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Misconceptions on Pollution and the Causes of Cancer*

The public has numerous misconceptions about the relationship between environmental pollution and human cancer. Underlying these misconceptions is an erroneous belief that nature is benign. In this article we highlight eight of these misconceptions and describe the scientific information that undermines each one.

1. Misconception No. 1 : Cancer Rates Are Soaring

According to the latest update from the National Cancer Institute (February 1988), "the age adjusted mortality rate for all cancers combined except lung cancer has been declining since 1950 for all individual age groups except 85 and above" [1]. That represents a 13-percent decrease overall, 44 000 deaths below expected, and a 0.1-percent increase in the over-85 group (unless otherwise noted, all statistics given in this article refer to the USA).

The types of cancer deaths that have been decreasing during this period are primarily stomach (by 75 percent, 37 000 deaths below expected), cervical (by 73 percent, 11 000 deaths below expected), uterine (by 60 percent, 9 000 deaths below expected), and rectal (by 65 percent, 13 000 deaths below expected). The types of cancer deaths that are increasing are primarily lung cancer (by 247 percent, 91 000 deaths above expected), which is due to smoking (as are 30 percent of all US cancer deaths), and non-Hodgkin's lymphoma (by 100 percent, 8 000 deaths above expected).

Changes in incidence rates and effects of treatment are also relevant in interpreting the changes in mortality rates [1, 2]. Incidence rates have been increasing for some types of cancer.

In their definitive study on cancer trends [2], Sir *Richard Doll* and *Richard Peto* point out that, although incidence rates are of interest, they should not be taken in isolation, because trends in the recorded incidence rates are biased by improvements in the level of registration and diagnosis. Even if particular types of cancer can be shown to be increasing or decreasing, establishing a causal relation among the many changing aspects of our lives is difficult [3-15]. There is no persuasive evidence that life in the modern industrial world has in general contributed to cancer deaths [2, 10, 13].

Cancer is fundamentally a degenerative disease of old age, although exogenous factors can increase cancer rates (e.g., cigarette smoking in humans) or decrease them (e.g., caloric restriction in rodents) [16-18]. For mammalian species, cumulative cancer risk increases with approximately the fourth power of age, both in short-lived species such as rats and mice (about 30 % have cancer by the end of their 2-year life span) and in long-lived species such as humans (about 30 % have cancer by the end of their 85-year life span) [2, 13, 19-21].

Life expectancy is steadily increasing in the United States and other industrial countries. Infant mortality is decreasing. Although the statistics are less adequate on birth defects, there is no evidence that they are increasing. Conclusion : Americans, Japanese, and Western Europeans are healthier now than they have been in their history.

2. Misconception No. 2 : Cancer Risks to Humans Can Be Assessed by Testing Chemicals at High Doses in Rodents

Results from animal cancer tests, which are conducted at near toxic doses of the test chemical, cannot predict the cancer risk to humans at the usually low levels of human exposures. Knowledge of the mechanisms of carcinogenesis is necessary for prediction and is now progressing rapidly. Recent understanding of these mechanisms undermines many of the assumptions of current regulatory policy towards rodent carcinogens and necessitates a rethinking of the utility and meaning of routine animal cancer tests. The following summarizes our current understanding of these mechanisms and how they relate to animal cancer tests.

2.1. Mutagenesis Can Cause Cancer, and Normal Rates of Mutagenesis Are High

Mutagens cause cancer by mutating the DNA of cells in ways that cause cells to proliferate in an uncontrolled manner. It is generally agreed that several mutations are necessary to convert a normal cell into a cancer cell capable of uncontrolled growth

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[22, 23]. Mutagens are often assumed to be exogenous agents (coming from outside the body), such as synthetic chemicals ; however, many endogenous mutagens (coming from inside the body) are formed naturally during normal metabolic processes like oxygen utilization, which produces DNA-damaging oxidants. These oxidants are the same as those produced by radiation, which itself is an oxidative mutagen. Thus, in a sense, breathing oxygen is equivalent to irradiating the body. Normal metabolism causes chronic, oxidative DNA damage : we estimate that the number of oxidative hits to DNA per cell per day is about 100 000 in rats and 10 000 in humans [21, 24, 25]. Endogenous rates of DNA damage are thus so high that it may be difficult for exogenous mutagens to increase this damage significantly at the normal levels of human exposure. All mammals have numerous defenses to counter this damage, such as enzymes that repair damaged DNA [20, 21, 26]. Nevertheless, this damage appears to be a major contributor to aging and to many of the degenerative diseases associated with aging, including cancer.

2.2. Chronic Cell Division Increases Mutagenesis and Carcinogenesis

"Promoters" of carcinogenesis have been recognized for many years, but the concept of "promotion" and its role in carcinogenesis have been fuzzy compared to the concept of mutagenesis and its role in carcinogenesis. This is primarily because the mechanisms of carcinogenesis have in the past not been well understood. Cell division (cell proliferation) promotes carcinogenesis by increasing the vulnerability of the DNA to mutation. A dividing cell is much more at risk from mutagens (either endogenous or exogenous) than is a nondividing, quiescent cell [26-32]. Agents that cause chronic cell division are therefore indirectly mutagenic (and commonly carcinogenic) [28-33]. Saccharin, for example, is not itself a mutagen, but high doses of saccharin given to rodents cause sufficient cell division to be carcinogenic [32]. Low doses, however, would be expected to have no carcinogenic effect. Agents that cause chronic cell division (e.g., by irritation and inflammation of tissues) appear to be important in many of the known causes of human cancer : hepatitis B or C viruses or alcohol in liver cancer, high salt or *Helicobacter (Campylobacter)* bacteria in stomach cancer [34-43], hormones in breast cancer, papilloma virus in cervical cancer [44], asbestos or tobacco smoke in lung cancer [45], and excess animal fat and low calcium in colon cancer [46]. For the chemicals associated with occupational cancer, worker exposures usually have been at near-toxic doses that would be likely to cause cell proliferation.

2.3. Animal Cancer Tests Are Primarily Measuring the Effects of Massive Cell Division

Animal cancer tests of chemicals are conducted at near toxic, chronic doses - the maximum tolerated dose (MTD). (Such high doses are used in order to increase the sensitivity of the test to detect a carcinogenic effect among small numbers of animals, because the tests are very expensive to conduct). Such high doses often cause chronic cell death and a consequent chronic cell division of neighboring cells that replace the dead cells. Chronic dosing at the MTD can be thought of as chronic wounding, which is known to be both a promoter of carcinogenesis in animals and a risk factor for cancer in humans [31, 47-49]. Thus, by causing chronic cell division, a high percentage of all chemicals might be excepted to be carcinogenic at chronic, near-toxic doses. This is exactly what is found (see Section 3). About *half* of all chemicals tested chronically at the MTD are carcinogens [3, 50-55]. The fact that about 40 % of rodent carcinogens are not mutagens is consistent with our understanding of the important role of cell division in carcinogenesis.

Although toxicity at or near the MTD often induces cell division, below a certain dose no such effect is observed. Therefore, if animal cancer tests are primarily measuring the effects of cell division, then the dose-response curve would be expected to curve steeply upward rather than be linear [3, 30-32, 56-58]. This means that a tenfold reduction in dose in a rodent experiment would produce much more than a tenfold reduction in cancer risk. This prediction is confirmed by several recent analyses [32, 59-61].

3. Misconception No. 3 : Most Carcinogens and Other Toxins Are Synthetic

About 99.99 % of all pesticides in the human diet are natural pesticides from plants [62]. All plants produce toxins to protect themselves against fungi, insects, and animal predators such as

TABLE I. - *Forty-nine natural pesticides (and metabolites) in cabbage. See [a] for remarks on the numbered compounds.*

Glucosinolates

prop-2-en-1-yl glucosinolate (sinigrin, **1**)
3-methylthiopropyl glucosinolate
3-methylsulfinylpropyl glucosinolate
but-3-en-1-yl glucosinolate
2-hydroxy-but-3-en-1-yl glucosinolate
4-methylthiobutyl glucosinolate
4-methylsulfinylbutyl glucosinolate
4-methylsulfonylbutyl glucosinolate
benzyl glucosinolate
2-phenylethyl glucosinolate
propyl glucosinolate
butyl glucosinolate

Indole glucosinolates and related indoles

3-indolylmethyl glucosinolate (glucobrassicin)
1-methoxy-3-indolylmethyl glucosinolate (neoglucobrassicin)
indole-3-carbinol (**2**)
indole-3-acetonitrile (**3**)
3,3'-diindolylmethane

Isothiocyanates and goitrin

allyl isothiocyanate (**4**)
3-methylthiopropyl isothiocyanate
3-methylsulfinylpropyl isothiocyanate
3-butenyl isothiocyanate
5-vinyloxazolidine-2-thione (goitrin, **5**)
4-methylthiobutyl isothiocyanate
4-methylsulfinylbutyl isothiocyanate
4-methylsulfonylbutyl isothiocyanate
4-pentenyl isothiocyanate
benzyl isothiocyanate
phenylethyl isothiocyanate

Cyanides

1-cyano-2,3-epithiopropane
1-cyano-3,4-epithiobutane
1-cyano-3,4-epithiopentane
threo-1-cyano-2-hydroxy-3,4-epithiobutane
erythro-1-cyano-2-hydroxy-3,4-épithiobutane
2-phenylpropionitrile
allyl cyanide (**6**)
1-cyano-2-hydroxy-3-butene
1-cyano-3(methylsulfinyl)propane
1-cyano-4(methylsulfinyl)butane

Terpenes

menthol
neomenthol
isomenthol
carvone (**7**)

Phenols

2-methoxyphenol
3-caffoylquinic acid (chlorogenic acid, **8**)
4-caffoylquinic acid (**9**)
5-caffoylquinic acid (neochlorogenic acid, **10**)
4-*p*-coumaroylquinic acid
5-*p*-coumaroylquinic acid
5-feruloylquinic acid

[a] *Clastogenicity :* Chlorogenic acid (**8**) [160] and allyl isothiocyanate (**4**) are positive [75]. Compound **8** and its metabolite caffeic acid are also mutagens [161-163], as is **4** [77]. *Carcinogenicity :* Allyl isothiocyanate (**4**) induced papillomas of the bladder in male rats (a neoplasm that is unusually rare in control rats) and was classified by the National Toxicology Program (NTP) as carcinogenic. There was no evidence of carcinogenicity in mice ; however, NTP indicated "the mice probably did not receive the MTD" [164, 165]. Sinigrin (**1** ; the glucosinolate, that is, thioglycoside of **4**) is cocarcinogenic for the rat pancreas [166]. Carvone (**7**) is negative in mice [167]. Indoleacetonitrile (**3**) has been shown to form a carcinogen, nitrosoindoleacetonitrile, in the presence of nitrite [168]. Caffeic acid is a carcinogen [169, 170] and clastogen [160] and is a metabolite of its esters **8-10**. *Metabolites :* Sinigrin (**1**) gives rise to **4** on eating raw cabbage (e.g., coleslaw) ; in cooked cabbage it also is metabolized to **6**, which is untested. Indolecarbinol (**2**) forms dimers and trimers on ingestion, which mimic dioxin (TCDD) (see Section 4.2) [71]. *Occurrence* [65, 68, 124, 171]. *Toxicology :* The mitogenic effects of **5** (which is goitrogenic) and various organic cyanides from cabbage suggest that they may be potential carcinogens [172, 173]. Aromatic cyanides related to those from cabbage have been shown to be mutagens and are metabolized to hydrogen cyanide and potentially mutagenic aldehydes [174].

man [62-71]. Tens of thousands of these natural pesticides have been discovered, and every species of plant contains its own set of different toxins, usually a few dozen. When plants are stressed or damaged (e.g., during a pest attack), they increase the levels of natural pesticides manyfold, occasionally to levels that are acutely toxic to humans. We estimate that Americans eat about 1 500 mg per person per day of natural pesticides, which is 10 000 times more than they eat of synthetic pesticide residues [62]. The concentration of natural pesticides is usually measured in parts per million (ppm), rather than parts per billion (ppb), which is the usual concentration of synthetic pesticide residues or of water pollutants. We also estimate that a person ingests annually about 5 000 to 10 000 different natural pesticides and their breakdown products [62]. *Table I* lists 49 natural pesticides (and breakdown products) ingested on eating cabbage and indicates which ones have been tested for carcinogenicity or clastogenicity (the ability to break chromosomes). Lima beans contain a different array of 23 natural toxins that, in stressed plants, range in concentration from 0.2 to 33 parts per thousand fresh weight : none appears to have been tested for carcinogenicity or teratogenicity (the ability to cause birth defects) [66]. A large literature has examined the toxicity of many of these compounds to herbivorous animals, such as humans and domestic animals [63-68].

Surprisingly few plant toxins have been tested in animal cancer tests, but among those tested in at least one species, about half (27/52) are carcinogenic [62]. A search in plant foods for the presence of just these 27 natural-pesticide rodent carcinogens indicates that they occur naturally in the following foods (those at concentrations greater than 10 000 ppb of a single carcinogen are listed in italics) : *anise, apple,* banana, *basil,* broccoli, *Brussels sprouts, cabbage,* cantaloupe, *caraway, carrot, cauliflower, celery, cherry,* cinnamon, cloves, cocoa, *coffee (brewed), comfrey tea, dill, eggplant, endive, fennel, grapefruit juice, grape, honey,* honeydew melon, *horseradish,* kale, *lettuce, mace, mango, mushroom, mustard (brown), nutmeg, orange juice, parsley, parsnip,* peach, *pear, pepper (black),* pineapple, *plum, potato,* radish, raspberry, *rosemary, sage, sesame seeds (heated),* strawberry, *tarragon, thyme,* and turnip *(Table II).*

Thus, it is probable that almost every plant product in the supermarket contains natural carcinogens. The ppm levels of the known natural carcinogens in the above plants are commonly thousands of times higher than the ppb levels of man-made pesticides. The occurrence in the diet of natural pesticides that are rodent carcinogens should be interpreted cautiously. We need not be alarmed by the presence of low doses of synthetic toxins and a plethora of natural toxins in our food. As will be discussed in Section 5.1, humans are well protected against low doses of toxins by many layers of inducible, general defenses that do not distinguish between synthetic and natural toxins.

Dietary exposures to natural toxins are not necessarily of much relevance to human cancer. Indeed, a diet rich in fruit and vegetables is associated with lower cancer rates [72, 73]. This may be because anticarcinogenic vitamins and antioxidants come from plants [72, 73]. What is important in our analysis is that chronic exposures to natural rodent carcinogens may cast doubt on the relevance of far lower levels of exposures to synthetic rodent carcinogens.

3.1. Teratogens and Clastogens Are Common

It is also reasonable to assume that a sizable percentage of both natural and synthetic chemicals will be reproductive toxins at high doses because a high proportion of positives is reported for rodent teratogenicity tests. One-third of the 2 800 chemicals tested in laboratory animals have been shown to cause reproductive damage in the standard, high-dose protocol [74].

Results from other types of tests also indicate that the natural world should not be ignored and that positive results are commonly observed in high-dose tests. Ishidate *et al.* [75] reviewed experiments on the clastogenicity (chromosome breakage) of 951 chemicals in mammalian cell cultures. Of these 951 chemicals, we identified 72 as natural plant pesticides. Among these, 48 % (35/72) were positive for clastogenicity in some or all tests. This is similar to the results of the remaining chemicals ; 53 % (467/879) were positive in some or all tests. Thus, about half of the chemicals tested - whether synthetic or natural - have been shown to break chromosomes at high dose. These in vitro experiments do not necessarily simulate in vivo conditions, and chromosome breakage is probably much less extensive in tissues of the body than in laboratory tissue cultures.

TABLE II. - *Concentrations of some natural pesticides that are rodent carcinogens. 1 ppm = 1 000 ppb.*

Plant food	Rodent carcinogen	Concentration [ppm]
Parsley	5-and 8-methoxypsoralen	14
Parsnip, cooked		32
Celery		0.8
Celery, new cultivar		6.2
Celery, stressed		25
Mushroom, commercial	*p*-hydrazinobenzoate	11
Mushroom, commercial	glutamyl-*p*-hydrazinobenzoate	42
Cabbage	sinigrin **1** (allyl isothiocyanate, **4**) [a]	35-590
Collard greens		250-788
Cauliflower		12-66
Brussels sprouts		110-1 560
Mustard (brown)		16 000-72 000
Horseradish		4 500
Orange juice	limonene	31
Mango		40
Pepper, black		8 000
Basil	estragole	3 800
Fennel		3 000
Nutmeg	safrole	3 000
Mace		10 000
Pepper, black		100
Pineapple	ethyl acrylate	0.07
Sesame seeds (heated oil)	sesamol	75
Cocoa	α-methylbenzyl alcohol	1.3
Basil	benzyl acetate	82
Jasmine tea		230
Honey		15
Coffee (roasted beans)	catechol	100
Apple, carrot, celery, cherry, eggplant, endive, grapes, lettuce, pear, plum, potato	caffeic acid	> 1 000
Absinthe, anise, basil, caraway, dill, marjoram, rosemary, sage, savory, tarragon, thyme		
Coffee (roasted beans)		1 800
Apricot, cherry, peach, plum	chlorogenic acid **8** (caffeic acid) [b]	50-500
Coffee (roasted beans)		21 600
Apple, apricot, broccoli, brussels sprouts, cabbage, cherry, kale, peach, pear, plum	neochlorogenic acid **10** (caffeic acid) [b]	50-500
Coffee (roasted beans)		11 600

[a] Sinigrin (**1**) is a cocarcinogen [166] and is metabolized to the rodent carcinogen **4**, although no adequate test has been done on **1** itself. The proportion of **1** converted into **4** or into allyl cyanide (**6**) depends on food preparation [123, 124, 171]. Chlorogenic acid (**8**) and neochlorogenic acid (**10**) are metabolized to the carcinogens caffeic acid and catechol (a metabolite of quinic acid), but have not been tested for carcinogenicity themselves. The clastogenicity and mutagenicity of the above compounds are discussed in *Table I.*

Of particular interest are the levels at which some of the carcinogenic plant toxins in *Table II* were clastogenic [75] :

(1) Allyl isothiocyanate (**4**) was clastogenic at a concentration of 0.0005 ppm, which is about 200 000 times less than the concentration of its glucosinolate, sinigrin (the parent compound **1**), in cabbage. Allyl isothiocyanate (**4**) was among the most potent chemicals in the compendium [75] and is also effective at unusually low levels in transforming [76] and mutating animal cells [77]. (See also the discussion of cancer tests in the legend to *Table I*).

(2) Safrole was clastogenic at a concentration of about 100 ppm, which is 30 times less than the concentration in nutmeg, and roughly equal to the concentration in black pepper. The rodent carcinogens safrole and estragole, and a number of other related dietary natural pesticides that have not been tested in animal cancer tests, have been shown to produce DNA adducts (damaged DNA bases) in mice [78].

(3) Caffeic acid was clastogenic at a concentration of 260 and 500 ppm, which is less than its concentration in roasted coffee beans and close to its concentration in apples, lettuce, endive, and potato skin. Chlorogenic acid (**8**), a precursor of caffeic acid, was clastogenic at a concentration of 150 ppm, which is 100 times less than its concentration in roasted coffee beans and similar to its concentration in apples, pears, plums, peaches, cherries, and apricots. Chlorogenic acid (**8**) and its metabolite caffeic acid are also mutagens *(Table I)*. The toxicity of coffee to the DNA in mammalian cells has been demonstrated [79].

3.2. Cooking Food

The cooking of food is also a major dietary source of potential rodent carcinogens. Cooking produces about 2 000 mg per person per day of mostly untested burnt material that contains many rodent carcinogens [3, 69, 70, 80-85). Roasted coffee, for example, is known to contain about 825 volatile chemicals [69]. Only 22 have been tested, and 17 are rodent carcinogens [51-54]. In addition, roasted coffee also contains hundreds of nonvolatile chemicals : caffeic acid has been tested and is a carcinogen. With just these few chemicals tested, the carcinogens total 10 mg per cup of coffee (40 000 ppb). (There is some, but not sufficient evidence to conclude that coffee causes cancer in humans) [72, 80]. When proteins or amino acids are heated, certain mutagens known as heterocyclic amines are sometimes produced. Thus far, ten of these heterocyclic amines have been shown to be carcinogens in rodents, and many others are in the process of being isolated and tested [86, 87]. In addition, cooked food contains a plethora of other mutagens as well as rodent carcinogens (polycyclic hydrocarbons, furfural, and nitrosamines) [3, 69, 70, 80-85].

The total amount of browned and burnt material consumed per person in a typical day is at least several hundred times more than that inhaled in a day from severe outdoor air pollution [71]. Three mutagenic nitropyrenes present in diesel exhaust have now been shown to be rodent carcinogens [88], but the intake of these carcinogenic nitropyrenes has been estimated to be much higher from grilled chicken than from air pollution [86, 87, 89]. Gas flames generate NO_2, which can form both carcinogenic nitropyrenes [3] and nitrosamines in foods that are cooked in gas ovens. Food cooked in gas ovens may be a major source of dietary nitropyrenes and nitrosamines.

3.3. Residues of Man-made Pesticides

By contrast, human exposures to man-made pesticide residues are minuscule. The Food and Drug Administration (FDA) assayed food for residues of the 200 synthetic compounds thought to be of greatest importance, including most synthetic pesticides and a few industrial chemicals [90]. The FDA estimates that the intake of these residues averages about 0.09 mg per person per day and other analyses are similar [91]. For comparison, we estimate that the intake of natural pesticides averages about 1 500 mg per person per day [62]. About half of the intake of synthetic residues is composed of four chemicals (ethylhexyl diphenyl phosphate, dicloran, malathion, and chlorpropham) [90] that were not carcinogenic in rodent tests [51, 92]. Thus, the intake of carcinogens from synthetic residues (0.05 mg a day, if one assumes that all the other residues are carcinogenic, which is unlikely) is extremely tiny relative to the background of natural substances ; this 0.05 mg intake is equivalent to about 60 ppb of synthetic residues in plant food consumed daily.

4. Misconception No. 4 : Synthetic Toxins Pose Greater Risks than Natural Toxins

The possible carcinogenic hazards from synthetic pesticides (at normal exposures) are minimal compared with the background hazards of nature's pesticides. Even though an overwhelming number of the chemicals that humans eat are natural, the natural world of chemicals has never been tested systematically. Synthetic chemicals account for 350 (82 %) of the 427 chemicals tested chronically at high doses in both rats and mice [3, 50-55]. Of the 77 *natural* chemicals tested, the proportion carcinogenic is about *half* (37/77), that is, similar to that of synthetic chemicals (212/350) [3, 50-54]. It is unlikely that the high proportion of carcinogens in rodent studies is due simply to selection of suspicious chemical structures : while some synthetic or natural chemicals were selected precisely because of suspect structures, most chemicals were selected because they were widely used industrially ; for example they were high-volume chemicals, pesticides, drugs, dyes, or food additives [50]. The natural world of chemicals has never been looked at systematically.

In recent years, we have tried to formulate a method of setting priorities among possible carcinogenic hazards [3]. The potencies of different carcinogens vary more than 10^7 - fold in rodent tests, and the comparison of possible hazards from various carcinogens ingested by humans must take this into account. We have analyzed animal cancer tests from our Carcinogenic Potency Database [51-54] and, for each chemical, have calculated the TD_{50} (Tumorigenic Dose 50), which is essentially the daily dose of the chemical estimated to give half of the animals tumors. We have constructed an index to rank possible carcinogenic hazards : first, we estimate a reasonable daily lifetime human exposure to each chemical and express that as milligrams (of the chemical) per kilogram of body weight. Then, that mg kg^{-1} human exposure is expressed as a percentage of the rodent TD_{50} dose (mg kg^{-1}) for each carcinogen. We call this percentage the HERP value (Human Exposure dose/Rodent Potency dose). Because rodent data are all calculated on the basis of lifetime exposure at the indicated daily dose rates [8, 51], the human exposure data are similarly expressed as lifelong daily exposure rates, even though the human exposure is likely to be less than daily for a lifetime *(Table III)*.

The HERP values do not estimate human risk directly, because it is impossible to extrapolate to low doses (see Section 1), but they do offer a way of comparing possible hazards and thus of putting exposures into a relative context so that priorities can be more reasonably set. (Carcinogens clearly do not all work in the same way, and as we learn more about mechanisms, HERP comparisons can be refined, as can risk assessments). Our results suggest that alcohol at moderate doses should be high on our priority list for epidemiological studies on cancer. The HERP analysis further suggests that the possible carcinogenic hazard of synthetic chemicals that humans ingest from pesticide residues or water pollution appears to be trivial relative to the background of carcinogenic hazards from natural chemicals and chemicals formed by cooking food [3, 71, 93].

TABLE III. - *Ranking possible carcinogenic hazards [a].*

Possible hazard HERP [%] [b]	Daily human exposure	Carcinogen dose for a 70-kg human
Environmental pollution		
0.001*	Tap water, 1 liter	Chloroform, 83 μg (U.S. average)
0.004*	Well water, 1 liter contaminated (worst well in Silicon Valley, CA, USA)	Trichloroethylene (TCE), 2 800 μg
0.0004*	Well water, 1 liter contaminated (Woburn, MA, USA)	Trichloroethylene, 267 μg
0.0002*		Chloroform, 12 μg
0.0003*		Tetrachloroethylene (perc), 21 μg
0.008*	Swimming pool, 1 hour (for child)	Chloroform, 250 (average pool) μg
0.6	Conventional home air (14 h per day)	Formaldehyde, 598 μg
0.004		Benzene, 155 μg
2.1	Mobile home air (14 h per day)	Formaldehyde, 2.2 mg
Pesticides and other residues [c]		
0.0002*	PCBs : daily dietary intake	PCBs, 0.2 μg (U.S. average)
0.0003*	DDE/DDT : daily dietary intake	DDE, 2.2 μg (U.S. average)
0.0004	1,2-dibromoethane (EDB) : daily dietary intake (from grains and grain products)	EDB, 0.42 μg (U.S. average)
Natural pesticides and dietary toxins		
0.003	Bacon, cooked (100 g)	Dimethylnitrosamine 0.3 μg
0.006		Diethylnitrosamine, 0.1 μg
0.003	Sake (250 mL)	Urethane, 43 μg
0.03	Comfrey herb tea, 1 cup	Symphytine, 38 μg (750 μg pyrrolizidine alkaloids)
0.03	Peanut butter (32 g ; one sandwich)	Afltoxin, 64 ng (U.S. average, 2 ppb)
0.06	Dried squid, broiled in gas oven (54 g)	Dimethylnitrosamine, 7.9 μg
0.07	Brown mustard (5 g)	Allyl isothiocyanate (4), 4.6 mg
0.1	Basil (1 g of dried leaf)	Estragole, 3.8 mg
0.1	Mushroom, one raw (15 g) *(Agaricus bisporus)*	Mixture of hydrazines, etc.
0.2	Natural root beer (12 oz ; 354 mL) (now banned)	Safrole, 6.6 mg
0.008	Beer, before 1979 (12 oz ; 354 mL)	Dimethylnitrosamine, 1 μg
2.8*	Beer (12 oz ; 254 mL)	Ethanol, 18 mL
4.7*	Wine (250 mL)	Ethanol, 30 mL
6.2	Comfrey-pepsin tablets (nine daily)	Comfrey root, 2 700 mg
1.3	Comfrey-pepsin tablets (nine daily)	Symphytine, 1.8 mg
Food additives		
0.0002	AF-2 : daily dietary intake before banning	AF-2 (furylfuramide), 4.8 μg
0.06*	Diet cola (12 oz ; 354 mL)	Saccharin, 95 mg
Drugs		
[0.3]	Phenacetin pill (average dose)	Phenacetin, 300 mg
[5.6]	Metronidazole (therapeutic dose)	Metronidazole, 2 000 mg
[14]	Isoniazid pill (prophylactic dose)	Isoniazid, 300 mg
16*	Phenobarbital, one sleeping pill	Phenobarbital, 60 mg
17*	Clofibrate (average daily dose)	Clofibrate, 2 000 mg
Occupational exposure		
5.8	Formaldehyde : Workers' average daily intake	Formaldehyde, 6.1 mg
141	EDB : Workers's daily intake (high exposure)	EDB, 150 mg

[a] We have tried to use average or reasonable daily intakes to facilitate comparisons [3]. In several cases, such as contaminated well water or factory exposure to EDB, this is difficult to determine, and we give the value for the worst exposure found. The calculations assume a daily dose for a lifetime ; where drugs are normally taken for only a short period, we have bracketed the HERP value. [b] The asterisk means that the HERP value is from carcinogens thought to be nogenotoxic. [c] PCBs = polychlorinated biphenyls, DDE = 1,1-dichloro-2,2-bis(4-chlorphenyl)ethylene, DDT = 1,1,1-trichloro-2,2bis(4-chlorphenyl)ethane.

4.1. Water Pollution

The possible hazards from carcinogens in contaminated well water in places like California's Santa Clara ("Silicon") Valley or Woburn, Massachusetts [94-99], should be compared with the possible hazards of ordinary tap water [3]. Of the 35 wells that were shut down in Santa Clara Valley because of a supposed carcinogenic hazard to humans (low traces of trichloroethylene), only two were of a possible hazard greater than ordinary tap water. Well water is not usually chlorinated and therefore lacks the 83 ppb of chloroform present in average chlorinated tap water in the US [3]. Water from the most polluted well in the Santa Clara Valley had a relative hazard that was orders of magnitude less than that for an equal volume of coffee, beer, or wine [3]. The consumption of tap water is only about one or two liters per day, and animal evidence [3] provides no good reason to expect that either the chloroform produced in water by chlorination or the current levels of synthetic pollutants in water would pose a significant carcinogenic hazard [3]. Natural arsenic appears to be the most significant carcinogen in both well water and tap water and is often present at quite high levels [100]. Arsenic is a known human carcinogen.

The trace amounts of chemicals found in polluted wells are likely to be a negligible cause of birth defects, in comparison to the background level of known teratogens such as alcohol. The important risk factors for birth defects and reproductive damage in humans are the age of the mother, her consumption of alcohol, her smoking habits, and her exposure to the rubella virus.

4.2. TCDD (Dioxin) Compared with Broccoli and Alcohol

Cabbage and broccoli contain a chemical whose break-down products bind to the body's Ah receptor, induce enzymes, and possibly cause cell division - just a does dioxin (TCDD), one of the most feared industrial contaminants. TCDD is of great public concern because it is carcinogenic and teratogenic in rodents at extremely low doses. The doses humans ingest, however, are far lower than the lowest doses that have been shown to cause cancer and reproductive damage in rodents.

TCDD exerts many or all of its harmful effects in mammalian cells through binding to the Ah receptor [101]. A wide variety of natural substances also bind to the Ah receptor (e.g., tryptophan oxidation products [102]) and, insofar as they have been examined, they have similar properties to TCDD. A cooked steak, for example, contains polycyclic hydrocarbons that bind to the Ah receptor and mimic TCDD. In addition, a variety of other plant substances in the diet also bind to the Ah receptor. Indole carbinol (**2**), for example, is present in large amounts in broccoli (500 ppm), cabblage [103], cauliflower, and other members of the *Brassica* family. At the pH of the stomach, **2** forms chemical structures (known as dimers and trimers) that induce the same set of detoxifying enzymes as TCDD [104-106]. Like TCDD, **2** protects against carcinogenesis when given *before* aflatoxin or other carcinogens [106-108]. However, when given *after* aflatoxin or other carcinogens, **2**, like TCDD, stimulates carcinogenesis [105]. This stimulation of carcinogenesis has also been shown for cabbage itself [109]. These derivatives of **2** appear to be much more of a potential hazard than TCDD. The Environmental Protection Agency's human "reference dose" (formerly "acceptable dose limit") of TCDD is 6 femtograms per kilogram per day. This should be compared with 25 mg of **2** per 100 g of broccoli (one portion) (see also cabbage) [62, 103]. Although the affinity of the indole derivatives in binding to Ah receptors is less than that of TCDD by a factor of about 8 000, the effective dose to the Ah receptor from a portion of broccoli would be about 1 500 times higher than that of TCDD, taking into account another factor of 1 000 for the very long lifetime of TCDD in the body (several years) and assuming that the lifetime of the hydrophobic indole dimers is a short as one day. However, it is not clear whether, at the low doses of human exposure, *either* **2** or TCDD is hazardous. It seems likely that many more of these natural "dioxin simulators" will be discovered in the future.

If TCDD is compared with alcohol, it seems of minor interest as a teratogen or carcinogen. Alcohol is the most important known human chemical teratogen [72]. In contrast, there is no persuasive evidence that TCDD is either carcinogenic or teratogenic in humans, although it is both at neartoxic doses in rodents. If one compares the teratogenic potential of TCDD to that of alcohol for causing birth defects (after adjusting for their respective potency as determined in rodent tests), then a daily consumption of the EPA reference dose of TCDD (6 fg) would be equivalent in teratogenic potential to a daily consumption of alcohol from 1/3 000 000 of a beer. That is equivalent to drinking a single beer (15 g of ethanol) over a period of 8 000 years.

In humans alcoholic beverages are carcinogenic [110] as well as teratogenic. A comparison of the rodent carcinogenic potential of TCDD with that of alcohol (adjusting for the potency in rodents) shows that ingesting the TCDD reference dose of 6 fg per kilogram per day is equivalent to a man ingesting one beer every 345 years. Since the average consumption of alcohol in the United States is equivalent to more than one beer per person per day, and since five drinks a day are a carcinogenic risk in humans, the experimental evidence does not of itself seem to justify the great concern over TCDD at levels in the range of the reference dose.

5. Misconception No. 5 : The Toxicology of Man-made Chemicals Is Different from That of Natural Chemicals

It is often assumed that, because plants are part of human evolutionary history, whereas industrial chemicals are not, the mechanisms that animals have evolved to cope with the toxicity of natural chemicals will succeed in protecting them against natural chemicals, yet will fail to protect against synthetic chemicals : "For the first time in the history of the world, every human being is now subjected to contact with dangerous chemicals, from the moment of conception until death" (Rachel Carson : *Silent Spring*, 1962). We find this assumption flawed for several reasons.

5.1. Defenses That Animals Have Evolved Are Mostly of a General Type

Since the number of natural chemicals that might have toxic effects is so large, general defenses offer protection not only against natural but also against synthetic chemicals, making humans well buffered against toxins [3, 7, 103, 111]. These defenses include the following :

(1) The continuous shedding of cells exposed to toxins : the surface layers of the mouth, esophagus, stomach, intestine, colon, skin, and lungs are discarded every few days.

(2) The induction of a wide variety of general detoxifying enzymes, such as antioxidant enzymes [20, 21, 112] or the glutathione transferases for detoxifying alkylating agents [113] : human cells that are exposed to small doses of an oxidant, such as radiation or hydrogen peroxide, induce antioxidant defenses and become more resistant to higher doses [114-118]. These defenses can be induced by both synthetic oxidants (e.g., the herbicide paraquat) and natural oxidants and are effective against both.

(3) The active excretion of planar hydrophobic molecules (natural or synthetic) out of liver and intestinal cells [119].

(4) DNA repair : this is effective against DNA adducts formed from both synthetic and natural chemicals and is inducible in response to DNA damage [26].

(5) Animals' olfactory and gustatory perception of bitter, acrid, astringent, and pungent chemicals : these defenses warn against a wide range of toxins and could possibly be more effective in warning against some natural toxins that have been important in food toxicity during evolution than against some synthetic toxins. However, it seems likely that these stimuli are also general defenses and are monitoring particular structures correlated with toxicity ; some synthetic toxic compounds are also pungent, acrid, or astringent. Even though mustard, pepper, garlic, onions, etc., have some of these attributes, humans often ignore the warnings.

The fact that defenses are usually general, rather than specific for each chemical, makes good evolutionary sense. Predators of plants evolved general defenses against toxins presumably to be prepared to counter a diverse and everchanging array of plant toxins in an evolving world ; if a herbivore had defenses only against a set of specific toxins it would be at a great disadvantage in obtaining new plant foods when favored plant foods became scarce or evolved new toxins.

5.2. Various Natural Toxins, Some of Which Have Been Present throughout Vertebrate Evolutionary History, Nevertheless Cause Cancer in Vertebrates

Mold aflatoxins, for example, have been shown to cause cancer in trout, rats, mice, monkeys, and, possibly, humans [3, 110]. Eleven mold toxins have been reported to be carcinogenic [103] and nineteen mold toxins have been shown to be clastogenic [75]. Many of the common elements are carcinogenic (e.g., salts of lead, cadmium, beryllium, nickel, chromium, selenium, and arsenic) or clastogenic [75] at high doses, despite their presence throughout evolution.

Furthermore, epidemiological studies from various parts of the world show that certain natural chemicals in food may be carcinogenic risks to humans : the chewing of betel nuts with tobacco around the world has been correlated with oral cancer [110, 120]. The phorbol esters present in the Euphorbiacea, some of which are used as folk remedies or herb teas, are potent mitogens (inducers of cell proliferation) that are thought to be a cause of

nasopharyngeal cancer in China and esophageal cancer in Curacao [121, 122]. Pyrrolidizine toxins are mutagens that are found in comfrey tea, various herbal medicines, and some foods ; they are hepatocarcinogens in rats and may cause liver cirrhosis and other pathologies in humans [120].

Plants have been evolving and refining their chemical weapons for at least 500 million years and incur large fitness costs in producing these chemicals. If these chemicals were not effective in deterring predators, plants would not have been naturally selected to produce them.

5.3. Humans Have Not Had Time to Evolve into a "Toxic Harmony" with All of the Plants in Their Diet

Indeed, very few of the plants that humans eat would have been present in an African hunter-gatherer's diet. The human diet has changed drastically in the last few thousand years, and people are eating many recently introduced plants that their ancestors did not, for example, coffee, cocoa, tea, potatoes, tomatoes, corn, avocados, mangoes, olives, and kiwi fruit. In addition, cruciferous vegetables such as cabbage, broccoli, kale, cauliflower, and mustard were used in ancient times "primarily for medicinal purposes" and were spread as foods across Europe only in the Middle Ages [123, 124]. Natural selection works far too slowly for humans to have evolved specific resistance to the food toxins in these newly introduced plants.

5.4. Poisoning from Plant Toxins in the Milk of Foraging Animals Was Quite Common in Previous Centuries

In nonindustrial societies, cow or goat milk and other ingested dairy products were contaminated by the natural toxins from plants that were eaten by foraging animals, because toxins that are absorbed through the animal's gut are often secreted in the milk. Since the plants foraged by cows vary from place to place and are usually inedible for human consumption, the plant toxins that are secreted in the milk are, in general, not toxins to which humans could have easily adapted. Abraham Lincoln's mother, for example, died from drinking cow's milk that had been contaminated with toxins from the snakeroot plant [125]. When cows and goats forage on lupine, their offspring may have teratogenic abnormalities, such as "crooked calf" syndrome caused by the anagyrine in lupine [126-128]. Such significant amounts of these teratogens can be transferred to the animals' milk that drinking the milk during pregnancy is teratogenic for humans [126-128] : in one rural California family, a baby boy, a litter of puppies, and goat kids all had a "crooked" bone birth defect. The pregnant woman and the pregnant dog had both been drinking milk obtained from family goats that had been foraging on lupine, the main forage in winter [126-128].

5.5. Anticarcinogenic Chemicals in the Diet May Help to Protect Humans Equally Well against Synthetic and Natural Carcinogens

Although plants contain anticarcinogenic chemicals (e.g., antioxidants) that may protect against carcinogens [129, 130], these anticarcinogens *do not distinguish* whether carcinogens are synthetic or natural in origin.

5.6. Although Synergism between Synthetic Carcinogens Could Multiply Hazards, This Is Also True of Natural Chemicals

Natural chemicals are by far the major source of chemicals in the diet.

5.7. Although the Synthetic Pesticide DDT Bioconcentrates in the Food Chain Due to Its Unusual Fat Solubility, Natural Toxins Can Also Bioconcentrate

DDT is often viewed as the typically dangerous synthetic pesticide because it persists for years ; it was representative of a class of chlorinated pesticides. Natural pesticides, however, also bioconcentrate if fat-soluble : the teratogens solanine (and its aglycone solanidine) and chaconine, for example, are found in the tissues of potato eaters [131-133]. Although DDT was unusual with respect to bioconcentration, it was remarkably nontoxic to mammals, saved millions of lives, and has not been shown to cause harm to humans [134]. To a large extent DDT, the first major synthetic insecticide, replaced lead arsenate, a major carcinogenic pesticide used before the modern era ; lead arsenate is even more persistent than DDT. When the undesirable bioconcentration and persistence of DDT and its lethal effects on some birds were recognized, it was prudently phased out and less persistent chemicals were developed to replace it. Examples of these newer chemicals are the synthetic pyrethroids that disrupt the same sodium channel in insects as DDT [135], are degraded rapidly in the environment, and can often be used at a concentration as low as a few grams per acre.

6. Misconception No. 6 : Storks Bring Babies and Pollution Causes Cancer and Birth Defects

The number of storks in Europe has been decreasing for decades. At the same time, the European birth rate also has been decreasing. We would be foolish to accept this high correlation [136] as evidence that storks bring babies. The science of epidemiology tries to sort out the meaningful correlations from the numerous chance correlations. That is, epidemiology attempts to determine correlations that may indicate cause and effect. However, it is not easy to obtain persuasive cause-and-effect evidence by epidemiological methods, because of inherent methodological difficulties [10]. There are many sources of bias in observational data, and chance variation is also important. For example, because there are so many different types of cancer and birth defects, by chance alone one might expect some of them to occur at a high frequency in a small community here and there. Toxicology provides evidence that can help us decide whether an observed correlation might be causal or accidental.

There is no persuasive evidence from epidemiology or toxicology that pollution is a significant cause of birth defects or cancer. For example, the epidemiological studies of the Love Canal toxic waste dump in Niagara Falls, New York, or of dioxin in Agent Orange [137, 138], or of pollutants produced by the refineries in Contra Costa County, California [139, 140], or of the contaminants in the wells of Silicon Valley [141] or Woburn, Massachusetts [94-99], or of the nowbanned pesticide DDT, provide no persuasive evidence that pollution was the cause of human cancer in any of these well-publicized exposures. At Love Canal, where people were living next to a toxic waste dump. The epidemiological evidence for an effect on public health is equivocal. Analyses of the toxicology data on many of these cases suggest that the amounts of the chemicals involved were much too low relative to the background of naturally occurring carcinogens and carcinogens from cooking food to be credible sources of increased cancer in humans [3]. With respect to birth defects, a comparative analysis of teratogens using a HERP-type index, which would express the human exposure level as a percentage of the dose level known to cause reproductive damage in rodents, would be of interest. Such an analysis has not been done in a systematic way.

Environmental exposures to industrial chemical pollutants are thousands of times lower than some occupational exposures to these same agents [3, 8]. Thus, if ppb levels of these pollutants

were causing cancer or birth defects, one might expect to see an effect in the workplace. So far, however, epidemological studies on these chemicals do not suggest an association with cancer [142].

Historically, for chemicals that have been shown to increase cancer in the workplace, exposures were at high levels. For example, in California the levels of the fumigant ethylene dibromide (EDB) that workers were allowed to breathe in were once shockingly high [3]. We testified in 1981 that our calculations showed that the workers were allowed to breathe in a dose higher than the dose that gave half of the test rats cancer. California lowered the permissible worker exposure more than a hundredfold. Despite the fact that the epidemiology on EDB in highly exposed workers does not show any significant effect, the uncertainties of our knowledge make it important to have strict rules about workers, because they can be exposed chronically to extremely high doses.

7. Misconception No. 7 : Trade-offs Are Not Necessary in Eliminating Pesticides

Since no plot of land is immune to attack by insects, plants need chemical defenses - either natural or synthetic - in order to survive pest attack. "It has been suggested that one consequence of crop plant domestication is the deliberate or inadvertent selection for reduced levels of secondary compounds that are distasteful or toxic. Insofar as many of these chemicals are involved in the defense of plants against their enemies, the reduction due to artificial selection in these defenses may account at least in part for the increased susceptibility of crop plants to herbivores and pathogens..." [143]. Thus, there is a trade-off between natural pesticides and man-made pesticides.

Cultivated plant foods commonly contain fewer natural toxins than do their wild counterparts. For example, the wild potato, the progenitor of cultivated strains of potato, has a glycoalkaloid content about three times that of cultivated strains and is more toxic [144, 145]. The leaves of the wild cabbage (the progenitor of cabbage, broccoli, and cauliflower) contain about twice as many glucosinolates as cultivated cabbage [146]. The wild bean contains about three times as many cyanogenic glucosides as does the cultivated bean [147]. Similar reductions in toxicity through agriculture have been reported in lettuce, lima bean, mango, and cassava [65].

One consequence of disproportionate concern about synthetic pesticide residues is that some plant breeders are currently developing plants that are more insect-resistant and, thus, higher in natural toxins. Two recent cases illustrate the potential hazards of this approach to pest control.

(1) When a major grower introduced a new variety of highly insect-resistant celery into commerce, a flurry of complaints were made to the Centers for Disease Control from all over the country, because people who handled the celery developed rashes when they were subsequently exposed to sunlight. Some detective work found that the pest-resistant celery contained 6 200 ppb of carcinogenic (and mutagenic) psoralens instead of the 800 ppb present in normal celery *(Table II)* [64, 103, 148, 149]. It is not known whether other natural pesticides in the celery were increased as well. The celery is still on the market.

(2) A new potato, developed at a cost of millions of dollars, had to be withdrawn from the market because of its acute toxicity to humans when grown under particular soil conditions - a consequence of higher levels of the natural toxins solanine and chaconine. Solanine and chaconine inhibit cholinesterase, thereby blocking nerve transmission, and are known rodent teratogens. They were widely introduced into the world diet about 400 years ago with the dissemination of the potato from the Andes. Total toxins are present in normal potatoes at a level of 15 mg per 200-g potato (75 ppm), which is less than a tenfold safety margin from the measurably toxic daily dose level for humans [144]. Neither solanine nor chaconine has been tested for carcinogenicity. In contrast, the cholinesterase inhibitor malathion, the main synthetic organophosphate pesticide residue in our diet (0.006 mg per day), has been tested and is not a carcinogen in rats or mice. Common cultivars of plants differ widely in the level of particular natural toxins *(Table II)* [103], and other factors in the plant also play a part in pest resistance. Breeding or genetic engineering can be used to increase or decrease specific chemicals or other factors.

Certain cultivated crops have become popular in developing countries because they thrive without costly synthetic pesticides. However, the trade-offs of cultivating some of these naturally pest-resistant crops are that they are highly toxic and require extensive processing to detoxify them. For example, cassava root, a major food crop in Africa and South America, is quite resistant to pests and disease ; however, it contains cyanide at such high levels that only a laborious process of washing, grinding, fermenting, and heating can make it edible ; ataxia due to chronic cyanide poisoning is endemic in many of the cassava-eating areas of Africa [150]. In one part of India, the pest-resistant grain *Lathyrus sativus* is cultivated to make some types of dahli. Its seeds contain the neurotoxin ß-*N*-oxalylaminoalanine, which causes a crippling nervous system disorder, neurolathyrism [151].

As an alternative to synthetic pesticides, it is legal for "organic farmers" to use the natural pesticides from one plant species against pests that attack a different plant species : for example, rotenone (which Indians used to poison fish) or the pyrethrins from chrysanthemum plants. These naturally derived pesticides have not been tested as extensively for carcinogenicity (rotenone is negative, however), mutagenicity, or teratogenicity as have synthetic pesticides ; therefore, their safety compared to synthetically derived pesticides should not be prematurely assumed.

There is a tendency for nonscientists to think of *chemicals* as being only synthetic and to characterize synthetic chemicals as toxic, as if every natural chemical were not also toxic at some dose. Even a recent National Research Council report [152] states : "Advances in classical plant breeding... offer some promise for nonchemical pest control in the future. Nonchemical approaches will be encouraged by tolerance revocations...". The report was concerned with pesticide residues in tomatoes, but ignored the natural pesticides in tomatoes. Tomatine, one of the natural toxins in tomatoes, is a recent chemical, too, since it was introduced to the world diet from Peru 400 years ago. Neither tomatine nor its aglycone, tomatidine, an antifungal steroidlike molecule, has been tested in rodent cancer bioassays. Tomatine is present at 36 mg per 100-g tomato (360 ppm), a concentration that is much closer to the acutely toxic level in humans than are the concentrations of man-made pesticide residues [144].

Efforts to prevent hypothetical carcinogenic risks of 1 in a million could be counterproductive if the risks of the alternatives are worse. For example, Alar was withdrawn from the market after the EPA proposed cancellation hearings on it and after the Natural Resources Defense Council (NRDC) went to the media to get the process accelerated [93]. However, we incur various risks by withdrawing Alar, and these risks should be addressed. Alar is a growth regulator that delays ripening of apples so that they do not drop prematurely, and it also delays overripening in storage. Alar plays a role in reducing pesticide use on some types of apples, particularly in the Northeast [153]. Without Alar, the danger of fruit fall from the pests known as leafminers is greater, and more pesticides are required to control pests. When fruit falls prematurely, pests on the apples remain in the orchard to attack the crop the next summer, and more pesticides must be used. Since Alar produces healthier apples that stay on the trees, Alar-treated fruit is less susceptible to molds. Therefore, it is likely that the amounts and variety of mold toxins present in apple juice (e.g., patulin [154-157] will be higher in juice made from untreated apples. The carcinogenicity of patulin has not been adequately examined [158]. Another trade-off of eliminating Alar is decreasing the availability of domestically grown,

fresh apples throughout the year and increasing the price of apples, which might lead consumers to substitute less healthy foods.

Synthetic pesticides have markedly lowered the cost of plant food, thus promoting increased consumption. Eating more fruits and vegetables, and less fat, may be the best way to lower risks of cancer and heart disease (other than giving up smoking).

8. Misconception No. 8 : Technology Is Harmful to Public Health

Modern technologies are almost always replacing older, more hazardous technologies. Billions of pounds of trichloroethylene (TCE), one of the most important nonflammable, industrial solvents, and perchloroethylene (perc), the main drycleaning solvent in the United States, are used because they are low in toxicity and are not flammable. Chlorinated solvents replaced flammable solvents in industry and in dry cleaning ; this was a major advance in fire safety, with a minor trade-off of an occasional ppb contamination in water.

Eliminating a carcinogen may have unwanted effects. For example, 1,2-dibromoethane (ethylene dibromide, EDB), the main fumigant in the United States before it was banned in 1984, was present in trivial amounts (about 0.4 ppb) in our food : the average daily intake was a possible carcinogenic hazard, about one-tenth that of the aflatoxin in the average peanut butter sandwich, itself a minimal possible hazard *(Table III)* [3]. It is possible that the elimination of EDB fumigation will result in greater insect infestation and contamination of grain by carcinogen-producing molds. This would result in a reduction in public health, not an advance, and would greatly increase costs. Furthermore, alternative fumigants to replace EDB do not appear satisfactory and may be more hazardous and expensive.

Similarly, modern synthetic pesticides replaced more hazardous substances, such as lead arsenate, one of the major pesticides before the modern era. Lead and arsenic are both natural, highly toxic, and carcinogenic. Pesticides have increased crop yields and have brought down the price of foods, a major public health advance. Each new generation of synthetic pesticides is more environmentally and toxicologically benign.

Every living thing and every industry "pollutes" to some extent. The fact that scientists have developed methods to measure part per billion levels of chemicals and are developing methods to measure parts per trillion, makes us more aware of toxicity, but does not mean that exposure to toxins is necessarily increasing or that detected chemicals are causing human disease. Minimizing pollution is clearly desirable for other reasons, but is a separate issue from cancer prevention ; getting the most pollution reduction for the lowest economic cost is, of course, important [159].

Focusing on minor rather than major health risks is counterproductive. If we divert too much of our attention to traces of pollution as a public health concern we dot not improve public health - and, in the confusion, the important hazards may be neglected : for example, smoking (400 000 deaths per year), alcohol (100 000 deaths per year), eating unbalanced diets) such as too much saturated fat and cholesterol and too few fruits and vegetables), AIDS, radioactive radon released from the soil into homes, and high-dose occupational exposures to chemicals.

It is the inexorable progress of modern technology and scientific research that is likely to lead to a decrease in cancer death rates, a decrease in the incidence of birth defects, and an increase in the average human life span.

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