyrosine to tyramine. A cheese and wine party could be disastrous if high tyramine substances such as cheddar cheese and Chianti wine were freely consumed. There are other high tyramine cheeses as well as wines and beers (Sen, 1969; Bassuk and Schoonover, 1977, p. 41; Maga, 1978). Tyramine releases pressor catecholamines (Editorial, 1965).

It is interesting that some varieties of ripe cheddar and Cheshire cheese, plain chocolate, and to a small extent some wines, precipitate migraine attacks and this is due to *2-phenylethylamine* (Chaytor et al., 1975).

## FOODS DISTURBING NEUROLOGIC MECHANISMS

Certain foods are cholinesterase inhibitors and thus disturb nerve impulse transmission. Such foods include potatoes (*solanine* effect), roots of tomatoes, beets, apples and eggplants (Salunkhe and Wu, 1977). Bananas in excess affect transmission of impulses because they contain serotonin and catecholamines.

Some foods produce hallucinations. Examples are nutmeg seeds and mace, which contain *myristicin*.

The methylated xanthines in tea, coffee, cocoa and cola drinks overstimulate sensitive individuals. The drugs include *caffeine*, *theophylline* and *theobromine*.

The neurologic effects of coffee are very controversial. A 5-ounce cup of coffee contains up to 90 mg of caffeine which can produce nervous excitement and cardiac stimulation, but only in a sensitive individual. Ingestion of one gram (11 cups) could seriously affect such an individual. The potential toxicity of caffeine is offset by the fact that when ingested in ordinary amounts it does not accumulate excessively in the body.

## OTHER ASPECTS OF FOOD POISONING

Our discussions hardly scratch the surface. There is a large literature on food and drug interactions, making physicians take caution when prescribing antibiotics, anticoagulants, tranquilizers, and certain laboratory tests. The literature on foods as allergens is extensive. Problems in irradiation of food are still greatly unsolved. Food contamination by microorganisms is a continual and severe threat. The poisoning of animals by food toxicants and the transmission in the food chain to man is under perpetual surveillance.

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