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Abstract: Discusses several proposals to defeat global industrial toxic terrorism which causes cancer and poses a major threat to public health and environmental integrity. Prohibition of the authorization of potentially carcinogenic products and processes; Reduction of toxic products in use; Development of international rules to restrict industry claims of confidentiality and trade secrecy; Implementation of policies relating to product labeling.

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REVERSING THE CANCER EPIDEMIC

We are losing the winnable war against cancer. Over recent decades, the incidence of cancer in industrialized nations has escalated to epidemic proportions, with lifetime cancer risks in the United States now approaching one in two for men and one in three for women. For 2001, the estimated number of new cancer cases was 1.3 million; the estimated number of deaths from cancer, 550,000 (Greenlee et al., 2001). The overall increase in the incidence of all cancers among whites in the United States from 1950-1997 was 58 percent, of which lung cancer, primarily attributed to smoking, accounted for about 25 percent [Surveillance, Epidemiology and End Results (SEER), 1973-1997]. Similarly, a survey of 17 other major industrialized nations has shown that non-smoking related cancers are responsible for about 75 percent of the overall increased incidence of cancer since 1950 (Davis and Hoel, 1990). Over the same period, nonsmoking cancers in the United States increased approximately as follows: prostate cancer, non-Hodgkin's lymphoma and multiple myeloma, 200 percent; thyroid cancer, 155 percent; testis cancer, 120 percent; adult brain and nervous system cancer, 70 per cent; female breast cancer, 60 percent; and childhood cancer, 35 percent. Similar trends are reflected in federal incidence rates from 1973 onwards.

While cancer rates have escalated, our ability to treat and cure most cancers (with the notable exception of the relatively rare childhood and testicular cancers), has remained largely unchanged for decades. Despite general impressions, the five-year survival rates for all cancers in the U.S. population from 1974 to 1990 only increased from 49 percent to 54 percent for all races, and from 39 percent to a mere 40 percent for blacks.

The modern cancer epidemic cannot be explained away on the basis that longevity has increased. Cancer registers like SEER are adjusted to reflect this trend (technically speaking, incidence and mortality rates are age-standardized). In short, the numbers already take into account the fact that we are all getting older; they show that cancer rates have increased more than would be expected if the population simply lived longer and cancer rates stayed the same.

Nor can the epidemic be largely attributed to faulty personal lifestyle factors such as smoking. Although smoking is clearly the single most important cause of cancer, the incidence of lung cancer in men (though not women) is

declining because there has been a notable reduction in smoking (at least among men). While lung cancer in men has diminished, however, the incidence of a wide range of nonsmoking cancers is increasing at proportionately greater rates. Something besides smoking is causing this increase.

Nor can the role of high fat diets be incriminated as a major cause of cancer, in sharp contrast to heart disease. In the case of breast cancer, for example, epidemiological studies over the past two decades have consistently failed to establish any causal relationship between breast cancer and the consumption of fat per se, excluding consideration of meat and dairy fats heavily contaminated with carcinogenic pesticides and industrial pollutants (Epstein et al., 1998; Willet, 1987; Hunter 1996).

Finally, increasing cancer rates cannot be attributed to genetic factors. Genetics are directly implicated in well under 10 percent of all cancers. Though some types of cancers may be attributed to genetics, it is impossible that a sudden rise in cancer could be attributed to genetics, as the genetics of human populations cannot possibly have materially changed within just the last few decades.

What then is the predominant cause of the modern cancer epidemic? A strong body of scientific evidence points to the role of run-away industrial technologies, particularly the petrochemical and radionuclear, whose explosive growth since the 1940s has, to varying degrees in different nations, outstripped the development of social control infrastructures and mechanisms. The result is that our total environment--air, water, consumer and medicinal products, and the workplace--has become pervasively contaminated with a wide range of industrial carcinogens, particularly persistent organic pollutants (POPS) such as organochlorine pesticides. As a consequence, the public-at-large has been and continues to be unknowingly exposed to avoidable chemical and radionuclear carcinogens from conception to death.

These conclusions have been strikingly confirmed by the results of a large scale study on identical twins in Sweden, Denmark and Finland (Lichtenstein et al., 2000). Published in the New England Journal of Medicine, that study concludes: "The overwhelming contribution to the causation of cancer in the population of [90,000] twins that we studied was the environment. Even for cancers for which there is statistically significant evidence of a heritable component, most pairs of twins were discordant for the cancer, indicating that the increase in the risk of cancer even among close relatives is generally moderate."

We are thus faced with an unparalleled crisis of our own making--an epidemic of cancer caused by our own technological innovations. This crisis will be further exacerbated with the growing industrialization of relatively underdeveloped European nations, such as Greece, Spain, and Portugal, not to mention the slow but steady industrialization of behemoths like China and India. The solution must thus not be limited to one nation, but be extensible internationally.

Nations, of course, prefer to keep sovereignty rights over the products they produce and export. Yet many governments are recognizing the need for international regulation even when it may infringe on these rights. For example, French President Jacques Chirac, at a 1998 meeting of the World Conservation Union, proposed increasing the powers of the United Nations Environment Program to avoid sovereignty disputes that hamper the global fight against pollution. President Chirac warned that countries around the world were holding on to an outdated idea of sovereignty, while environmental pollution ignored national borders. The time for international regulation of toxic products has come.

To address the environmental causes of cancer and the need to focus on prevention, I have developed a series of six legislative proposals that can be implemented on national and international levels. Not all these proposals are original to me; some are already under consideration in various Parliaments and Congresses worldwide. Together, however, these proposals form an interlocking complex, the whole of which is greater than the sum of its parts. The proposals, in brief, are as follows: The Precautionary Principle; Reduction of Toxics in Use; The Right-to-Know; Transparent Decision-Making; Prosecution of White Collar Crime; and the Establishment of an International Citizen Health and Safety Agency.

While my focus is primarily directed to cancer and to avoidable and involuntary carcinogenic exposures, the majority of carcinogens also induce other chronic toxic effects--including reproductive, endocrine, neurotoxic and immunotoxic effects--for which there are no comparable systematic data on incidence trends. Cancer, in effect, thus represents a quantifiable paradigm of the adverse public health and environmental impacts of all run-away industrial technologies, including petrochemical and radionuclear technologies. The proposals also address the potential adverse public health and environmental impact of emerging technologies, particularly genetic engineering. If we can address these toxic technologies in order to reduce their carcinogenic effects, we will most likely be rewarded with a parallel reduction in the incidence of other chronic, environmentally-induced diseases. The broadest aim of the proposals is to defeat global industrial toxic terrorism, which poses a major threat to public health and environmental integrity.

1. The Precautionary Principle

Under the terms of the 1948 UN Universal Declaration of Human Rights, the right to life and its corollary right to health are the first and most important of all fundamental rights recognized by many international conventions. This Declaration mandates that legislation is needed to ensure that considerations of health take absolute precedence over economics and trade.

The first line of defense against avoidable carcinogenic exposure is to prohibit the authorization of any new potentially carcinogenic products and processes. This zero-risk policy--the Precautionary Principle--was initially invoked by the EU in 1980 with regard to chlorofluorohydrocarbons, and again more recently by the German government, in 1994 at the Second North Sea Conference, in relation to marine dumping of toxic wastes (Thorpe, 1999).

The Precautionary Principle would mandate the categorical responsibility of industry to provide unequivocal evidence on the safety of any new candidate product and process, thereby ensuring that they do not pose potential or recognized human or environmental risks. This principle further absolves citizens and regulatory agencies from the heavy burden for proving risks in response to industry challenges, and allows the banning of suspect products in circumstances of scientific uncertainty. As such, this Principle is particularly relevant to genetically engineered food for which industry claims of safety are based on "trust us" assurances, rather than published scientific data.

The Precautionary Principle is clearly preferable to our current policy of deliberately accepting risks and then attempting to "manage" them by reducing exposures to levels claimed "acceptable" by self-interested industry or complicit regulatory agencies. The need to prevent rather than "manage" risk is especially apparent when we review the well-documented and decades-old track record of obfuscation and denial of toxic effects in a wide range of petrochemical and other industries. A recent illustrative example is afforded by the review of 161 studies in the National Library of Medicine files on four heavily regulated industrial chemicals: formaldehyde, perchloroethylene, atrazine, and alachlor. While only 14 percent of industry studies reported toxic or carcinogenic effects, such effects were disclosed in 71 percent of independent studies (Fagin and Lavelle, 1996). That's why, under the Precautionary Principle, the raw data on the basis of which industry claims of safety are based, apart from their interpretation, must be fully disclosed and evaluated at industry's expense by an independent agency with qualified representation of non-governmental organizations (NGO's) and their scientific consultants.

In 1997, the Swedish Chemicals Policy Committee, established by the Swedish government in May 1996, published a revolutionary document entitled "Towards A Sustainable Chemicals Policy." In their official report to the government, the committee embraced the fullest implementation of the Precautionary Principle ever proposed for policies regarding industrial chemicals. Prime Minister Goran Persson is expected to present a version of these new policies in the spring of 2002 to Parliament which is expected to approve them. These policies will shift the burden of proof of safety away from the public to industry. Industry will have to produce detailed evidence that all new chemicals proposed for use pose no carcinogenic, mutagenic or endocrine disruptive adverse public health effects and environmental impacts, including persistence and bioaccumulation. The new law will also ban persistent organic pollutants (POPS) and other persistent chemicals such as lead and require the phasing out of chlorinated paraffins, such as plasticisers and flame retardants. Swedish companies will have five years to test the estimated 2,500 chemicals that they use in quantities over 1,000 tons per year for such effects. By 2010, chemicals used in less amounts will also have to be tested.

2. Reduction of Toxics in Use

The second line of defense against avoidable carcinogenic exposures is the reduction or phase-out of toxics in use. Phasing out the manufacture, use, and disposal of carcinogenic and otherwise toxic chemicals, coupled with their replacement by safe alternative technologies, is not only a practical but a cost-effective strategy. The effectiveness of such a strategy clearly depends on the establishment of an explicitly defined schedule for the shortest feasible phase-out time, and on the establishment of a plan to monitor industry compliance.

Toxics use reduction is based on the principle of risk prevention, which is in sharp contrast to the "risk management" strategies strongly favored by industry, by a growing battery of right-wing think tanks (including the Harvard Center for Risk Analysis, The Hudson, Cato and Competitive Enterprise Institutes, The American Policy Center, and the International Life Sciences Institute), and by complicit regulatory agencies (Rampton and Stauber, 2000). Risk management accepts the inevitability of risk from industrial processes and products while claiming that such risks can be managed to levels variously described as "acceptable," "insignificant," or "minimal." These claims are derived from highly dubious, if not manipulated, risk assessment mathematical formulae shaped by predetermined financial or regulatory interests which predict minimal deaths anticipated from any particular carcinogenic exposure.

Following a well-organized political campaign by environmental groups, the Commonwealth of Massachusetts

unanimously passed the Toxics Use Reduction Act in 1989 which created the Massachusetts Toxics Use Reduction Program (TURA, 1989). The Act is a specific form of pollution prevention that focuses on reducing the use of toxic chemicals and generation of hazardous waste by improving and redesigning industrial products and processes. The Toxics Use Reduction Institute of the University of Massachusetts, Lowell, played an important role in developing the Act by providing education, training, research on new materials and processes, a technical library and information source, and specialized laboratories for evaluating alternative safe technologies. The achievements of this Act include reducing the generation of toxic wastes from 1989 to 1997 by 50 per cent by reducing toxics use by 20 per cent; establishing toxics use reduction as the preferred means for achieving compliance with federal and state environmental statutes; promoting reduction in the production and use of toxic chemicals; enhancing and strengthening the enforcement of existing environmental laws; promoting co-ordination between state agencies administering toxics-related programs; and sustaining and promoting the competitiveness of Massachusetts industry (Massachusetts Department of Environmental Protection, 1997).

The Massachusetts Act could also serve as a useful model for international, national, and state legislation. The active interest of mainstream industry in such initiatives could well be encouraged by granting tax incentives for the urgent development of safe alternatives to conventional toxic-based technologies, and tax penalties for failure to adopt available safe alternative technologies.

The relatively new trend to voluntary and economy-driven corporate environmentalism may prove at least as potent as ideologically and legislatively-driven toxics use reduction. Many businesses are now seeking to provide services and functions rather than products. For instance, the Atlanta-based Interface, Inc. leases floor covering services and recycles old carpets rather than selling new carpets that would eventually need to be incinerated or dumped in landfills (Interface, Inc., 1999). Similarly, Xerox now leases copiers and recycles old models. An article in the June 7, 1999 edition of the International Herald Tribune identified a parallel development known as Eco-efficiency and Pollution Prevention (E2 P2), typified by the growing investment of Royal Dutch Shell, Amoco, and British Petroleum in renewable sustainable energy sources, including wind, solar power, and fuel cells, and in extending product ranges to improved gasoline mixes. While citizen groups may well be cynical, considering the past environmental track record of these companies, these initiatives should nevertheless be welcomed. Legislation can and should be designed to reinforce businesses willing to embrace this sort of corporate environmentalism.

A further example of the role of marketplace pressures which merits legislative recognition and support relates to consumer products, especially food, cosmetics, toiletries, and household products. The growth of organic and non-toxic non-mainstream products in U.S. markets has reached double digit annual figures over the last decade. A 1995 published rating of some 4,000 conventional mainstream and safe non-mainstream products for undisclosed carcinogenic ingredients and contaminants has resulted in a significant market shift away from hazardous to safe products which are becoming more price competitive (Epstein, 1998).

Even non-price competitive safe products have been successful recently. For an example we need only look at the booming sales of a leading sportswear manufacturer, Patagonia, which has completely converted to organic cotton by the use of well-established integrated pest management strategies; this is particularly important, as cotton is the most pesticide-intensive U.S. crop, accounting for 10 percent of all national pesticide use. The idea of using marketplace pressure to reduce carcinogenic exposure has recently been amplified and extended by Paul Hawken, Amory Lovins, and Hunter Lovins into a new paradigm they call "natural capitalism," which has set a landmark agenda for a rational and ecologically sound concept of industrial development (Hawken et al., 1999).

3. Right-To-Know

Clearly, such health-driven marketplace pressure to develop non-toxic products and processes depends on a fully informed public. The right-to-know is, or should be, an inalienable and fundamental democratic principle (acknowledging probable exceptions for national security concerns). Industry claims of confidentiality and trade secrecy are often a serious deterrent to the recognition of potential risks from carcinogenic and otherwise toxic products. We must develop international rules to restrict these industry claims of confidentiality. Industries would still be allowed protect independently validated proprietary information. However, all information on the carcinogenic and otherwise toxic risks of a product, drug, or process must be automatically and fully released and made available to the public.

Implementing the right-to-know in the home countries of these industries is not sufficient. We must extend right-to-know requirements and legislation to the overseas operations of major corporations, especially when these operations take place in lesser developed countries. Such requirements should encompass occupational, environmental, and human rights practices. A good model for such legislation is the Right-to-Know program designed by Friends of the Earth organizer Lisa Archer.

Recently, right-to-know requirements have focused on product labeling. Labeling per se, however, is inadequate unless accompanied by an explicit "red flag" warning of recognized cancer and other health, environmental, and

occupational risks. Furthermore, labeling should not be used as a justification for the authorization of new candidate carcinogens or for the continued use of carcinogenic products already in commerce. Labeling is no substitute for a moratorium or ban. Indeed, labeling is not only discriminatory to uneducated and lower socio-economic population groups, but may encourage industry to target such groups and penetrate national markets by price regulation strategies.

There are four areas in which right-to-know legislation is especially needed--consumer products, prescription drugs, occupational exposure, and environmental exposure. (See Table 1 at left.)

Consumer product legislation, in particular, is well overdue. All foods grown with the application of carcinogenic pesticides should be clearly labeled with a cancer warning, the name of each carcinogenic pesticide, and the concentrations of its residues. Of particular concern are the high residues of multiple carcinogenic pesticides in grains, vegetables and fruit. Recent estimates indicate that by the age of one, cancer risks from residues of just eight common pesticides in twenty infant foods exceed the lifetime "acceptable" cancer risks estimated by the U.S. Environmental Protection Agency. U.S. meat should also be clearly labeled as contaminated with residues of carcinogenic sex hormones (Epstein, 1998), as should U.S. milk be labeled as a genetically engineered product, for which the public health hazards have been fully documented (Epstein, 2001). Similarly, irradiated meat, poultry, eggs, and produce should be prominently labeled as "irradiated," especially in view of their carcinogenic, mutagenic, nutritional, and other risks. This requirement is in sharp contrast to efforts by industry, with complicity of the United States Food and Drug Administration and Department of Agriculture, to use labels with misleading euphemistic absurdities such as "cold pasteurization" or "electronic pasteurization" (Epstein and Hauter, 2001).

While ingredients of cosmetics and personal care products are generally identified on their labels by a long list of chemicals, this is meaningless to the overwhelming majority of consumers in the absence of any "red flag" warning of the wide range of multiple carcinogenic ingredients, contaminants, and precursors in most products. Similarly, the complete composition of all household cleaning and other products, including home, lawn, and garden pesticides, should also be clearly labeled, together with cancer warnings for each listed carcinogenic ingredient. Consumer product legislation should require data and affidavits in support of claims of safety for organic or other products. Consideration should also be given to the granting of tax incentives to the manufacturers of safe alternative products.

Clear labeling is also needed for prescription drugs. A recent survey of 241 high-volume U.S. prescription drugs reported that nearly half posed cancer risks based on carcinogenicity tests designed by their manufacturers to prove safety (Moore, 1998). Many carcinogenic drugs have been identified at low test dosages, near or at therapeutic levels. These risks are compounded by the fact that carcinogenic drugs are often administered individually or in various combinations to tens of millions of patients, sometimes for decades and starting in childhood. The author of this study, Thomas Moore, has claimed that prescription drugs may pose the single most important class of unrecognized and avoidable carcinogenic risks for the entire U.S. population.

To argue that such risks are more than justified by their very real benefits is to posit a false dilemma, especially in view of the fact that patients are rarely affirmatively and explicitly informed of these risks, and of the availability of safer and effective alternatives. Legislation is urgently required to ensure that the pharmaceutical industry provides clear and explicit information on carcinogenic prescription and non-prescription drugs, which should also be labeled with clear warnings of such risks. Physicians should also be required to endorse these warnings, provide patients with information on safe and effective alternatives, and be held accountable for failure to do so.

Many of the most toxic substances are those we do not purchase. Instead, they are present in the environment around us or as occupational hazards in our workplaces. Workers and their representatives have inalienable rights to be given full information on the identity of all carcinogens, including raw materials, intermediates, impurities and final products, to which they are exposed by providing explicit labeling and posting. Additionally, they are entitled to quantitative information on levels of inhalation and skin exposure for each carcinogen. All such information should be made available to workers on a daily basis and also reported to the responsible regulatory authorities.

Citizens, too, are entitled to full access to information from local and national government on their avoidable carcinogenic exposures from air and water. Such information is likely to encourage industry to reduce environmental emissions and discharges of carcinogenic and toxic pollutants and also to encourage more stringent governmental regulation.

Every regional municipal authority should be required to provide consumers with a complete list of carcinogenic contaminants and their concentrations in drinking water together with each water bill. Similarly, every chemical, mining, and nuclear industry should be required to disclose to local communities and regional and national governments a complete listing of all carcinogens, including intermediates and products, they use, process, manufacture, and dispose. They should also be required to disclose the amounts of each carcinogen they discharge into surrounding air and water. No industry should be allowed to operate unless it provides ongoing quantitative

information on smokestack and other atmospheric emissions of carcinogens in the air of its perimeter and in the local community.

4. Transparent Decision-Making

Key governmental decisions and policies are generally determined by the recommendations of governmental scientific institutions, designated expert committees, and regulatory bodies. Their independence, integrity, expertise and accountability are thus matters of critical concern. In addition, all institutions receiving government or tax-exempt funds (such as the cancer establishment) should be required to provide clear and audited budgetary statements defining their sources of funding and their expenditures on basic molecular research, diagnosis and treatment, and primary prevention.

For instance, budgetary information on prevention should specify allocations for the following: research primarily directed to investigating avoidable causes of cancer; research on all possible risk factors for each type of cancer whose incidence has increased substantially over recent decades; research on cancer risks from carcinogens identified in well-designed animal tests and/or listed by the International Agency for Research on Cancer; activities with regard to the development of a comprehensive registry for all carcinogens to which general populations and populations at high risk may be exposed; and outreach activities providing Congress or Parliaments, governmental agencies and the public with available information on all avoidable carcinogenic exposures and actions that may be taken to reduce or avoid such exposures.

Legislation to ensure full accountability and transparency of all cancer institutions involved in cancer research and related activities is long overdue.

In the United States, the predominant complex of institutions charged with fighting cancer, known as the "cancer establishment," is comprised of the governmental National Cancer Institute (NCI) and the private "charity," the American Cancer Society (ACS), together with their national network of funded university scientists and Comprehensive Cancer Centers. The cancer establishment has massive resources at its disposal. The 2001 budget of the NCI is $3.8 billion, up from $220 million in 1971 when President Nixon declared the War Against Cancer. The current budget of the ACS is about $700 million, with cash reserves and other assets of $900 million.

The policies and priorities of the cancer establishment are narrowly fixated on damage control--diagnosis and treatment--and on basic molecular research with a not always benign indifference to cancer prevention. For the ACS, this indifference has reached the level of overt hostility that I've described elsewhere (see, for example, TIKKUN Nov/Dec, 2000). These and other concerns relating to fiscal malpractice have led the Chronicle of Philanthropy, the authoritative U.S. charity watch dog, to charge that the ACS is "more interested in accumulating wealth than saving lives." ACS allocations for all primary prevention activities are under 0.1 percent of its budget. NCI's budgetary allocation for occupational cancer, the most avoidable of all cancers, which according to conservative estimates is responsible for about 10 percent of all U.S. cancer deaths besides being a major cause of childhood cancer, is only one percent; the budget for research and outreach to African American and other ethnic minorities, with their disproportionately high cancer rates, is also only one percent of NCI's budget. NCI's allocations for all primary prevention activities total well under five percent.

The establishment's professional mindset and priorities are compounded by disturbing conflicts of interest with the cancer drug and other industries. As NCI's previous director Dr. Samuel Broder recently admitted, the NCI has become "what amounts to a governmental pharmaceutical company" (Epstein, 1998). The establishment's myopic mindset is further illustrated by a succession of widely publicized misleading claims to have turned "the tide against cancer," and for the latest "miracle" or "magic bullet" cancer drugs, claims which have rarely been substantiated, let alone recanted, over the last four decades (Epstein, 1998).

Most seriously, the poorly accountable U.S. cancer establishment has failed to provide Congress, regulatory agencies, and the public with available scientific information on a wide range of avoidable carcinogenic exposures. As a result, corrective legislative and regulatory action has still not been taken, and the public has been and still is denied its right to such information and the opportunity to take action to reduce their own risk of cancer.

The track record of U.S. and U.K. cancer establishments makes it clear that only drastic reforms of their policies, priorities and leadership will achieve such objectives, and belatedly restore an overdue sense of mission and balance to winning the losing war against cancer.

Similar reforms are needed for national and international regulatory bodies. The 1972 U.S. Federal Advisory Committee Act requires that the composition of regulatory agency advisory committees reflect balanced and qualified representation of all concerned interests and that meetings must be publicized in advance and open to the public. However, in practice, these requirements are more often breached than observed. For example, in an ominous development, a secret World Science Court or Global Science Advisory Board has been created under the

leadership of Dr. Bruce Alberts, president of the U.S. National Academy of Sciences (Epstein, 2000). Alberts has fought tooth and nail against complying with the Federal Advisory Committee Act's requirements for transparency of operations and balanced representation. The World Science Court, now known as the InterAcademy Council and based in Amsterdam, is at this moment organizing expert panels to provide scientific advice to the United Nations, World Bank, and other international organizations on issues ranging from food safety to emerging diseases.

The sort of secrecy, sadly, is not new. In a 1997 U.S. and Canadian challenge against the EU ban on hormonal meat before the World Trade Organization (WTO), I served, together with other international scientists, as the public health consultant to the EU in defense of its ban. Apart from documenting the scientific evidence for the risks from high residues of sex hormones in meat, I analyzed the reports and composition of the relevant FAO/WHO committees, particularly the 1988 Joint Expert Committee on Food Additives (JECFA), which had claimed that hormonal meat was safe, and on whose authority the U.S. and Canadian legal action was largely based. I concluded that "the membership of these committees reflects disproportionate representation of U.S. senior regulatory officials and of veterinary and food scientists, with minimal if any involvement of independent experts in preventive medicine, public health and carcinogenesis. The European Commission Scientific Conference of November 29-December 1, 1995 also reflects such imbalanced representation. While Conference participation of 'scientists directly employed' by industry was 'generally refused,' no apparent attempt was made to identify or exclude industry consultants, contractees, or grantees. Furthermore, the Conference based its findings and conclusions largely on unpublished industry data."

In his own report to the European Commission, John Verall also concluded that the FAO/WHO advisory committees represent a sanitized front for powerful industry interests and pre-determined regulatory decisions, rather than bodies ready to determine sound science and consumer safety (Verall, 1999). Clearly, legislation is needed to require that expert scientific committees, such as JECFA, and regulatory agencies dealing with health and environmental concerns such as the Codex Alimentarius, International Office of Epizootics/FAO, and WHO/ILO, conform to basic requirements to ensure unbiased and sound scientific findings and appropriate subsequent regulatory decisions (Verall, 1999; Castleman and Lemen, 1998).

How can we achieve transparent decision-making in such regulatory bodies and citizen-funded institutions? First, absolute rights should be given by law to grant consumer, environmental, occupational, cancer prevention, and other concerned NGO's full membership on scientific and advisory committees of regulatory bodies. They should also be given full right to participate in the evaluation and selection of scientists performing risk assessment, and financial support to appoint their own experts to work with scientific and regulatory committees charged with safety evaluation of industrial products and processes, medicinal drugs, consumer products, and emerging technologies, notably genetically-engineered foods.

Similar and equally rigorous legislation is needed for the executive, advisory, and scientific committees of all cancer institutions--governmental, charitable and academic--to ensure full accountability and transparency of their deliberations and to ensure that maximal priority be directed to cancer prevention, rather than virtually exclusively to damage control, diagnosis and treatment, and basic molecular research.

Second, transparency of all scientific and regulatory proceedings should further be ensured by providing advanced public information on scheduled committee meetings, which should be open without restriction to the public.

The European Commission (EC) has recently implemented a new policy of openness by publicizing the already mandated declarations of interest made annually by members of their influential and supposedly independent scientific committees (Watson, 2000). This move followed a lengthy campaign by the British advocacy group Baby Milk Action, the U.K. partner of the International Baby Food Action Network, with support from U.K. Labour members of the European Parliament. The EC has always claimed that the members of its various scientific committees act independently, make annual declarations of interest, and declare conflicts of interest at each meeting. However, even if that were the case, this information has never before been made public.

Now, the declarations of the nineteen members of the Scientific Committee for Food, established in 1974 to advise on consumer health and food safety, are the first to be made widely available. According to Baby Milk Action, four members of the Committee--Professor Albert Flyn (Ireland), Professor Ronald Walker (United Kingdom), Tim H.M. Saris (the Netherlands), and Professor Anna Ferro Luzzi (Italy)--have declared "economic or ethical interests which might be considered prejudicial" to their independence. Seven other scientific committees, and their overall steering committees, are now likely to follow suit. The EC insists, however, that contacts between the committees' members and commercial organizations are "part of normal and professional life" and should not be treated as "undesirable" (Watson, 2000). At least now, with a transparent decision-making process in place, those of us who disagree have the facts we need to make our argument.

5. White Collar Crime

There is an overwhelming disparity between the force of criminal law directed at perpetrators of theft, property damage, or personal violence and the lenient civil proceedings against managers and executives of industries and their consultants who knowingly manipulate, distort, or suppress information on the environmental, occupational and consumer hazards of their products and processes. As Ralph Nader has aptly commented, there are two standards of justice in modern industrialized society: "jail for crime in the streets, but bail for crime in the suites." This flagrant inequity in our dual system of justice is exacerbated by the major socioeconomic differences between the two classes of offenders. Furthermore, the obvious one-to-one direct and immediate impact of blue-collar crime on a single victim is generally in striking contrast with white-collar industry crime, the effects of which are largely sanitized by the non-personal and indirect relationship between the criminal and multiple victims and by the usually long latency between crime and effect.

Over two decades ago, Congressman John Conyers, the distinguished Democratic chairman of the U.S. Congress House Committee on the Judiciary, invited me to assist in drafting legislation and to testify on white collar crime, as defined by "nondisclosure of certain matters by certain business entities and personnel" in relation to environmental and health concerns. Congressman Conyers' bill, which urged criminal penalties, including imprisonment, for such corporate crimes, was presented to Congress on July 26, 1979. However, its passage was blocked by Republican committee members and has not since been reintroduced.

In testimony on this proposed legislation, I stated that my investigations had revealed a pattern of gross negligence, manipulation, distortion, suppression, and destruction of data. I found that those involved in the generation and interpretation of this tainted data included not only the businesses concerned, but also a complex of commercial testing and consulting laboratories, and academic consultants, supported by a network of industry front organizations and quasi-professional societies. It was this kind of data, I testified, which allowed industries to minimize or deny the risk to workers and the public-at-large, and to maximize product or process efficacy to the detriment of public health and the environment.

The legislation I supported then and continue to support today offers business the opportunity to explicitly reassert its highest ethical standards and, by policing itself, to preclude or limit the need for further regulatory policing. Such a bill would impose no unreasonable restraints on commerce or on technological innovation but would instead seek to encourage honest disclosure of "lethal defects" and to deter and punish those who knowingly commit criminal acts on "nondisclosure." In so doing, such a bill would discourage the introduction of products and processes with "lethal defects," and thus prevent the attendant economic dislocation following their subsequent withdrawal once these defects become recognized. Successful self-policing by business would also act as a major brake to burgeoning product liability suits. Finally, a bill like the one Conyers introduced would offer a unique opportunity to restore the eroding public confidence in big business in general, and the chemical industry in particular, and thus reverse the growing and nationally damaging trend of polarization and confrontation between business, the general public, and labor.

In the absence of a legislative disincentive like the Conyers bill, environmental and health safety white collar crime has continued unabated and has extended into global markets. Such misconduct, which I have investigated over three decades, includes:

- Suppression and manipulation by Vesicol Chemical Company of the carcinogenic and other chronic toxic effects of the pesticides chlordane and heptachlor, which have been extensively used for termite treatment of wood (Epstein, 1990).
- Monsanto's suppression and denial of clear evidence of adverse veterinary and public health effects of genetically-engineered milk hormone (rBGH/rBST) and of excess levels of a growth factor, IGF-1, in hormonal milk which poses serious cancer and other risks to consumers (Epstein, 1998; Epstein, 2001).
- The cancer risks of silicone gel breast implants, particularly those coated with polyurethane foam, long-standing evidence of which had been suppressed by Dow Corning Company, Bristol-Myers Squibb, and other manufacturers, by plastic surgeons and their professional associations (Epstein, 1998, Appendix V; Epstein, 1995).
- Suppression by Eli Lilly Company of its own evidence on the grave risks of ovarian cancer from its aggressively promoted and advertised new drug Evista (raloxifene) used for the prevention of postmenopausal osteoporosis (Epstein, 1998, Appendix V).

Among more recent examples of corporate misconduct is the reckless behavior of the tobacco industry, now the subject of federal, state, and civil litigation. The most egregious examples of such conduct have been detailed in extensive secret documents obtained from R.J. Reynolds' Company in the course of civil litigation and released to the public in January, 1998 (Superior Courts of the State of California, 1998). The Company's "Joe Camel" advertising campaign deliberately targeted underage smokers in calculated efforts to recruit lifetime adult smokers, most of whom start smoking or become addicted by the age of eighteen. With huge promotional expenditures from 1987-1998, R.J. Reynolds recruited about 560,000 underage U.S. smokers. No criminal charges have yet been brought against this industry despite the devastating scourge of future disease and death anticipated from the Camel campaign, including cancers of the lung and other sites, cardiovascular disease, stroke, chronic obstructive lung disease and adverse complications of pregnancy, apart from inflationary medical and loss of productivity costs.

Clearly, white collar environmental and health crime legislation is critically needed and well overdue world-wide. Congressman Conyers' 1979 bill could still serve as a useful model. Consideration should also be directed to the establishment of an International Public Health Crimes Court, modeled along the lines of the International War Crimes Tribunal, for the investigation and indictment of transnational corporations whose products and processes pose recognized or potential dangers to public health and environmental integrity.

Apart from criminal prosecution of white collar crime, legislation is also needed to empower citizens who become aware of undisclosed carcinogenic hazards in consumer products to take civil action to enjoin their distribution and sale and receive as a benefit a share of past illegal sales together with some type of mandatory financial sanctions. One precedent for such an initiative is Proposition 65, passed by California in 1986.

6. Independent Citizen Health and Safety Agency

The five preceding principles point to the critical and long overdue need for the establishment of an Independent Citizen Safety Agency. This Agency should be given wide powers to police the effectiveness of current health and safety regulations, and to act as intermediary between consumers, workers, and their NGO's on the one hand and regulatory authorities and industry on the other. The Agency should be empowered with responsibilities including the establishment of a clearinghouse for receiving and evaluating complaints from individual consumers, workers, and their interest groups on all health related issues; collecting, systematizing and evaluating new scientific data and assessing their implications for current and proposed new regulations; publication and dissemination of information, in explicit and simple language, on possible health and environmental risks from regulated products and processes and the proposed authorization of new products and processes.

The Agency should be established on the models of antitrust and cartel agencies with wide powers of investigation, decision making and fining of violators. The Agency should be a public watchdog, an ombudsman with teeth, directly accountable only to Congress or Parliament.

ILLUSTRATION (BLACK & WHITE)

TABLE 1: The dirty dozen consumer products.

Mainstream industry consumer products--foods and beverages, cosmetics and toiletries, and household products including home, lawn and garden pesticides--contain a wide range of undisclosed carcinogens which pose major, but generally unrecognized, avoidable risks of cancer.

FOOD

Beef Frankfurters--(e.g. Oscar Mayer Foods Corporation)

- Unlabeled toxic ingredients: Benzene Hexachloride, carcinogenic; Dacthal, carcinogenic (can be contaminated with dioxin); Dieldrin, carcinogenic; DDT, carcinogenic; Heptachlor, carcinogenic; Hexachlorobenzene, carcinogenic; Lindane, carcinogenic; hormones, carcinogenic and feminizing; antibiotics (some are carcinogenic, e.g. Sulfamethazine).
- Labeled toxic ingredient:--Nitrite (interacts with meat amines to form carcinogenic nitrosamines).
- Note: Substantive evidence of causal relation to childhood cancer.

Whole Milk--(e.g. Borden or Lucerne)

• Unlabeled toxic ingredients: DDT, carcinogenic; Dieldrin, carcinogenic; Heptachlor, carcinogenic; Hexachloro-benzene, carcinogenic; antibiotics (some are carcinogenic); Recombinant Bovine Growth Hormone and IGF-1 (evidence of breast and colon cancer promotion).

COSMETICS and TOILETRIES

Talcum Powder--(e.g. Johnson & Johnson, Inc.)

- Labelled toxic ingredient: Talc, carcinogenic.
- Note: Substantive evidence of causal relation to ovarian cancer.

Cover Girl Replenishing Natural Finish Make-up (Foundation)--Procter & Gamble, Inc.

• Labelled toxic ingredients: BHA, carcinogenic; Talc, carcinogenic; Titanium Dioxide, carcinogenic; Triethanolamine (TEA) (interacts with nitrites to form carcinogenic nitrosamines); Lanolin (often contaminated with DDT and other carcinogenic pesticides).

Crest Tartar Control Toothpaste--Procter & Gamble. Inc.

• Labelled toxic ingredients: FD & C Blue #1, carcinogenic; Saccharin, carcinogenic; Fluoride, possible carcinogen.

Alberto VO5 Conditioner (Essence of Neutral Henna)--Alberto-Culver USA, Inc.

• Labelled toxic ingredients: Formaldehyde, carcinogenic; Polysorbate 80 (can be contaminated with the carcinogen 1,4-dioxane); FD & C Red #4, carcinogenic.

Clairol Nice 'n East (Permanent Haircolor)--Clairol, Inc.

- Labelled toxic ingredients: Quaternium-15, Formaldehyde releaser, carcinogenic; Diethanolamine (DEA) (interacts with nitrites to form a carcinogenic nitrosamine); Phenylene-Diamines (includes carcinogens and other ingredients inadequately tested for carcinogenicity).
- Note: Substantive evidence of causal relation to lymphoma, multiple myeloma, and other cancers.

HOUSEHOLD PRODUCTS

Ajax Cleanser--Colgate-Palmolive, Inc.

• Unlabeled toxic ingredient: Crystalline Silica, carcinogenic.

Zud Heavy Duty Cleanser--Reckitt & Colman, Inc.

• Unlabeled toxic ingredient: Crystalline Silica, carcinogenic.

Lysol Disinfectant Spray--Reckitt & Colman, Inc.

• Labelled or unlabeled toxic ingredient: Orthophenylphenol (OPP), carcinogenic.

Zodiac Cat & Dog Flea Collar--Sandoz Agro, Inc.

• Labelled toxic ingredient: Propoxur, carcinogenic.

Ortho Weed-B-Gon Lawn Weed Killer--Monsanto Co.

- Labelled toxic ingredient: Sodium 2,4- Dichlorophenoxyacetic acid (2,4-D), carcinogenic.
- Note: Substantive evidence of causal relation to lymphoma, soft tissue sarcoma, and other cancers.

This table is reprinted from Table 17.4 of my book, The Politics of Cancer Revisited, © 1998 East Ridge Press.

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THE CAUSES AND PREVENTION OF CANCER: GAINING PERSPECTIVE

Epidemiological studies have identified several factors that are likely to have a major effect on reducing rates of cancer: reduction of smoking, increased consumption of fruits and vegetables, and control of infections. Other factors include avoidance of intense sun exposure, increased physical activity, and reduced consumption of alcohol and possibly red meat. Risks of many types of cancer can already be reduced, and the potential for further reductions is great. In the United States, cancer death rates for all cancers combined are decreasing, if lung cancer (90% of which is due to smoking), is excluded from the analysis. We review the research on causes of cancer and show why much cancer is preventable. The idea that traces of synthetic chemicals, such as DDT, are major contributors to human cancer is not supported by the evidence, yet public concern and resource allocation for reduction of chemical pollution are very high, in part because standard risk assessment uses linear extrapolation from limited data in high-dose animal cancer tests. These tests are done at the maximum tolerated dose (MTD) and are typically misinterpreted to mean that low doses of synthetic chemicals and industrial pollutants are relevant to human cancer. About half the chemicals tested, whether synthetic or natural, are carcinogenic to rodents at such high doses. Almost all chemicals in the human diet are natural. For example, 99.99% of the pesticides we eat are naturally present in plants to ward off insects and other predators. Half of the natural pesticides that have been tested at the MTD are rodent carcinogens. Cooking food produces large numbers of natural dietary chemicals. Roasted coffee, for example, contains more than 1000 chemicals: of 27 tested, 19 are rodent carcinogens. Increasing evidence supports the idea that the high frequency of positive results in rodent bioassays is due to testing at the MTD, which frequently can cause chronic cell killing and consequent cell replacement--a risk factor for cancer that can be limited to high doses. Because default risk assessments use linear extrapolation, which ignores effects of the high dose itself, low-dose risks are often exaggerated. -- Environ Health Perspect 105(Suppl 4):865-873 (1997)

Key words: causes of cancer, environmental carninogens, diet and cancer

Cancer Trends

According to the National Cancer Institute's 1993 Surveillance, Epidemiology, and End Results Program (1), cancer caused 23% of the person-years of premature loss of life and about 530,000 deaths in the United States in 1993. Four major cancers--lung, colon-rectum, breast, and prostate--accounted for 55% of these deaths. Cancer death

rates in the United States are decreasing, after adjustment for age and exclusion of lung cancer. The age-adjusted mortality rate for all cancers combined (excluding lung and bronchus) has declined 14% from 1950 to 1990. Smoking, in addition to causing 90% of lung cancer, contributes to cancers of the mouth, esophagus, pancreas, bladder, and possibly colon; if these were taken into account, the decline would be greater.

Peto and colleagues, (2) have come to the same conclusion: "The common belief that there is an epidemic of death from cancer in developed countries is a myth, except for the effects of tobacco. In many countries cancer deaths from tobacco are going up, and in some they are at last coming down. But, if we take away the cancer deaths that are attributed to smoking then the cancer death rates that remain are, if anything, declining."

The number of people newly diagnosed with cancer (incidence rate) has been increasing for some types of cancer. In their comprehensive study on the causes of cancer, Doll and Peto (3) point out that incidence rates should not be taken in isolation because reported incidence rates for a disease might reflect increases in registration of cases and improvements in diagnosis. For example, the rapid increase in age-adjusted prostate cancer incidence without any major increases in mortality is mostly due to increased screening and incidental detection during prostatectomy for benign prostatic hypertrophy (4). Devesa et al. (5) discuss incidence and mortality trends by site in detail.

Major Contributors to Risk of Cancer

Two critical factors in the formation of mutations are lesions in DNA (produced when DNA is damaged) and cell division (which converts DNA lesions to mutations). Agents that increase either lesions or cell division in stem cells can increase mutations, and as a consequence increase cancer incidence (below) (4,6-8). Hormones stimulating cell division increase cancer incidence (e.g., estrogen in breast cancer and testosterone in prostate cancer); hormones may be a risk factor in about 20% of human cancer (4,6).

Oxidative Damage and the Degenerative Diseases of Aging

Aging and its degenerative diseases appear to be due in good part to the accumulation of oxidative damage to DNA and other macromolecules (9). By-products of normal metabolism--superoxide, hydrogen peroxide, and hydroxyl radical--are the same oxidative mutagens produced by radiation (10). Oxidative lesions in DNA accumulate with age, so that by the time a rat is old (2 years) it has about 1 million DNA lesions per cell, which is about twice the number in a young rat (9). Mutations also accumulate with age. DNA is oxidized in normal metabolism because antioxidant defenses, though numerous, are not perfect. Endogenously produced oxidants can damage proteins as well as DNA (11). In two human diseases associated with premature aging, Werner's syndrome and progeria, oxidized proteins accumulate at a much higher rate than normal (11).

Chronic inflammation from chronic infection results in release of oxidative mutagens from phagocytic cells and is a major contributor to cancer (below).

Antioxidant defenses against oxidative damage include vitamins C and E and carotenoids. To the extent that the major external risk factors for cancer--smoking, unbalanced diet, and chronic inflammation-are diminished, cancer will appear at a later age, and the proportion of cancer that is caused by normal metabolic processes will increase.

Diet

Doll and Peto (3) and others (6) estimate that diet accounts for about one-third of cancer risk, and current research is slowly clarifying specific factors.

Cancer Prevention by Calorie or Protein Restriction. In rodents, a calorie-restricted diet compared to ad libitum feeding markedly decreases tumor incidence and increases life span (12-14). Protein restriction appears to have a similar effect on rodents, although research is less extensive (15). An understanding of mechanisms for the marked effect of dietary restriction on aging and cancer is becoming clearer and may be due largely to reduced oxidative damage and reduced rates of cell division. Although epidemiological evidence on restriction in humans is sparse, the possible importance of growth restriction in human cancer is supported by epidemiological studies that indicate higher rates of breast cancer among taller persons (16,17). For example, Japanese women are now taller, menstruate earlier, and have increased breast cancer rates. Also, many of the variations in breast cancer rates among countries and trends over time within countries are compatible with changes in growth rates and attained adult height (18).

Cancer Prevention by Dietary Fruits and Vegetables. Adequate consumption of fruits and vegetables is associated with a lowered risk of degenerative diseases such as cancer, cardiovascular disease, cataracts, and brain and immune dysfunction (9). Nearly 200 studies in the epidemiological literature have been reviewed, and they show a consistent association between inadequate consumption of fruits and vegetables and cancer (19-21). The quarter of the population with the lowest dietary intake of fruits and vegetables has roughly twice the cancer risk for most types

of cancer (lung, larynx, oral cavity, esophagus, stomach, colon and rectum, bladder, pancreas, cervix, and ovary) compared with the quarter with the highest intake. For hormonally related cancers, the protective effect of consuming fruits and vegetables is weaker and less consistent: for breast cancer the protective effect appears to be about 30% (16,19,22). Laboratory studies suggest that antioxidants such as vitamins C and E and carotenoids account for a good part of the beneficial effect of fruits and vegetables (9); however, epidemiologists have difficulty disentangling the effects of dietary intakes of the antioxidants from other important vitamins and ingredients in fruits and vegetables (23,24).

A wide array of compounds in fruits and vegetables in addition to antioxidants may contribute significantly to the reduction of cancer. Folic acid may be particularly important. Low folic acid intake causes chromosome breaks in rodents (25) and in humans (26,27) and increases tumor incidence in some rodent models (28). Folic acid is essential for the synthesis of DNA. Low folate intake has been associated with several neoplasms including adenomas and cancers of the colon (29-31). Maternal deficiency of folate is associated with neural tube birth defects (32). Deficient intake of folic acid is common in U.S. diets. About 15% of the U.S. population (33) has a folate level at which chromosome breaks are seen (26). A study of adolescents (34) and elderly (35) from urban, low-income, predominantly African-American households, found that about half had such levels. Dietary fiber, obtained only from foods of plant origin, may contribute to lower risk of colon cancer (36). Plant foods also contain a wide variety of weak estrogens that may act as antiestrogens by competing with estrogenic hormones (20,24,37).

Other Aspects of Diet. Although epidemiological studies most clearly support the benefits of fruits and vegetables in the prevention of cancer, strong international correlations suggest that animal (but not vegetable) fat and red meat may increase the incidence of cancers of the breast, colon, and prostate (38). However, large prospective studies have consistently shown either a weak association or a lack of association between fat intake and breast cancer (16). Consumption of animal fat and red meat have been correlated with risk of colon cancer internationally, but the relation with fat intake has not been supported in most case-control and cohort studies (39,40); the association with meat consumption appears more consistent (40-43). Consumption of animal fat and red meat has been associated with risk of prostate cancer (42,44). Mechanisms for these associations are not clear, but may include the effects of dietary fats on endogenous hormone levels (4), the local effects of bile acids on the colonic mucosa, the effects of carcinogens produced by cooking meat, and excessive iron intake from red meat. Excess iron absorption, particularly heme iron from meat, is a plausible, though unproven, contributor to the production of oxygen radicals (9). Some of the large geographical differences in colon cancer rates that have been attributed to dietary factors are probably due to differences in physical activity, which is inversely related to colon cancer risk in many studies (45-47).

Alcoholic beverages cause inflammation and cirrhosis of the liver, leading to liver cancer (48). Alcohol is an important cause of oral and esophageal cancer and is also synergistic with smoking (48) and possibly contributes to colorectal cancer (31,49).

Cooking food is plausible as a contributor to cancer (50). Cooking forms a wide variety of chemicals. Four groups of chemicals that cause tumors in rodents have attracted attention because of mutagenicity, potency, or concentration: nitrosamines, heterocyclic amines, polycyclic hydrocarbons, and furfural and similar furans. Epidemiological studies on cooking are difficult and so far are inadequate to evaluate a carcinogenic effect in humans (51).

Tobacco

Smoking contributes to about one-third of cancer, about one-quarter of heart disease, and about 400,000 premature deaths per year in the United States (52). Tobacco is a known cause of cancer of the lung, bladder, mouth, pharynx, pancreas, stomach, larynx, esophagus (2), and possibly colon (53-55). Tobacco causes even more deaths by diseases other than cancer. The evidence for environmental tobacco smoke as a cause of cancer is much weaker. Studies have estimated that environmental tobacco smoke causes up to 3000 additional cases of cancer a year (56,57), although this estimate has been disputed (58).

The carcinogenic mechanisms of tobacco smoking are not well understood. Smoke contains a wide variety of mutagens and rodent carcinogens, and smoking is a severe oxidative stress and causes inflammation in the lung. The oxidants in cigarette smoke--mainly nitrogen oxides--deplete the body's antioxidants. Thus, smokers must ingest two to three times more ascorbate than nonsmokers to achieve the same level of ascorbate in blood, but they rarely do (59-61). Men with inadequate diets or who smoke may damage both their somatic DNA and the DNA of their sperm. When the level of dietary ascorbate is insufficient to keep seminal fluid ascorbate at an adequate level, the oxidative lesions in sperm DNA are increased 2.5 times (62). Inadequate concentration of ascorbate in plasma is more common among single males, the poor, and smokers (63). Paternal smoking may plausibly increase the risk of birth defects and childhood cancer in offspring (64).

Cancer from Inflammation Caused by Chronic Infection

White cells and other phagocytic cells of the immune system combat bacteria, parasites, and virus-infected cells by destroying them with potent mutagenic oxidizing agents. The oxidants protect humans from immediate death from infection; but they also cause oxidative damage to DNA, mutation, and chronic cell killing with compensatory cell division (65,66) and thus contribute to the carcinogenic process. Antioxidants appear to inhibit some of the pathology of chronic inflammation (9).

We estimate that chronic infections contribute to about one-third of the world's cancer. Hepatitis B and C viruses are a major cause of chronic inflammation leading to liver cancer--one of the most common cancers in Asia and Africa (67-69). Hepatitis B and C viruses infect about 500 million people worldwide. Nearly half the world's liver cancer occurs in China (70). Vaccinating babies at birth is potentially an effective method to reduce liver cancer and is routinely done for hepatitis B in Taiwan. The mutagenicmold toxin, aflatoxin, which is found in moldy peanut and corn products, interacts with chronic hepatitis infection in liver cancer development (71-73).

Another major chronic infection is schistosomiasis, which is widespread in Egypt and Asia. In Egypt, the eggs of Schistosorna haernatobium, deposited in the bladder, cause inflammation and bladder cancer (74). In Asia, the eggs of Schistosoma japonicum, deposited in the colonic mucosa, cause inflammation, and there is limited epidemiological evidence for an association with colon cancer (74). Opisthorchis viverrini, a liver fluke, infects millions of people in Thailand and Malaysia. The flukes lodge in bile ducts and increase the risk of cholangiocarcinoma (74). Chlonorchis sinensis infects millions of people in China and increases the risk for biliary tract cancer (74). Helicobacter pylori bacteria, which infect the stomachs of more than one-third of the world's population, are a major cause of stomach cancer, ulcers, and gastritis (74). In the United States the infection is often asymptomatic, which suggests that inflammation may be at least partially suppressed, possibly by adequate levels of dietary antioxidants (75).

Human papilloma virus, a major risk factor for cervical cancer, does not appear to work through an inflammatory mechanism (76). It is spread by sexual contact, an effective method of transmitting viruses.

Chronic inflammation resulting from noninfectious sources can also lead to cancer. For example, asbestos exposure leading to chronic inflammation may be in good part the reason that asbestos is a significant risk factor for lung cancer (77,78).

Hormones

Henderson et al. have reviewed the extensive literature on hormones and cancer, which indicates that endogenous reproductive hormones play a large role in cancer, possibly contributing to as much as one-third of all cancer, including breast, prostate, ovary, and endometrium (4). Hormones are likely to act by causing cell division (79).

Less Important Contributors to Risk of Cancer

We have discussed elsewhere some of the less important contributors to cancer, including hereditary factors, sun exposure, and medical interventions (6). Here we discuss occupation and pollution because the scientific basis for concern needs clarification.

Occupation

The International Agency for Research on Cancer of the World Health Organization evaluates potential cancer risks to humans from a range of chemical exposures (80). Half of the 60 chemicals and chemical mixtures the agency has evaluated as having sufficient evidence of carcinogenicity in humans represent occupational exposures, which tend to be concentrated among small groups of people who have been chronically exposed at high levels. These include workplace exposures such as rubber industry or coke production, as well as exposure to specific aromatic amines, petrochemicals, and metals. How much cancer can be attributed to occupational exposure has been a controversial issue, but a few percent seems a reasonable estimate. Doll and Peto (3) have discussed difficulties in making such estimates, including the lack of accurate data on the history of exposure and current exposures, as well as confounding factors such as socioeconomic status and smoking. Lung cancer was by far the largest contributor to Doll and Peto's estimate of the proportion of cancers due to occupation. The preeminence of smoking as a cause of lung cancer confounds the interpretation of rates in terms of particular workplace exposures to substances such as asbestos; asbestos appears to multiply rather than just add to the effect of smoking. In contrast, asbestos alone is a known risk factor for mesothelioma. Doll and Peto (3) estimated that asbestos caused a high proportion of occupational cancers, but recent estimates for asbestos-related cancer are lower (81,82).

Exposures to substances in the workplace can be high in comparison with other chemical exposures in food, air, or water. Past occupational exposures have often been high and comparatively little quantitative extrapolation may be required for risk assessment from high-dose rodent tests to high-dose occupational exposures. Because

occupational cancer is concentrated among small groups exposed at high levels, there is an opportunity to control or eliminate risks once they are identified. The U.S. Occupational Safety and Health Administration (U.S. OSHA), however, unlike other federal agencies such as the U.S. Environmental Protection Agency (U.S. EPA), regulates few chemicals as potential human carcinogens. For 75 rodent carcinogens regulated by U.S. OSHA with permissible exposure limits, we recently ranked potential carcinogenic hazards on an index that compares the permitted dose rate for workers with the carcinogenic dose for rodents (83). We found that for 9 chemicals the permitted exposures were within a factor of 10 of the rodent carcinogenic dose and for 17 they were between 10 and 100 times lower. These values are high in comparison with hypothetical risks regulated by other federal agencies. An additional 120 rodent carcinogens to which workers are exposed had no U.S. OSHA permissible exposure limit, which suggests the need for further regulatory attention and research on mechanism of carcinogenesis.

Pollution

Much of the public fears synthetic pollutants as major causes of cancer, but this fear is based on a misconception. Even assuming that the U.S. EPA's worst-case risk estimates for synthetic pollutants arc true risks, the proportion of cancer that the U.S. EPA could prevent by regulation would be tiny (84). Epidemiological studies of pollutants, moreover, are difficult to conduct because of inadequacies in assessing low-level exposures and failure to account for confounding factors like smoking, diet, and geographic mobility of the population. Since the focus of this section is on cancer causation, we shall not discuss other issues in environmental protection.

Air Pollution

Indoor air is generally of greater concern than outside air because people spend 90% of their time indoors and because the concentrations of pollutants indoors tend to be higher than outdoors. Radon is likely to be the most important carcinogenic air pollutant. It occurs naturally as a radioactive gas that is generated as a decay product of the radium present in trace quantities in the earth's crust. Radon primarily enters houses in air that is drawn from the underlying soil. On the basis of epidemiological studies of high exposures of underground miners, researchers have estimated that radon causes as many as 15,000 lung cancers per year in the United States, mostly among smokers because of the synergistic effect with smoking (85-87). Epidemiological studies of radon exposures in homes (88,89) have failed to demonstrate convincingly an excessive risk. About 50,000 to 100,000 of the homes in the United States (0.1%) are estimated to have annual average radon levels approximately 20 times the national average, and inhabitants receive annual radiation doses that exceed the current occupational standard for underground miners. Efforts to identify houses with high levels of radon indicate that they occur most frequently in concentrated geographic areas (90). In areas with high levels of radon, individuals can perform a measurement in their homes for about $20, and if high levels are found, they can be reduced substantially--using available contractors--for perhaps $1500 (86). With respect to outdoor air pollution, a recent large study has reported an association with lung cancer when sulfates are used as an index, but not when fine particles are used; the study did not control for diet (91).

Water Pollution

Water pollution as a risk factor for cancer appears small. Among potential hazards that have been of concern, the most important are radon (exposure is small compared to air) and arsenate. Natural arsenate is a known human carcinogen at high doses (92,93), and further research is needed to determine mechanisms of carcinogenesis and the dose response in humans. Chlorination of water, an important public health intervention, produces large numbers of chlorine-containing chemicals as by-products, some of which are rodent carcinogens. Evidence that chlorination of water increases cancer has been judged inadequate (94). A recent case-control interview study did not confirm earlier associations with bladder and colon cancer but did find an association with rectal cancer (95).

Animal Cancer Tests and the Rachel Carson Fallacy

Neither toxicology nor epidemiology supports the idea that synthetic industrial chemicals are causing an epidemic of human cancer. Although some epidemiological studies find an association between cancer and low levels of industrial pollutants, the associations are usually weak, the results are usually conflicting, and the studies do not correct for diet, which is a potentially large confounding factor. Moreover, the levels of synthetic pollutants are low and rarely seem plausible as a causal factor when compared to the background of natural chemicals that are rodent carcinogens (7).

Rachel Carson's fundamental misconception was, "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" (96). She was wrong: The vast bulk of the chemicals to which humans are exposed are natural, and for every chemical some amount is dangerous. Carson thus lacked perspective about the wide variety of naturally occurring chemicals to which all people are exposed and did not address the fact that, outside the workplace, exposures to synthetic pollutants are extremely low relative to the natural background.

Animal cancer tests are conducted on synthetic chemicals at the maximum tolerated dose (MTD) of the chemical, and regulatory agencies use the results to predict human risk at low levels of exposure. Since the vast proportion of human exposures are to naturally occurring chemicals, while the vast proportion of chemicals tested for carcinogenicity are synthetic, there is an imbalance in data and perception about chemicals and cancer.

The great bulk of chemicals ingested by humans is natural by both weight and number. We estimate that 99.99% of the pesticides in the diet are naturally present in plants to ward off insects and other predators (97). Half the natural pesticides tested--35 of 64--are rodent carcinogens (7,98,99). Reducing exposure to the 0.01% of pesticides that are synthetic, either individual chemicals or mixtures, will not appreciably reduce cancer rates. On the contrary, fruits and vegetables are important for reducing cancer; making them more expensive by reducing use of synthetic pesticides is likely to increase cancer. People with low incomes eat fewer fruits and vegetables (100) and spend a higher percentage of their income on food.

Humans also ingest large numbers of natural chemicals from cooking food. Of the more than 1000 chemicals identified in roasted coffee, over half of those tested--19 of 27--are rodent carcinogens (99). There are more natural rodent carcinogens by weight in a single cup of coffee than potentially carcinogenic synthetic pesticide residues in the average U.S. diet in a year, and there are still about 1000 known chemicals in roasted coffee that have not been tested. That does not necessarily mean that coffee is dangerous, but that high-dose animal cancer tests and worst-case risk assessments build in enormous safety factors and should not be considered true risks at the low dose of most human exposures.

Because of their unusual lipophilicity and long environmental persistence, there has been particular concern for a small group of polychlorinated synthetic chemicals such as DDT and polychlorinated biphenyls. There is no convincing epidemiological evidence (101), nor is there much toxicological plausibility (7), that the levels normally found in the environment are likely to contribute significantly to cancer. TCDD, which is produced naturally by burning when chloride ion is present, for example in forest and other fires, and as an industrial by-product, is an unusually potent rodent carcinogen but seems unlikely to be a significant human carcinogen at the levels to which the general population is exposed.

The reason humans can eat the tremendous variety of rodent carcinogens in our diet is that, like other animals, we are extremely well protected by many general defense enzymes, most of which are inducible--that is, whenever a defense enzyme is in use, the body produces more of it (102). Defense enzymes are effective against both natural and synthetic chemicals, including potentially mutagenic, reactive chemicals. One does not expect, nor does one find, a general difference between synthetic and natural chemicals in their ability to cause cancer in high-dose rodent tests (7,99,103).

We have ranked possible carcinogenic hazards from known rodent carcinogens by using an index that relates human exposure to carcinogenic potency in rodents (HERP) (7,99,104,105). Our ranking does not estimate risks because current science does not have the ability to do so. Instead, we put possible hazards of synthetic chemicals into perspective against the background of naturally occurring rodent carcinogens in typical portions and average exposures of common foods (99). The residues of synthetic pesticides or environmental pollutants rank low in comparison with the background of naturally occurring rodent carcinogens, despite the fact that such a comparison gives a minimal view of hypothetical background hazards because so few chemicals in the natural world have been tested for carcinogenicity in rodents. Our results indicate that many ordinary foods would not pass the regulatory criteria used for synthetic chemicals. Our analysis does not necessarily indicate that coffee consumption, for example, is a significant risk factor for human cancer even though chemicals in coffee have HERP values that rank much higher in possible hazard than the HERP that converts to the default one-in-a-million worst-case risk estimate used by the U.S. EPA (7). Adequate risk assessment from animal cancer tests requires more information about many aspects of toxicology, such as effects on cell division, induction of defense and repair systems, and species differences. The U.S. EPA has recently given attention to these factors in its newly proposed cancer risk assessment guidelines (106).

More than half the chemicals, whether synthetic or natural, that have been tested at the MTD under standard testing procedures are classified as carcinogenic. The high positivity rate is consistent for synthetic chemicals, natural chemicals, natural pesticides, and chemicals in roasted coffee, and has not changed through the years of testing (99,107,108). Half the drugs in the Physician's Desk Reference that report animal cancer test results are carcinogenic (109). The 1969 Innes series of tests of 119 synthetic chemicals, mainly all of the commonly used pesticides of the time, is frequently cited as evidence that the proportion of carcinogens in the world of chemicals is low, as only 9% were judged positive. Gold et al. (99,107) pointed out that these tests were quite deficient in power compared to modern tests, and they have now reanalyzed Innes by asking whether any of the Innes-negative chemicals have been retested using current protocols. They found that 34 had been retested and 16 were judged carcinogenic, again about half (99).

What is the explanation for the high positivity rate in high-dose animal cancer tests? When the testing protocol was developed in the 1960s, it was expected that chemical carcinogens would be rare and that they would be mutagens. Bias in picking more suspicious chemicals does not appear to be the sole explanation for the high positivity rate for numerous reasons (107,108,110). There is, however, an explanation that is supported by an increasing array of papers: that the MTD of a chemical can cause chronic cell killing and cell replacement in the target tissue, a risk factor for cancer that can be limited to the high dose. This explanation is supported by a wide variety of evidence. For example, endogenous oxidative damage to DNA is enormous--over 1 million oxidative lesions per rat cell (9). Thus, from first principles, the cell division rate must be a factor in converting such lesions to mutations, thereby increasing cancer. Therefore, raising the level of either DNA lesions or cell division in the cells that can give rise to tumors will increase cancer. Just as DNA repair protects against lesions, p53 guards the cell cycle and protects against cell division if the lesion level gets too high; however, neither defense is perfect. Cell division is also a major factor in loss of heterozygosity through nondisjunction and other mechanisms (103,110,111).

In another line of evidence, many studies on rodent carcinogenicity show a correlation between cell division at the MTD and cancer. Cunningham and colleagues have analyzed 15 chemicals at the MTD, 8 mutagens and 7 nonmutagens, including several pairs of mutagenic isomers, one of which is a carcinogen and one of which is not (112-120). They have found a perfect correlation between cancer causation and cell division in the target tissue: when tested at the bioassay dose, the nine chemicals that cause cancer caused cell division in the target tissue and the six chemicals that do not cause cancer did not cause such cell division. A similar result has been found in an analysis of Mirsails et al. (121), e.g., both dimethyl nitrosamine (DMN) and methyl methane sulfonate (MMS) methylate liver DNA and cause unscheduled DNA synthesis; however, DMN causes both cell division and liver tumors, whereas MMS does neither. The induction of cell division at high dose would explain why a high proportion of the known rodent carcinogens (42%) are not mutagenic, which is otherwise not satisfactorily explained. There is a large body of literature on rodent studies reviewed by Cohen and Lawson (122), Cohen (123), and Ames et al. (9) showing that chronic cell division can induce cancer. Work on chloroform induction of mouse liver tumors by Larson et al. (124) also indicates the important role of increased cell division at bioassay doses. A large epidemiological literature reviewed by Preston-Martin et al. (79,125) shows that increased cell division by hormones and other agents can increase human cancer.

Thus it seems likely that a high proportion of the chemicals in the world may be carcinogens if tested in standard rodent bioassays at the MTD; but this will be primarily due to high-dose effects for nonmutagens, and a synergistic effect of cell division at high doses with DNA damage for mutagens. Ad libitum feeding in the standard bioassay, which also can increase cell division, may also contribute to the high positivity rate, as shown by a recent National Toxicology Program study (126). If tumor induction in bioassays is due to effects unique to high doses, much more information on mechanism is required to understand the causes of human cancer. The default risk assessment virtually safe dose is simply a factor of 740,000 times below the MTD, as shown by Gaylor and Gold (127). If tests are conducted primarily on synthetic chemicals and regulation is directed toward tiny traces of synthetic chemicals, as is now the case, resources will be diverted from more important issues. Thus, the positivity rate and the frequency of positive results that are unique to high doses are key questions in getting an overview of the world of chemicals, both natural and synthetic.

Linear extrapolation from the MTD in rodents to low-level exposure in humans for synthetic chemicals, while ignoring the enormous background of natural chemicals, has led to exaggerated estimates of cancer risk and to an imbalance in the perception of hazard and the allocation of resources. If the costs were minor, the issue of putting hypothetical risks into perspective would not be so important, but the costs are great (128,129) and escalate as cleanliness approaches perfection. Most attempts to deal with pollutants do not adequately deal with trade-offs; instead, policy makers assume that upper-bound risk assessment to one in a million protects the public. Reports by the Office of Management and Budget (130) and the Harvard Center for Risk Analysis (131) compared costs of risk reduction among government agencies and concluded that the money spent to save a hypothetical life under U.S. EPA regulations is often orders of magnitude higher than that spent on regulations of other government agencies. The uncertainties inextrapolations to low-dose assessments are great, and the true risk could be zero. Thus, the discrepancy between costs of U.S. EPA regulations and other agencies' may be even greater, e.g., permitted worker exposure limits regulated by U.S. OSHA can be dose to the carcinogenic dose rate in rodent bio-assays and little extrapolation is required. Many scholars have pointed out that expensive regulations intended to save lives may actually lead to increased deaths (132), in part because they divert resources from important health risks and in part because higher incomes are associated with lower mortality (133,134). Worst-case assumptions in risk assessment represent a policy decision, not a scientific one, and they confuse attempts to allocate money effectively for cancer prevention (135,136).

Discussion

Epidemiological evidence in humans is sufficient to identify several broad categories of cancer causation for which the evidence is strong and plausible. Because many of those risks are avoidable, it is possible to reduce rates of

many types of cancer. One approach to estimating the population impact of adopting major lifestyle factors associated with low cancer risk is to compare cancer incidence and mortality rates of the general population to those of Seventh-Day Adventists--who generally do not smoke, drink heavily, or eat much meat but do eat a diet rich in fruits and vegetables (137,138). Seventh-Day Adventists experience substantially lower mortality rates of lung, bladder, and colon cancers. Total cancer mortality is about half that of the general U.S. population. While this comparison has limitations--better use of medical services may contribute to reduced mortality, and imperfect compliance with recommendations may underestimate the impact of lifestyle--the results strongly suggest that a large portion of cancer deaths can be avoided by using knowledge at hand. Incidence rates rather than mortality rates provide a similar picture, although the differences are somewhat less. For breast cancer, the healthy behavior of Seventh-Day Adventists was not sufficient to have a major effect on risk.

Decreases in physical activity, and increases in smoking, obesity, and recreational sun exposure have contributed importantly to increases in some cancers in the modern industrial world, whereas improvements in hygiene have reduced other cancers related to infection. There is no good reason to believe that synthetic chemicals underlie the changes in incidence of some cancers. In the United States and other industrial countries, life expectancy has steadily increased and will increase even faster as smoking declines.

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Abbreviations used: DMN, dimethyl nitrosamine; HERP, human exposure to carcinogenic potency in rodents; MMS, methyl methane sulfonate; MTD, maximum tolerated dose; U.S. EPA, U.S. Environmental Protection Agency; U.S. OSHA, U.S. Occupational Safety and Health Administration.

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